

# Global Access to Medicines Day



**OUR LABS. OUR DRUGS.  
OUR RESPONSIBILIITY.**

***Access to Medicines and the Role of  
University Scientists***

**March 30<sup>th</sup>, 2009**

**Universities Allied for Essential Medicines**

*[www.essentialmedicine.org/action](http://www.essentialmedicine.org/action)*





## Table of Contents

Access to Medicines and the Role of Universities and University Scientists.....	3
Frequently Asked Questions from Scientists.....	6
Philadelphia Consensus Statement.....	8
Philadelphia Consensus Statement Signatories	10
Global Access Licensing Framework .....	12
Explanatory Notes	13
Common Questions & Explanations	17
Published Literature Regarding Global Access Licensing.....	
“The Scientist’s Story” <i>The New York Times</i>	24
“Leveraging University Research to Advance Global Health” <i>JAMA</i>	25
“Closing the access gap for health innovations: an open licensing proposal for universities” <i>Globalization and Health</i>	28
“Improving access to medicines in poor countries: The role of universities” <i>PloS Medicine</i>	35
Editorial: “Global Health and University Patents” <i>Science</i>	39

# UCGH AND UNIVERSITIES ALLIED FOR ESSENTIAL MEDICINES GLOBAL ACCESS TO MEDICINE DAY

## Access to Medicines and the Role of Universities of University Scientists

During the week of March 30, 2009, join students, faculty, and researchers at schools across the country for Global Access to Medicine Day by demanding that life-saving drugs developed in your campus laboratories be made available in poor countries and reach out to university scientists who create the medicines that are so needed in developing countries.

### PEOPLE ARE DYING BECAUSE THEY CANNOT ACCESS EXISTING MEDICINES

The World Health Organization estimates that ten million people die every year who could be saved by existing drugs but are simply too poor to afford them.

#### THE PROMISE: YALE AND STAVUDINE

Yale University created one of the first AIDS drugs, a molecule known as stavudine. Within a few years of its release, stavudine had revolutionized AIDS treatment, and helped change HIV/AIDS from a rapid death sentence to a manageable – if difficult – condition.

But – as the drug’s discoverer wrote in the editorial pages of the *New York Times* – it soon became clear that stavudine “was not reaching millions of desperately suffering people because they lacked the money to purchase it.”

Working with students on campus, *Médecins Sans Frontières* (MSF) urged Yale, as the patent-holder, to help increase access to the urgently needed drug. MSF’s request exploded into a student campaign that gave birth to Universities Allied for Essential Medicines.

Under pressure, Yale and Bristol-Myers Squibb jointly announced that they would allow generic manufacturers of Stavudine to compete in certain markets, thus lowering the price of the drug from \$1600 per patient per year to just \$55 – a 96% reduction.

promise of that success has gone largely unfulfilled.

### UNIVERSITIES AND THE GLOBAL HEALTH CRISIS

University scientists are major contributors in the drug development pipeline. Further, universities are committed to the creation and dissemination of knowledge in the public interest. We thus believe that universities have an opportunity and a responsibility to take part in finding solutions to the global access to medicines crisis by ensuring access to their health-related technologies.

#### Universities have a critical role to play.

- In 2000, a United States Senate report noted that 15 of the 21 drugs considered by experts to have the greatest therapeutic impact on society were developed using research funded by the United States government. In the United States, most government-funded research occurs at universities.
- Approximately 25% of all drugs classified as “[d]rugs used in the treatment of HIV infections” by the United States FDA include a university or hospital-held patent (35.7% for 2001-2006).

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#### UNIVERSITIES CAN CHANGE THIS

Because many of these life-saving drugs are developed in campus laboratories, universities wield substantial leverage when they license their drugs to pharmaceutical companies.

Our proposal is simple: Every university-developed drug, vaccine, or medical diagnostic should be licensed with a concrete, effective, and transparent strategy to make affordable versions available in poor countries for essential medical care. For example, when a university licenses a promising new drug candidate to a pharmaceutical company, it should demand that the company allow the drug to be made available in poor countries at the lowest possible cost. This would have virtually no financial impact on the company or university, but could ultimately save millions of lives.

Yale’s 2001 decision to release its patent on a critical AIDS drug showed the world that universities have the power to trigger substantial, immediate price reduction on lifesaving treatments (see sidebar). Yet the

- Universities, as nonprofit institutions, have committed to engaging in research that benefits the public interest.

## THIS WORK IS MORE IMPORTANT NOW THAN EVER BEFORE

We are at a crucial moment for global health. Constitutional litigation over a life-saving cancer drug has been used to threaten production of affordable medicines in India; in Thailand, Abbott Labs, a multinational pharmaceutical giant, has withdrawn registration of all new medicines as leverage in a struggle over compulsory licensing; and right here at home, Merck faces growing pressure to make its revolutionary cervical cancer vaccine available to women worldwide.

Every one of these struggles involves a university-developed medicine:

- In India, the drug at the center of the lawsuit was Gleevec, a lifesaving cancer treatment based on research by scientists at the Oregon Health & Sciences University and the Dana Farber Cancer Institute.
- In Thailand, one of the drugs that Abbott is using as political leverage—Zemplar—is based on a patent licensed out of the University of Wisconsin, Madison.
- And Merck’s cervical cancer vaccine is based on patents held by Georgetown, the University of Rochester, and the University of Queensland in Australia.

Research universities have an opportunity to intervene in the access-to-medicines crisis in poor countries. By virtue of their upstream contribution to the drug development pipeline—estimated at \$19.6 billion in 2002 for the United States alone—universities have considerable untapped influence. Both the number of patents held and the number of license agreements executed by universities more than doubled between 1991 and 2005.

## NOW IS THE TIME

Over the past two years, UAEM has brought these issues to the forefront, riding a wave of momentum:

- The launch of UAEM’s Statement of Principles (called the Philadelphia Consensus Statement) garnered the support of more than 100 luminaries in the field – including Jeffrey Sachs, Paul Farmer, Stephen Lewis, James Orbinski, ten Nobel Laureates, top intellectual property professors,– as well as thousands of other students and professors at over a hundred campuses around the world.
- *Nature*, *Science* the *Chronicle of Higher Education*, the *British Medical Journal*, and the *Financial Times* have all covered UAEM’s activities.
- Working with UAEM, Senator Patrick Leahy (VT) introduced legislation that would mandate humanitarian licensing terms modeled on the terms UAEM has urged universities to adopt voluntarily.
- The Stanford White Paper has been signed by forty five prominent universities and the Association of American Medical Colleges. In this, they have come together to publicly recognize their responsibility to ensure university research benefits the world’s poor, and to commit to the principles at the heart of our policy proposals.
- At the World Health Organization Intergovernmental Working Group on Public Health, Innovation and Intellectual Property UAEM worked alongside other key NGOs to ensure progressive innovation and access provisions are included in the WHO strategy.
- UAEM consultations with the Barack Obama campaign led to the adoption of a portion of UAEM humanitarian licensing policies into the Obama platform
- The University of British Columbia, catalyzed by their UAEM chapter, licensed its first medicine under their new access licensing principles which will make a new treatment for leishmaniasis and HIV related opportunistic infections available at low cost in developing countries

The patent rights contributing to several currently marketed HIV drugs are held by universities:

- stavudine (Yale University),
- abacavir (University of Minnesota),
- lamivudine (Emory University)
- emtricitabine (Emory University)
- enfuvirtide (Duke University).

Overall, university patents are associated with 10 of the 30 HIV drugs approved by the US FDA between 1987 and 2007.<sup>1</sup>

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- The University of Washington took its first steps in implementing humanitarian access licensing policies in 2007
- Emory University, working with their UAEM chapter, adopted Global Access Guiding Principles, which will guide how the university licenses medical technologies

But our work is far from over. Even as this language was being drafted, signatory universities continued to license drug candidates with no provisions for access. Principles are not enough. **And delay has a real human cost.**

## WHAT CAN YOU DO? 2009 Focus: Scientists

Join UAEM the week of March 30<sup>th</sup>: Call on universities to translate their rhetoric into action. Help us ensure that every health product developed in campus laboratories *reaches* those who need it most by raising awareness and reaching out to university scientists.

This year we are focusing on educating scientists about making their discoveries accessible. We are going to try to reach out to as many scientists as possible, while logging our new supporters.

**Why focus on scientists?** Scientists have an important role to play in regards to achieving global access licenses for health technologies. While the details at every university are different, scientists invariably have input on the patenting and licensing of their innovations but they often lack awareness of patenting and licensing issues. Their support for, or against, global accessing licensing could be pivotal in any agreement.

We need to create wide-spread awareness amongst university scientists about the access gap and the role of patents and licenses. By informing scientists how to get their medicines into the hands of those who need it most, we can create powerful allies in the fight for equitable access.

## TAKE ACTION!

Join students, faculty, and researchers at top research institutions in the U.S, Canada and the UK by demanding that lifesaving drugs developed in your campus laboratories be made available in poor countries.

### - Learn

- Screen a movie: show the film *Pills, Profits Protest* on your campus to teach your fellow students about the barriers to ensuring access to medicines
- Organize or attend a workshop on intellectual property, trade agreements and access to medicines.

### - Build

- Host a sign-on for the Philadelphia Consensus Statement (PCS) to add your campus' voices to the thousands already calling for universities to play their role in ensuring access to medicines. Log your new PCS signatures on <http://www.essentialmedicine.org/cs> to be counted as more voices calling for change.

### - Act

- Educate scientists at your university about how to make sure the fruits of their research reach those who need it. Email Gloria Tavera at [grtavera@ufl.edu](mailto:grtavera@ufl.edu) or Taylor Gilliland at [cgilliland@ucsd.edu](mailto:cgilliland@ucsd.edu) for a "Scientist Outreach" toolkit. You can also go to <http://www.essentialmedicine.org/action> to register your chapter for the action, download tools and access more resources.

### Time To Act

"Biomedical knowledge and achievement is growing at a tremendous pace, but is unmatched by ethical thinking about how to apply the results equitably, humanely and wisely.

The universities are forgetting their role as guardians of human wisdom, and instead are selling out to the highest bidders. UAEM has created consensus. Now it is time for the policy makers to act."

- Sir John Sulston, Nobel Laureate in Medicine

Register your chapter for action at <http://www.essentialmedicine.org/action> so we can send you materials!



## Frequently Asked Questions

### “Why are these students contacting me?”

We're from Universities Allied for Essential Medicines (UAEM). The organization grew from the idea that universities – powerhouses of upstream research and institutions acting in the public interest – have an opportunity to license their technologies (precursors of drugs, diagnostics, biologics) in a way that satisfies the needs for further development, for profit by industry, *AND for affordable access in developing countries*. We refer to these licensing strategies as “global access licensing.” In brief, these are a variety of licensing strategies that allow generic sales (or equivalent) of the downstream product in developing countries. This is possible since Low and Middle Income (LMI) countries account for only 5-7% of the overall pharmaceutical market,<sup>1</sup> allowing industry to still have a profit-incentive in high-income countries, while generic competition elsewhere will barely touch their bottom line. Though the problem of access to medicines is not solved by any silver bullet, global access licensing is a crucial step in that direction.

*We are contacting you in hopes that when you have a technology ready to be patented, licensed and developed, you will insist that global access licensing be a part of any licensing agreement. Thus, any product derived from your technology will reach all who might benefit from it – now, rather than a decade or more beyond.*

### “I don't have any product right now that I want to patent, license and have commercialized... does this apply to me, then?”

Yes! We still want you to be aware of the possibilities, so that when your lab is ready to pursue commercialization of a technology, a form of global access licensing is part of any agreement. And we aren't only talking of medicines for diseases such as HIV, tuberculosis, malaria... Global access licensing is a financially viable way for all stakeholders of addressing the overall health needs in developing countries, and as such, all technologies that could have a medical use should be tagged for such licensing strategies.

### “Global access licensing' sounds like a good, reasonable idea... why isn't my university already doing this? What concerns do they have?”

A few universities – Berkeley, Oxford, University of British Columbia – have started engaging in forms of global access licensing, testing it out – and with great success<sup>2,3</sup>. But these methods are relatively new and still need scientist-advocates to gain traction. Universities' main concerns have been over fears of lost revenues, fears of lost licenses, and parallel importation.

**Fear of lost revenue:** Pharmaceutical sales, and thus university royalties, are unlikely to be impacted by a global access license, because the provisions are only relevant to Low and Middle-Income (LMI) countries, where sales are minimal. Consumers in the US, EU, and Japan comprise 93.2% of all pharmaceutical revenues.<sup>4</sup> Mozambique, for instance, is home to at least 1,500,000 HIV positive persons<sup>5</sup>, yet per capita GNI is \$320.<sup>6</sup> Because there is no effective market in Mozambique, there exist no revenue streams to potentially disrupt.

**Fears of lost licenses:** Universities are some of the country's most successful licensors of technologies.<sup>7</sup> Global access strategies would not affect the likelihood of continued successes. Because >93% of revenues originate in countries ineligible for global access-provision, extra burdens on universities are unlikely to materialize. For example, University of British Columbia in the year following its formal adoption of Global Access Principles<sup>8</sup> in September 2007 saw funding for Sponsored Research from all sources, including government, non-profit, *as well as industry*, that was stable or increased from 2006-2008<sup>9</sup>. Its licensing actually

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<sup>1</sup> “Pathways to Biopharm Innov.” PhRMA. 40 (2005).

<sup>2</sup> UBC University-Industry Liaison Office 2007/08 Annual Report (p.4): [www.uilo.ubc.ca/pdf/UILO\\_AR\\_2008.pdf](http://www.uilo.ubc.ca/pdf/UILO_AR_2008.pdf)

<sup>3</sup> Ledford, Heidi. “IP: Ideas for Purchase?” *Berkeley Science Review*. Spring 2006. p 38.

<sup>4</sup> “The Pharm. Industry in Figures.” Euro Fed of Pharm. Ind. and Assoc. 2008 edition. p. 5.

<sup>5</sup> UNAIDS 2008.

<sup>6</sup> World Bank 2008.

<sup>7</sup> “Biotechnology Report 2007.” Marks and Clerk. 2007. London.

<sup>8</sup> UBC's Commitment to Global Access Licenses: [www.uilo.ubc.ca/global.asp](http://www.uilo.ubc.ca/global.asp)

<sup>9</sup> UBC University-Industry Liaison Office 2007/08 Annual Report (p.4): [www.uilo.ubc.ca/pdf/UILO\\_AR\\_2008.pdf](http://www.uilo.ubc.ca/pdf/UILO_AR_2008.pdf)

increased in the following year. Likewise, Yale saw no declines in licensing or funding following its renegotiation of the license for stavudine, nor has UC Berkeley seen declines in any metric since its adoption of Socially Responsible Licensing.

**Parallel importation.** New regulatory barriers and customs regulations have minimized the threat of generics returning to developed country markets. This concern finds little empirical support, and can be addressed in the same manner that the WTO has elected to treat the issue: requiring the use of different packaging, pill color, and shape in different countries to facilitate identification of illegal (re)importations.<sup>10</sup> Generic drugs have been produced in India for decades without resulting in the infiltration of or undermining of Western markets.<sup>11</sup>

**“My main concern is that when I do have a technology, demanding global access licensing hinder my ability to get it licensed and commercialized.”**

It should not. As >93% of industry revenues originate in countries ineligible for global access-provision, industry should not fear demands for these strategies. Some pharmaceutical companies have proven receptive to the idea and do allow sales of generics in a few developing countries.<sup>12</sup> UAEM’s idea have gained great support with professionals and researchers through the world, and UAEM may also be able connect you with institutions such as One World Health, Global Vaccines Inc, DNDi or even Novartis’ Vaccines Institute for Global Health in commercializing your technology.

**“Your proposal sounds well-thought out. But you all are just students... Are other professionals and researchers supporting these ideas?”**

Yes! Our proposals have been developed in conjunction with some of the most innovative minds in medicine, law, and policy, and have gained widespread support among researchers, public health experts and economists. For instance, Nobel Prize winners who have supported UAEM’s proposals include Peter Agre (2003, Chemistry), Kenneth Arrow (1972, Economics), Medecins Sans Frontieres (1999, Peace), Craig Mello (2006, Medicine), John Polanyi (1986, Chemistry), Oliver Smithies (2007, Medicine), Jack Steinberger (1988, Physics), Sir John Sulston (2002, Medicine), Harold Varmus (1989, Medicine), and Desmond Tutu (1984, Peace). We are happy to connect you with our faculty supporters around the nation in law, economics or policy if you would like more input from them. **[LIST FACULTY SUPPORTERS AT YOUR UNIVERSITY]**

**“Ok, I’m convinced that this is an idea worth supporting. When I do have a product ready for patenting and licensing, if my university technology transfer office won’t accept these ideas, what can I do?”**

We suggest you contact members of UAEM before you go to your university technology transfer office. We can offer advice on global access licensing and can connect you with professionals in research and technology transfer to do the same, so that your product might reach all who need it. Your university’s UAEM chapter can help with publicity and/or public pressure related to your desire to engage in global access licensing.

**“I’m sure this is only a brief overview of the issues. How can I learn more?”**

These are but a few articles related to global access licensing. Should you desire a more comprehensive bibliography, just let us know.

- Chokshi D. and Rajkumar. Leveraging University Research to Advance Global Health. *JAMA* October 24/31 2007;298(16): 1934.
- Kapczynski A., Crone E.T., Merson M. Global Health and University Patents. *Science* 2003;301(5640):1629.
- World Health Organization. “Access to Medicines.” WHO Drug Information Report. 2005 Nov 3; 19(3): 236-241. Available at: [www.who.int/druginformation/vol19num3\\_2005/DI19-3.pdf](http://www.who.int/druginformation/vol19num3_2005/DI19-3.pdf).
- Wainberg, MA. “Generic HIV drugs--enlightened policy for global health.” *N Engl J Med*. 2005 Feb 24; 352(8):747-50. *Yale Journal of Health Policy, Law, and Ethics*. 2003; 3:293.

**“How can I get in contact with this student group again if I want help in advocating for global access licensing for a future product of mine?”**

Feel free to contact us at any time at: **[YOUR EMAIL]** or **[YOUR PHONE NUMBER]**

<sup>10</sup> “Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health”, World Trade Organization 2003.

<sup>11</sup> Presentation at the Earth Institute, Columbia University, by Andrew Farlow: ‘Costs of Monopoly Pricing Under Patent Protection. December 4, 2003.

<sup>12</sup> “Gilead Announces Licensing Agreements.” Sept 22, 2006. [http://www.gilead.com/pr\\_908393](http://www.gilead.com/pr_908393)

## PHILADELPHIA CONSENSUS STATEMENT

### *On University Policies for Health-Related Innovations*

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According to the World Health Organization, ten million people—most of them in developing countries—die needlessly every year because they do not have access to existing medicines and vaccines. Countless others suffer from neglected tropical diseases such as sleeping sickness, lymphatic filariasis, and blinding trachoma. Because these neglected diseases predominantly affect the poor, they attract very little research and development funding, leading directly to a paucity of safe and effective treatment options.

We believe that access to medical care and treatment is a basic human right.<sup>1</sup> Lack of access to medical treatment in developing countries stems from several factors, including high prices for medicines, underfunded health care systems, and a global biomedical research agenda poorly matched to the health needs of the world's destitute sick. Comprehensive solutions are thus needed to increase both access to existing medicines and research on neglected diseases.

We believe that universities have an opportunity and a responsibility to take part in these solutions. University scientists are major contributors in the drug development pipeline. At the same time, universities are committed to the creation and dissemination of knowledge in the public interest. Global public health is a vital component of the public interest. Therefore, universities best realize their objectives when they promote both innovation and access to health-related technologies.

To this end, we, the signatories of this Statement, urge universities to adopt the following recommendations.

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As owners of intellectual property, universities have the ability to promote widespread availability of their technologies in the developing world. When university-owned intellectual property is necessary for the development of a health-related end product—including but not limited to drugs, vaccines, diagnostics, monitoring tools, know-how and technical expertise—universities should:

#### PROMOTE EQUAL ACCESS TO UNIVERSITY RESEARCH

- 1. Require the inclusion of licensing terms in exclusive technology transfer agreements that ensure low-cost access to health-related innovations in the developing world.** The Equitable Access License (EAL)<sup>2</sup> is one example of a model license promoting access to university intellectual property in which all qualified entities<sup>3</sup> are permitted to supply the product to public and private sector markets in low- and middle-income (LMI) countries.<sup>4</sup>
- 2. Develop a transparent, case-by-case global access strategy to ensure access to health-related technologies where licensing provisions like the EAL will not serve the access objectives defined above.** For example, biologicals (e.g., complex macromolecules and vaccines) and healthcare devices (e.g., diagnostic tests) are subject to different scientific and technical constraints than synthetic small molecules and may require different methods to ensure access. Components of a global access strategy could include (a) forgoing the university's share of royalties to incentivize the licensee to facilitate access by offering discounts in developing countries; (b) actively seeking a third-party organization to participate in research, development, and distribution to facilitate access in developing countries; and (c) incorporating licensing provisions, such as non-patenting requirements, that guarantee access to data and materials necessary to promote generic production or adaptations for developing countries.

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<sup>1</sup> See Article 25, Universal Declaration of Human Rights.

<sup>2</sup> See <http://www.essentialmedicine.org/EAL.pdf>.

<sup>3</sup> Qualified entities include, but are not limited to, public or private generic manufacturers registered in the country of production.

<sup>4</sup> We use the categories of low- and middle-income countries as defined by the World Bank at <http://www.worldbank.org/data/countryclass/classgroups.htm>.

Neglected diseases are those for which treatment options are inadequate or do not exist and for which drug-market potential is insufficient to attract a private-sector response. In order to advance the development of therapies for neglected diseases (ND), universities should:

### **PROMOTE RESEARCH AND DEVELOPMENT FOR NEGLECTED DISEASES**

- 1. Adopt policies promoting in-house ND research.** Universities should (a) adopt a classification system defining and prioritizing neglected diseases<sup>5</sup>; (b) support existing researchers engaged in ND work; (c) recruit talented ND researchers by establishing proper incentives and marketing their ND research programs; and (d) formalize annual review practices aimed at identifying new or currently shelved technologies with promising potential for application to ND end product development.
- 2. Engage with nontraditional partners to create new opportunities for ND drug development.** Universities should actively seek out nontraditional partners (e.g., public-private partnerships, grantmaking organizations, nonprofits, and developing-world companies or research institutions) to facilitate development of technologies applicable to neglected diseases. Example interactions include: patent donation, dual-market licensing, and straightforward exclusive/non-exclusive licensing. In order to access novel funding sources for neglected diseases, universities should remove any barriers, such as intellectual property restrictions, to accepting research grants from nontraditional funders.
- 3. Carve out an ND research exemption for any patents held or licenses executed.** Licensing terms should allow other non-profit institutions to conduct research for neglected diseases using the university's patented innovation.<sup>6</sup> Similarly, for any out-licensed technologies, universities should retain the right to non-exclusively license use of its intellectual property for neglected disease research and for distribution of any resulting products in developing countries.

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Given their avowed commitment to the public good, universities should measure success in technology transfer by impact on global human welfare rather than simply by financial return. The positive social impact from university innovations—particularly in poor countries—would go largely unnoticed if technology transfer were to be measured in dollars alone. In order to develop transparent criteria measuring access to health technologies and innovation in neglected-disease research, universities should:

### **MEASURE RESEARCH SUCCESS ACCORDING TO IMPACT ON HUMAN WELFARE**

- 1. Collect and make public statistics on university intellectual property practices related to global health access.** To further elucidate how university patenting and licensing strategies affect access to the end products of academic research in developing countries, universities should disclose all healthcare-related end products in which it holds any intellectual property. Data should also be published on patents applied for or granted in all low- and middle-income countries. Conversely, universities should make known the number of licensing agreements that include access-minded provisions<sup>7</sup> as well as details of nontraditional partnerships for ND research and development.
- 2. Collaborate with other universities and consortia to develop more robust technology transfer metrics that better gauge access to public health goods and innovation in neglected-disease research.**

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<sup>5</sup> For example, the United States Orphan Drug Act could provide a legal basis for defining a set of neglected diseases.

<sup>6</sup> See <http://www.essentialmedicine.org/EAL.pdf>.

<sup>7</sup> Access-minded provisions include, but are not limited to: (1) facilitation of generic competition, (2) mandatory sublicensing clauses for LMI markets, (3) specific access milestones, and (4) agreements that reduce royalty payments from the licensee to the university in exchange for fair pricing in LMI markets on the part of the licensee.

**NOBEL LAUREATES:** Peter Agre, 2003 Nobel Laureate in Chemistry, Vice Chancellor for Science and Technology, James B. Duke Professor of Cell Biology, Duke University Medical Center — Kenneth Arrow, PhD, 1972 Nobel Laureate in Economics, 2004 National Medal of Science, Professor of Economics (Emeritus), Stanford University — Medecins Sans Frontieres (MSF), 1999 Nobel Laureate in Peace, Campaign for Access to Essential Medicines — Craig Mello, PhD, 2006 Nobel Laureate in Medicine, Professor of Molecular Biology, University of Massachusetts Medical School — John Polanyi, PhD, DSc, 1986 Nobel Laureate in Chemistry, Professor, University of Toronto — Oliver Smithies, PhD, 2007 Nobel Laureate in Medicine, Excellence Professor, UNC-Chapel Hill. — Jack Steinberger, PhD, 1988 Nobel Laureate in Physics — Sir John Sulston, PhD, FRS, 2002 Nobel Laureate in Medicine, Faculty of Life Sciences, University of Manchester — Harold Varmus, MD, 1989 Nobel Laureate in Medicine; Co-founder of Public Library of Science (PLoS); Chairman of the Scientific Board of Grand Challenges in Global Health, President and chief executive officer of the Memorial Sloan-Kettering Cancer Center in New York City — The Most Reverend Desmond Tutu, 1984 Nobel Laureate in Peace

**SCIENCE AND MEDICINE:** Sir Richard Feacham, former Head of the Global Fund for HIV, TB, and Malaria, Professor of Global Health, UCSF and UC Berkeley — Marcia Angell, Former Editor-in-Chief of the New England Journal of Medicine; Member, Institute of Medicine; Senior Lecturer, Harvard Medical School — Jerry Avorn, Professor of Medicine, Harvard Medical School — Pierre Baldi, Professor of Computer Science in the School of Information and Computer Sciences; Director of Institute for Genomics and Bioinformatics, University of California, Irvine — Solomon Benatar, Professor of Medicine, University of Cape Town; Foreign Member, Institute of Medicine — Todd Capson, Associate Scientist, Smithsonian Tropical Research Institute — George Chandy, Professor, Physiology & Biophysics, University of California, Irvine — Partho Ghosh, Associate Professor, Department of Chemistry and Biochemistry, University of California at San Diego — Siamon Gordon, GlaxoWellcome Professor of Cellular Pathology, University of Oxford; Pediatric Dengue Initiative Grantee; Initiator, AIDS Education Booklet for Southern Africa — Victoria Hale, Founder and CEO, Institute for OneWorld Health — Robert E.W. Hancock, Professor, Department of Microbiology and Immunology, University of British Columbia — Barton F. Haynes, MD, Frederic M. Hanes Professor of Medicine and Immunology, Duke University School of Medicine — Wim G.J. Hol, Professor, Biochemistry and Biological Structure, Investigator Howard Hughes Medical Institute, University of Washington — Peter Hotez, Director, Human Hookworm Vaccine Initiative; Walter G. Ross Professor of Basic Science Research at The George Washington University — Warren D. Johnson, Jr, B.H. Kean Professor of Tropical Medicine, Cornell University — Phyllis Kanki, Professor of Immunology and Infectious Disease, Harvard School of Public Health — David Mayne, Emeritus Professor of Control Theory, Department of Electrical and Electronic Engineering, Imperial College London — J. Andrew McCammon, Investigator, Howard Hughes Medical Institute, Joseph E. Mayer Professor of Theoretical Chemistry, Professor of Pharmacology, UC San Diego — Thomas E. Novotny, MD, MPH, UCSF Global Health Sciences — W. Geoffrey Owen, Dean of Biological Sciences, University of California at Berkeley — John Polanyi, Professor, Nobel Laureate in Chemistry, University of Toronto — Arnold S. Relman, Former Editor-in-Chief of the New England Journal of Medicine; Professor Emeritus of Medicine, Harvard Medical School — Harold Simon, Professor of Family and Preventive Medicine, Chief of the Division of International Health and Cross-cultural Medicine, UC San Diego — Jack Steinberger, Nobel Laureate in Physics — Ken Stuart, President and Director of Seattle Biomedical Research Institute; Professor, University of Washington — Mark A. Wainberg, Professor of Medicine, Director, McGill AIDS Centre, McGill University — Gavin Yamey, Senior Editor, PLoS Medicine; Consulting Editor, PLoS Neglected Tropical Diseases

**LAW:** Brook K. Baker, Northeastern University School of Law, Program on Human Rights and the Global Economy; Health GAP — Yochai Benkler, Professor of Law, Yale Law School — James Boyle, William Neal Reynolds Professor of Law, Duke University — Edwin Cameron, Justice, South African Supreme Court of Appeal — Carlos M. Correa, Professor, University of Buenos Aires — Dan Hunter, Professor of Law, University of Melbourne Law School; Visiting Associate Professor of Law, New York Law School — Mark A. Lemley, William H. Neukom Professor of Law, Stanford Law School; Director, Stanford Program in Law, Science and Technology — Lawrence Lessig, Professor of Law at Stanford Law School — Peter Menell, Professor of Law and Director, Berkeley Center for Law & Technology — Robert P. Merges, Wilson Sonsini Goodrich & Rosati Professor of Law and Technology; Director, Berkeley Center for Law & Technology, University of California at Berkeley — Carol Mimura, Assistant Vice Chancellor for Intellectual Property and Industry Research Alliances, UC Berkeley — Beth Noveck, Director of the Institute for Information Law and Policy; and Associate Professor, New York Law School — Kevin Outterson, Professor of Law, West Virginia University — Daniel B. Ravicher, President and Executive Director, Public Patent Foundation (PUBPAT) — Pamela Samuelson, Richard M. Sherman Distinguished Professor of Law; Professor of Information Management;

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Rubenstein, Executive Director, Physicians for Human Rights ORGANIZATIONS: ACT UP East Bay, Oakland, CA — African Services Committee — AIDS Access Foundation (AAF) — AIDS Law Project — American Medical Student Association — American Medical Women's Association — Canadian HIV/AIDS Legal Network — Central and Eastern European Harm Reduction Network (CEEHRN) — Community HIV/AIDS Mobilization Project (CHAMP) — Development Research and Action Group (DRAG) — Dignitas International — Diverse Women For Diversity — ENGAGE — European AIDS Treatment Group, Brussels, Belgium — Global AIDS Alliance — Global Health Council — Health GAP — Initiative for Medicines, Access, and Knowledge (I-MAK) — International Peoples Health Council (South Asia) — Lawyers Collective HIV/AIDS Unit — Oxfam International — Partners in Health — Research Foundation For Science Technology & Ecology — Society for the Study of Social Problems — Sociologists without Borders — Southern Initiatives — Stop HIV/AIDS in India Initiative — Students Against Global AIDS — Student Campaign for Child Survival — Student Global AIDS Campaign — Thai Network For People Living with HIV/AIDS (TNP+) — University of California-Irvine Associated Graduate Students — Yale University Graduate & Professional Student Senate



## GLOBAL ACCESS LICENSING FRAMEWORK

Every university-developed technology with potential for further development into a drug, vaccine, or medical diagnostic should be licensed with a concrete and transparent strategy to make affordable versions available in resource-limited countries for essential medical care. Licenses are complex and each will be unique. Universities should therefore implement Global Access Policies that adhere to the following five principles:

1. Access to medicines and health-related technologies for all is the primary purpose of technology transfer of health-related innovations.
2. Technology transfer should protect access to the final end product needed by patients (e.g., formulated pills or vaccines).
3. Generic provision is the best way to ensure access in resource-limited countries for products that also have markets in developed countries. Legal barriers to generic production of these products for use in resource-limited countries should therefore be removed. In the cases of biologic compounds or other drugs where generic provision is forecast to be technically or economically infeasible, “at-cost” or other provisioning requirements should be used as a supplement to generic provisioning terms but should never replace those terms.
4. Proactive licensing provisions are essential to ensure that follow-on patents and data exclusivity cannot be used to block generic production. Other barriers may need to be addressed for the licensing of biologics.
5. University licensing should be systematic in its approach, sufficiently transparent to verify its effectiveness, and based on explicit metrics that measure the success of technology transfer by its impact on access and continued innovation.



## GLOBAL ACCESS LICENSING FRAMEWORK EXPLANATORY NOTES

### ***Every drug license must contain access provisions.***

Access concerns are not limited to diseases such as HIV/AIDS, tuberculosis, malaria, and other communicable diseases. The World Health Organization reports that chronic diseases such as cardiovascular disease, chronic respiratory diseases, cancer, and diabetes made up 60% of the 58 million annual worldwide deaths, 80% of which occur in low and middle income countries. Over three times as many people die annually from cardiovascular diseases as from HIV/AIDS, tuberculosis, and malaria combined.<sup>1</sup> To ensure access for all essential medicines, it is important that every drug, vaccine, and medical diagnostic license contains access provisions.

Universities Allied for Essential Medicines (UAEM) is sensitive to the opinion that generic production is not essential for medicines indicated for “lifestyle” conditions such as hair loss, acne, or erectile dysfunction. However, because it can be difficult to know at licensing time whether a product will eventually have an essential medical use, even products that are originally licensed for lifestyle indications should have access provisions in their license. These provisions should automatically allow for generic production in the event that any new, non-lifestyle use is demonstrated to be effective via a meta-analysis published in a peer-reviewed journal. Lifestyle uses should be defined narrowly.

### **The Global Access Licensing Framework should apply to all low and middle income countries.**

The choice of which countries to include in a license has grave human consequences. Universities, committed to the public good, should err on the side of over-inclusion. Resource-limited countries should be defined to include low and middle income countries on the World Bank's List of Economies.<sup>2</sup> These classifications are based on gross national income (GNI) per capita and are revised each year on July 1.

### **Generic provision is the best way to ensure access.**

Generic provision of drugs is the most effective means of driving down prices and increasing access.<sup>3</sup> There are several reasons that generic provisions should be required in all licenses for products that also have markets in developed countries:

1. Generic provision enlists competitive market forces to develop the cheapest, most efficient ways to get drugs to patients and providers. Generic companies are in the business of supplying a large volume of drugs as cheaply as possible. In contrast, pharmaceutical companies' drug donation programs do not provide an effective long-term solution—charitable providers have

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<sup>1</sup> *Preventing Chronic Disease: A Vital Investment*, World Health Organization (2005), [http://www.who.int/chp/chronic\\_disease\\_report/en/](http://www.who.int/chp/chronic_disease_report/en/).

<sup>2</sup> World Bank Data & Statistics, Country Classification, <http://go.worldbank.org/K2CKM78CC0>.

<sup>3</sup> *Report to Congress by the U.S. Global AIDS Coordinator on the Use of Generic Drugs in the President's Emergency Plan for AIDS Relief*, PEPFAR (May 2008), <http://www.pepfar.gov/documents/organization/105842.pdf>.



- fewer incentives to drive down their costs and do not have the expertise or distribution networks that are necessary to get drugs to patients in resource-limited countries.<sup>4</sup>
2. Generic provision eliminates the measurement and enforcement problems inherent in “at-cost” approaches.<sup>5</sup>
  3. Generic licensing approaches foster important innovations specific to the developing-world. For example, such approaches allow generic companies to create pediatric and heat-stable formulations of new drugs.<sup>6</sup>

### **Generic provisions for resource-limited countries will have a negligible financial impact on the pharmaceutical industry.**

The financial impact to pharmaceutical companies of allowing generic competition in resource-limited countries is negligible, especially when revenues from royalties on the generics are taken into account. Drugs with a global market generate only a tiny fraction of their revenue in resource-limited countries. For example, the Pharmaceutical Research and Manufacturers of America (PhRMA) estimates that Africa is only 0.4% of their market, China is only 0.4%, and India is only 0.2%.<sup>7</sup> Consumers in the United States, European Union, and Japan produced 93.2% of all pharmaceutical revenues for new medicines launched between 2002 and 2007.<sup>8</sup>

To ensure a fully competitive market, production of generics should be allowed in any country, so long as the products are sold only in resource-limited countries, as defined above. This approach is consistent with the framework adopted in the World Trade Organization’s Doha Declaration.<sup>9</sup> Differential appearance and packaging requirements can be used to ensure that products destined for developing world market are not illegally sold elsewhere.<sup>10</sup>

A subset of the pharmaceutical industry is increasingly hospitable to controlled licensing of their drugs for generic use in developing world settings. For example, Gilead recently provided an open voluntary license of its important AIDS medication tenofovir to generic producers in India,<sup>11</sup> and both Gilead and Johnson & Johnson announced at the 2008 World AIDS conference that they would be willing to donate intellectual property to a new patent pool being created by UNITAID to allow further generic

<sup>4</sup> E-mail from Daniel Berman et al., MSF, to Robert Lefebvre, Bristol-Myers Squibb (Feb. 8, 2002), <http://www.essentialdrugs.org/edrug/archive/200202/msg00055.php>.

<sup>5</sup> Amy Kapczynski et al., *Addressing Global Health Inequities: An Open Licensing Approach for University Innovations*, Berkeley Tech. L.J., 20, 1031 (2005).

<sup>6</sup> *UNITAID and CHAI Announce Lower Prices for AIDS Drugs and Affordable Formulations for Children*, UNITAID (Apr. 28, 2008), <http://www.unitaid.eu/index.php/en/NEWS/UNITAID-and-CHAI-announce-Lower-Prices-for-AIDS-Drugs-and-Affordable-Formulations-for-Children.html>.

<sup>7</sup> *Industry Profile 2008*, PhRMA, <http://www.phrma.org/files/2008%20Profile.pdf>.

<sup>8</sup> *The Pharmaceutical Industry in Figures*, European Federation of Pharmaceutical Industries and Associations (2008), p. 5, <http://www.efpia.eu/Content/Default.asp?PageID=559&DocID=4883>.

<sup>9</sup> *Ministerial Declaration*, World Trade Organization (Nov. 14, 2001), [http://www.wto.org/english/thewto\\_e/minist\\_e/min01\\_e/mindecl\\_e.htm](http://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_e.htm).

<sup>10</sup> Kevin Outterson, *Pharmaceutical Arbitrage: Balancing Access and Innovation in International Prescription Drug Markets*, 5 Yale J. Health Pol’y L. & Ethics 193, 261-265 (2005).

<sup>11</sup> *Gilead Announces Licensing Agreements*, Gilead (Sep. 22, 2006), [http://www.gilead.com/pr\\_908393](http://www.gilead.com/pr_908393).



production of AIDS medications.<sup>12</sup> Even where pharmaceutical companies are initially resistant to a generic production arrangement, universities can and should insist on such terms as critical to the overall licensing goal of getting innovations to patients, just as they now insist on due diligence terms and measurable development milestones to ensure licensed innovations reach wealthier patients in primary markets.

### **Additional legal barriers exist to prevent access to the end product needed by patients must be removed.**

Some universities have argued that simply not patenting their own discoveries in resource-limited countries constitutes a sufficient access policy. However, if a university does **not** include specific access provisions in its license, there are still several ways licensees could block a generic company from producing the drug for use in resource-limited countries:

**Follow-On Patents:** Licensees can patent many of the incremental developments inherent in turning the basic licensed compound into a finished marketable drug, creating barriers to access. Several kinds of “follow-on” patents exist:

- *Product patents* cover marginal new chemical additions to the original compound, such as those required to make it dissolve.
- *Process patents* cover the techniques, paths, and intermediates that producers use to synthesize the chemical compound at scale.
- *Use patents* cover the use of the drug for a particular indication.

**Data Exclusivity:** It currently takes years for a generic company to gain the right to refer to the clinical trial data of drugs that are “bioequivalent” to its own, delaying its ability to provide these drugs in developing countries. In order to sell its drugs to the public, an originator pharmaceutical company must show that the drug is safe and effective by performing clinical trials. A generic company, in contrast, can sell a drug without performing such trials by proving that its drug is bioequivalent to a previously approved drug. In order to do so, it must make reference to the originator pharmaceutical company’s clinical trial data. This “right of reference” is limited by law; in the United States, for example, generic companies must wait five years before referring to clinical trials already registered with the FDA. This delay is particularly problematic for drugs that treat diseases like HIV, where resistance to first- and second-line therapies develops rapidly.

There are a number of strategies to address the issues of follow-on patents and data exclusivity, including non-assert clauses, sublicensing agreements, patent pools, data waivers, and grantback provisions.<sup>13</sup>

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<sup>12</sup> James Love, *The Health Impact Fund and product monopolies*, Knowledge Ecology International (Nov. 17, 2008), <http://www.keionline.org/blogs/2008/11/17/health-impact-fund-monopolies/>.

<sup>13</sup> April E. Effort and Ashley J. Stevens, *The Critical Role of Academic Licensing in Promoting Global Social Responsibility* (2008); Kapczynski et al., *supra*; UNITAID Mission (2005), <http://www.unitaid.eu/index.php/en/UNITAID-Mission.html>.



## **At-cost or other access provisions are sometimes necessary, but they should rarely replace generic provisions.**

At-cost provisions, which require the licensee to sell the licensed technology in resource-limited countries for no profit, may be necessary:

1. When the drug, process, technology, diagnostic, or other component of the licensed product is too complex to be feasible for replication and generic production. For example, many biologics may require at-cost provisions.
2. When the demand for the product in resource-limited countries is too small to induce a generic company to enter into production. Causes of a small demand could include a very small affected patient population as in rare genetic diseases, or an isolated or constrained geographic distribution.

For products that have a market in developed countries, at-cost provisions should never replace generic provisions in licenses. For products that only have a market in resource-limited countries—such as those for “neglected diseases” that are primarily prevalent in resource-limited countries—a geographic market division strategy may not be feasible.<sup>14</sup> Licensees for such drugs are likely to be to non-profit entities, public-private partnerships, or other organizations that are already committed to global access, and a comprehensive strategy for ensuring such access should be established working with each licensee on a case-by-case basis.

## **Additional barriers to access must be overcome for biologics.**

While there is a clear paradigm for the production of small molecule generics, there are a number of important issues related to the production of generic vaccines and other biologics that this framework does not address; there are multiple additional barriers—many of which are non-proprietary—that need to be addressed in order to ensure efficient, cost-effective generic development. Complicating this issue is the ongoing debate in the United States Congress regarding the development of a pathway of FDA approval for generic biologics (known as biosimilars or follow-on biologics). It is currently unclear how this debate will be resolved. Because of the evolving nature of the law, the regulations that are in place at the time that a license is executed could be significantly different from those in place at the time that a licensee has completed end-product development. Therefore, to an even greater extent than for small molecules, it is critical to consider access licensing provisions for biologics on a case-by-case basis.

Still, universities that license biologics should follow the same basic principle: generic provision is the best method for ensuring access, and biologic licenses should do as much to facilitate generic provision as possible. In particular, universities should seek commitments from licensees to transfer materials and know-how to follow-on producers when necessary.<sup>15</sup> Where such agreements are impractical or impossible; when they may be insufficient to ensure follow-on provision; and while there remains no established legal pathway for follow-on biologics, at-cost provisioning commitments should be required.

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<sup>14</sup> Jean O. Lanjouw, *Ensuring Access to Low-Cost Drugs in a Patent-Protected World*, Development Outreach, World Bank (2006), <http://www1.worldbank.org/devoutreach/february06/article.asp?id=356>.

<sup>15</sup> Sara E. Crager, Ethan Guillen, and Matt Price, *University contributions to HPV vaccines and implications for access in developing countries: Potential models for improving access to university discovered vaccines*, *American Journal of Law & Medicine* 110-132 (forthcoming, 2009).



## Global Access License Policy Common Questions & Explanations

February 2009

### **Will Universities lose royalty revenue from a Global Access License (“GAL”)?**

Pharmaceutical sales, and therefore royalties, are unlikely to be impacted by a Global Access License, because the GAL is only relevant to Low and Middle-Income (LMI) countries where pharmaceutical companies sell nearly nothing. Consumers in the US, EU, and Japan comprise 93.2% of all pharmaceutical revenues.<sup>1</sup> While countries where a GAL would facilitate access have few consumers, they contain the world’s vast majority of patients; patients here are simply too impoverished to afford treatment. Mozambique, for instance, is home to at least 1,500,000 HIV positive persons<sup>2</sup>, yet per capita GNI is \$320.<sup>3</sup> Despite Poverty Reduction Strategies and Millennium Development Goal efforts and given the degree of their impoverishment, Mozambicans will clearly not become actual consumers in the near or medium term. Indeed it is doubtful whether poverty can be overcome without access to improved health care.<sup>4</sup> The only royalty revenue that could come from treating these persons with pharmaceuticals will originate in multilateral funding agencies – the Global Fund, UNTAID, the Gates Foundation, etc – whose impact depends largely upon their ability to negotiate prices at or near cost.

Because there is no effective market in Mozambique, there exist no revenue streams for a GAL to potentially disrupt. As much was reiterated by Yale's Dean of Public Health Michael Merson after Yale dropped its demand for stavudine royalties: “[t]his change was made at Yale without any negative consequences for the University – financial or otherwise.”<sup>5</sup>

### **Because of the economic crisis and endowment and budget declines, universities simply cannot prioritize global health.**

Because revenue streams from licensing agreements would not be impacted by a GAL – US consumers spend twenty times more on pharmaceuticals than the United Republic of Tanzania's entire gross domestic product – we reiterate that current financial challenges are unlikely to be impacted by the provision of a generic anti-retroviral in Honduras or Tanzania. While UAEM is aware that budgets are tighter than ever, the need and opportunity for our universities to improve access to treatment for the world’s poor has never been greater. Moreover, should incorporation of a GAL into all technology transfer agreements be postponed until the nation's financial crises desist, we would argue that this is essentially a postponement ad infinitum.

Current financial challenges are, of course, not limited to universities. Especially in moments of economic contraction, a reduction in pharmaceutical expenses becomes even more important to patients dependent on donor and multilateral funders.

### **Will global access principles cause the university to license fewer things?**

Universities are some of the country's most successful licensors of technologies, precisely because they are powerhouses of innovation. For example, the most prolific source of innovation in the US is the University of California system<sup>6</sup>, second globally only to the Japan Science and Technology Agency in aggregate patents issued, and first in the world in the issuing of biotechnology patents. Among the ten most frequently-cited patents are those assigned to Harvard, MIT, Yale and Rockefeller Universities.<sup>7</sup> The University of Texas,

<sup>1</sup> “The Pharm. Industry in Figures.” Euro Fed of Pharm. Ind. and Assoc. 2008 edition. p. 5.

<sup>2</sup> UNAIDS 2008.

<sup>3</sup> World Bank 2008.

<sup>4</sup> Sachs, J, and Palaney, P. “The Economic and Social Costs of Malaria.” *Nature*. Vol. 415. 7 February 2002. pp 680-85; Report of the Commission for Macroeconomics and Health, World Health Organization. Geneva: 2001.

<sup>5</sup> Kapczynski et al. “Addressing Global Health Inequities.” 20 *Berk. Tech. L. J* 1031, 1089 (2005).

<sup>6</sup> “Biotechnology Report 2007.” Marks and Clerk. 2007. London.

<sup>7</sup> Id. at 20.



Duke, Stanford, Johns Hopkins, Columbia, UPENN, University of Michigan, University of Washington, University of Illinois, and University of Florida all are among the most prolific patenting institutions on earth.<sup>8</sup> Nothing in the GAL affects this nor the likelihood of continued successes. The GAL, rather, is crucial for each university because they will continue to license earth-moving technologies, and bringing each university's biomedical innovations to the world is unlikely without a GAL. We also note that universities carry out more than half of the basic research in the US, and more than 1/6 total R&D domestically.<sup>9</sup> “At least a third of drugs marketed by the major drug companies are now licensed from universities or small biotech companies, and these tend to be the most innovative.”<sup>10</sup> Looking farther back, 15 of the “most important” drugs sold between 1965 and 1992 “were developed using knowledge and techniques from federally funded research.”<sup>11</sup>

We are mindful, however, that technology transfer officers work in a buyer's market, and that a GAL could be seen as a tax on all university-licensed property. These concerns, however, are not supported by any biotech revenue data available to UAEM. Because >93% of revenues originate in countries ineligible for GAL-provision, and the essential pharmaceuticals in question overwhelmingly treat impoverished patients, GAL-imposed burdens are unlikely to materialize. We applaud the researchers whose tireless work produces essential medicines – it's our common desire to see their innovations in universal action that motivates a GAL.

One cause for encouragement is the funding experience of the University of British Columbia in the year following the formal adoption of its Global Access Principles<sup>12</sup> in September 2007. Funding for Sponsored Research from all sources, including government, non-profit, *as well as industry*, was stable or increased from the period 2006-2007 to 2007-2008<sup>13</sup>.

### **Does the University have the bargaining power to do this? Won't pharmaceutical companies just avoid the University?**

Were a pharmaceutical company to avoid university innovations, that company would abandon some of the most successful licensors of technologies in the country. Because the GAL does not affect the markets constituting over 93% of the pharmaceutical industry's revenue sources, (for example, while there is a patient population in Mali, they do not constitute a market with an ability to pay), the prospects of pharmaceutical recrimination are vanishingly few. Moreover, there is abundant interest within industry to pursue some level of these policies: Gilead has already signed generic licenses for its enormously popularly – and lucrative – ARV tenofovir (Viread)<sup>14</sup>, and Gilead, Johnson & Johnson and Tibotec are all participating in patent pool discussions with UAEM and UNITAID.

### **Isn't this a problem for Congress? Why aren't you lobbying our Senators to rewrite Bayh-Dole?**

UAEM continues to work lobby the Congress to revise the Bayh-Dole Act?<sup>15</sup> Revising Bayh-Dole, though important, will not revise local technology transfer policies. Our policies are not federally mandated – they are our own. The methods with which the University shares its advancements with citizens in the state, nation, and the rest of the world are our responsibility. These are our labs. These are our PIs. These are our creations, and we are proud of them. The licensing policies of American universities *are global policies*. It's in

<sup>8</sup> Id. at 14.

<sup>9</sup> Nat'l. Sci. Bd. Sci. and Eng. Indicators 2004, at 5-5, 5-8; Mowery et al. “Growth of Patenting and Licensing by US Univ.” 30 *Res. Pol'y* 99, 101 (2001).

<sup>10</sup> Angel, Marcia. “The Truth About the Drug Companies.” *NY Review of Books*. Vol. 51. No. 12, p. 4, citing An Industry in Evolution, 3rd ed., Mary Jo Lamberti, ed. CenterWatch, 2001. p. 22.

<sup>11</sup> Congressional Joint Economic Committee [Senator Connie Mack, chair]. “The benefits of medical research and the role of the NIH.” May 2000. available online at [http://opa.faseb.org/pdf/2008/nih\\_research\\_benefits.pdf](http://opa.faseb.org/pdf/2008/nih_research_benefits.pdf)

<sup>12</sup> In which UBC commits to implement Global Access Licensing whenever possible: [www.uilo.ubc.ca/global.asp](http://www.uilo.ubc.ca/global.asp)

<sup>13</sup> UBC University-Industry Liaison Office 2007/08 Annual Report (p.4): [www.uilo.ubc.ca/pdf/UILO\\_AR\\_2008.pdf](http://www.uilo.ubc.ca/pdf/UILO_AR_2008.pdf)

<sup>14</sup> “Gilead Announces Licensing Agreements.” Sept 22, 2006. [http://www.gilead.com/pr\\_908393](http://www.gilead.com/pr_908393)

<sup>15</sup> 35 USC §200-12 (2000).



part this innovation and initiative that has resulted in over 25% of anti-retrovirals originating on university campuses.<sup>16</sup>

### What about parallel importation?

Parallel importation involves low-priced generics finding their way into the black market in developed countries. New regulatory barriers and customs regulations have minimized this threat. In addition, this concern finds little empirical support, and can be addressed in the same manner that the WTO has elected to treat the issue: requiring the use of different packaging, pill color, and shape in different countries to facilitate identification of illegal (re)importations.<sup>17</sup> Chris Viehbacher, Glaxo President of Pharmaceuticals for Europe, said Glaxo "is seriously concerned" about the illegal shipments, "but is this going to shake our commitment to the program? Not at this time. The human need is too big."<sup>18</sup>

Diversion from poor countries is rarely observed. Generic drugs have been produced in India for decades without resulting in the infiltration of or undermining of Western markets.<sup>19</sup> Likewise, "there is no empirical evidence of any substantial flows of medicines from LMI to rich countries"<sup>20</sup> Insofar as diversion is a concern, it can be addressed in the same manner that the WTO has—by requiring use of different packaging, pill color, and pill shape in different countries to facilitate the identification of illegal imports.<sup>21</sup>

### Why not let our licensees determine global policies?

Two reasons: economics and history.

Bulk essential pharmaceuticals are most cheaply produced by generic manufactures in India, Brazil and South Africa. If you've taken acyclovir, your wallet knows this. Moreover, they are best administered and distributed by groups like Doctors Without Borders, the WHO, Gates Foundation, and similar international providers that specialize in therapy provisions in resource-constricted settings. The pharmaceutical firms that license university-IP are also talented – but in an entirely different niche. The production, marketing, and distribution of novel therapies in highly-developed countries have been perfected by the US pharmaceutical industry. But they are not design, and nor are they equipped, to provide the quantities of essential medicines at generic rates, the foundation of effective therapy scale-ups.

Bristol-Myers Squibb's history in Thailand explains the second answer – the company licensed a compound (didanosine) from the Department of Health and Human Services, added an antacid to improve effectiveness, and applied for exclusive rights of sale across the globe. When the company became dissatisfied with its original filing in Thailand, it sought to expand its patent, and prevent generic competitors from pursuing the businesses Bristol had itself declined to pursue, as per its patent prosecution. Nearly a decade of litigation later, Bristol returned the patent to Thailand – which was unable to produce didanosine for years because of the pending litigation. Bristol still refuses any differential pricing policies for its pediatric formulation,<sup>22</sup> and refuses pricing differentials for Bolivia, El Salvador, and other countries whose patients it does not consider poor enough. This, we add, is with a compound developed at the National Cancer Institute with taxpayer dollars, and still it remains unavailable in countries where per capita incomes barely crest \$1/day. With domestic patents already expired for didanosine, BMS continues to seek rents for the NCI's innovation (in

<sup>16</sup> Sampat, Bhaven. "Academic Patents and Access to Medicines in Developing Countries." *American Journal of Public Health*. January 2009, Vol. 99, No. 1. p. 15.

<sup>17</sup> "Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health", World Trade Organization 2003."

<sup>18</sup> *Washington Post*, 10-03-02.

<sup>19</sup> Presentation at the Earth Institute, Columbia University, by Andrew Farlow, Oxford University: 'Costs of Monopoly Pricing Under Patent Protection. December 4, 2003.

<sup>20</sup> Kapczynski et al, p. 1078, see also Outtersson, Kevin. "Pharm. Arbitrage: Balancing Access and Innovation in Int'l Prescription Drug Markets." *Yale Journal of Health Policy, Law, and Ethics*. Vol 5. Issue 1. January 2005.

<sup>21</sup> "Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health." World Trade Organization 2003.

<sup>22</sup> *Untangling the Web*. Doctors Without Borders. 2008. p. 15.



LMI countries) – with appalling consequences.

Highly relevant is the fact that the DHHS' initial license to BMS required a "reasonable relationship between licensee's pricing of licensed product and the health and safety needs of the public and that this relationship be supported by evidence."<sup>23</sup> The need for revisions to existing licensing arrangements is made clear when highly profitable pharmaceutical firms take major steps to prevent severely impoverished nations from importing reduced-cost ARVs, as GlaxoSmithKline attempted to do in Uganda and Ghana.<sup>24</sup> We strongly believe that a GAL is the most practical and effective means to bring about part of the solution to the global access to medicines crisis, and that it must be initiated at the university level where many medical innovations begin.

Existing donation programs also regularly fail to meet demand, and include discarded pharmaceuticals. This represents an obscene reduction in the standard of care. In 1991, *Pharmaciens Sans Frontieres* found that it had to burn 80% of the donations it received.<sup>25</sup> Another analysis of pharmaceuticals donated to Bosnia and Herzegovina observed that up to 60% of all donated medical supplies were "inappropriate" and had to be burned at a cost of \$2,000 per metric ton (paid by aid organizations).<sup>26</sup>

### **What about middle income countries, and developing markets?**

Middle-income countries are usually characterized by extreme economic inequalities (e.g. Brazil and South Africa), wherein a few citizens are potential consumers for pharmaceuticals, while the vast majority remain severely impoverished. Here, we should acknowledge that it was South Africa, a middle-income country, home to more HIV-positive persons than any other country on earth, where the decisions of Bristol and Yale resulted in extensions of human lives. No doubt the needs for generic ARVs is greatest in countries lacking some of the infrastructure South Africa possesses, but nothing about relative wealth of a very small percentage of the country's population should prevent the delivery of essential medicines. Delays in delivery in one country – South Africa – resulted in over 330,000 preventable deaths.<sup>27</sup> Are there any examples of university action making a difference?

Yale and Bristol Meyers Squib reduced the price of stavudine (d4T) in South Africa by more than 95% by agreeing not to enforce the patent there. Though it required pressure from students, the researcher who discovered the drug, and Doctors Without Borders, both Yale and BMS benefited from the positive publicity generated by their arrangement. These trailblazing efforts led the way for price reductions of many other drugs, which together enabled non-governmental organizations as well as governments to begin treating people infected with HIV in developing countries. Yale continues to have strong and healthy ties to the pharmaceutical industry, and Pfizer has recently built a new \$35 million Clinical Research Unit in cooperation with Yale. Closer to home, UCSB donated patent rights to cardiovascular medicines for the treatment of schistosomiasis to the not-for-profit pharmaceutical company OneWorld Health in 2004 – this affirmative action offers great promise to the 200,000 patients who will die, every year, from the parasite. A GAL would multiply this singular event into broad policy. UC-Berkeley pursued royalty-free licenses for dengue diagnosis technology, and artemisinin, a malaria therapy. The University of British Columbia issues a royalty-free license for a novel, oral formulation of amphotericin B, the drug of choice for leishmaniasis, a neglected, often lethal parasitic infection affecting millions world-wide.

### **Will universities or pharmaceutical companies be liable for drugs produced generically under a GAL?**

As there will be no direct relationships between pharmaceutical developers and generic manufacturers as part

<sup>23</sup> Ford et al. "The Role of Civil Society." *The Lancet*. Vol 363. 14 February 2004.

<sup>24</sup> Shoofs. "Glaxo Enters Fight in Ghana on AIDS Drug." *Wall St. J.* Dec. 1, 2000, at A3.

<sup>25</sup> Snell, Beverly. "Inappropriate drug donations: the need for reforms." *The Lancet*. Vol 358. August 18, 2001. 578-80.

<sup>26</sup> Aplenc, R, et al. "Inappropriate Drug-Donation Practices in Bosnia and Herzegovina." *N Engl J Med* 1998; 338; 1472-1474.

<sup>27</sup> Chugwedere et al. "Estimating the Lost Benefits of ARV Drug Use in South Africa." *J-AIDS*. December 1, 2008.



of the GAL, and the creation of the generic market is automatic and open, neither universities nor the pharmaceutical developer should be in any way legally liable for the actions of generic manufacturers. Implementing GAL does not necessitate any unique liability situations not currently seen in the pharmaceutical market.

**Will this completely solve the problem of access?**

No. Lowering thresholds for the provision of essential medicines does not erase global health disparities – but, importantly, it facilitates access. Obviously, existing funding mechanisms and NGOs that provide health care in developing countries are financially constrained – reducing their costs allows their efforts to reach more patients. Moreover, reducing the costs of some pharmaceuticals also allows new classes of drugs and therapies to reach patients. Though the “problem of access” is not solved by any silver bullet, a GAL is a crucial step in that direction. At least ten million patients die, every year, from lack of access to therapies – preventable deaths are legion. ARVs cut AIDS-related mortality by seventy percent in the US<sup>28</sup> – it is within our grasp and responsibility to make these therapies cheaper, and thus more available.

**If many drugs are not patented in the world's poorest countries how is GAL relevant in these situations?**

Even if there are no patents in a specific country other barriers may exist. Under a GAL, ideally regulatory barriers would be lifted through open licensing of any proprietary data held by the university or licensee. Importantly, since a country may not have the infrastructure to manufacture a drug within its own borders a GAL should take steps to lift manufacturing barriers. A GAL should provide for open licensing of the right to manufacture in any country for export to low and middle income countries. For example, India and Brazil are some of the largest manufacturers of generic medicines that are distributed throughout the developing world. The licensing barriers they face need to be lifted so they can supply those people who do not generate a sufficient financial incentive for the major branded pharmaceutical industry with low-cost medications.

**If universities ultimately hold the patent for a given drug, why is it necessary to even negotiate with drug companies to allow for generic manufacture and distribution? Couldn't universities simply directly license their patents to third parties for generic distribution?**

It is very rare that only one patent goes into making a new drug and that therefore the power is solely in the hands of a university. More often the case is that the university holds a patent for a very early stage component of a drug. In developing the drug the pharmaceutical company will take out several more patents for further developments along the way. In addition to those additional patents taken out in the initial manufacturing of the drug, any subsequent improvements on the drug (such as an improved, once-per-day dosage or pediatric formulation) will also be separately patented. In a traditional licensing agreement the university has very little power over the pharmaceutical company's patents related to the drug.

**What part of the market are we talking about, exactly?**

Low and Middle Income (LMI) countries, which make up 88.3% of the world's population, account for only 5-7% of the overall pharmaceutical market.<sup>29</sup> This is overall bulk sales, however. Pharmaceutical companies make only a tiny part of their profits in these countries, either because of lower prices or because there is simply not enough demand in particular countries. These statistics represent the market failure that is causing many of the world's neediest populations to lack necessary medicines. The flip side of this point is that pharmaceutical companies still have a profit-incentive to develop drugs for only high-income countries, while allowing generic competition in the rest of the world. Drastic price cuts for ARVs in sub-Saharan Africa were estimated by one WHO official at no more than “three days’ fluctuation of exchange rates.”<sup>30</sup>

<sup>28</sup> Palella et al, 338 *NEJM* 853 (1998).

<sup>29</sup> “Pathways to Biopharm Innov.” *PhRMA*. 40 (2005).

<sup>30</sup> Gellman, Barton. “An Unequal Calculus of Life and Death.” *Washington Post*. December 27, 2000. Page A01.



### **If drug companies are already implementing some differential pricing schemes, what role can universities play?**

Some pharmaceutical companies have enacted price differentials for selected drugs in the developing world and in some cases allow generic production of particular drugs. Yet the access gap persists. While the cost of a year's worth of anti-retroviral drugs in South Africa has been lowered to US\$99 in recent years, second-line therapy remains unattainable at US\$2,500 per year. Second-line therapies are essential components of treatment for HIV/AIDS, because patients acquire drug resistance. It is for this reason that patients in the US and EU can expect no fewer than four separate classes of therapies, with a range of lines therein. The WHO's 2007 ARV forecast, however, indicates that fewer than 4% of LMI patients are receiving second-line therapies; the 96% routinely receive therapies that are no longer recommended – even as alternative therapies – in the US/EU because of known toxicity and inferiority issues.<sup>31</sup>

This is a pattern seen in most new drugs, which arrive in the developing world decades after they save lives in high-income countries. Today, fewer than 30% of Africans in need of treatment for HIV infection are receiving even basic care.<sup>32</sup> Universities, which are at the forefront of creating new medical innovations, can change this outcome beginning at the first step in the drug pipeline. A GAL will ensure that any product that results from their innovations are made affordable via generic production.

### **Are there anti-trust concerns about universities conspiring to set prices?**

No. Federal Courts have heard cases concerning open-source and general public licenses, and challenges to them on the basis that companies “conspire” to eliminate competition. The precedent is *Wallace v. IBM, Inc.*<sup>33</sup> Wallace sued IBM and two prominent software manufacturers, Red Hat and Linux, for their use of a license devised by the Free Software Foundation, that allowed users to obtain the product free-of-charge, and for derivative products to be created for the same price. Judge Easterbrook of the Seventh Circuit Court of Appeals found, “[c]opyright and patent laws give authors a right to charge more, so that they can recover their fixed costs (and thus promote innovation), but they do not require authors to charge more. No more does antitrust law require higher prices.”<sup>34</sup> Though the plaintiff sued because the license agreements would “eliminate competition in the operating system market by making Linux available at an unbeatable price” (free), the suit was rejected because the licensees in question “have nothing to fear from the antitrust laws” as “[e]mploying antitrust law to drive prices up would turn the Sherman Act on its head.”<sup>35</sup>

A related case against the Free Software Foundation was also dismissed by US Federal Court Judge Daniel Wallace, who ordered the plaintiff to pay for defendant's fees (an indication of a baseless suit). Wallace wrote, “the GPL encourages, rather than discourages, free competition and the distribution of computer operating systems, the benefits of which directly pass to consumers. These benefits include lower prices, better access and more innovation.”<sup>36</sup>

Patent pools for intellectual property have also been considered in light of existing anti-trust concerns. The Department of Justice's analysis thereof, however, concludes that pools “can have procompetitive benefits, for example, by exploiting economies of scale and integrating complementary capabilities of the pool members.”<sup>37</sup>

### **Could this impact NIH funding?**

The GAL would not change any framework required by the NIH, and NIH funding is unrelated to

<sup>31</sup> WHO p. 17; Department of Health and Human Services ART Guidelines, November 2008.

<sup>32</sup> UNAIDS 2008.

<sup>33</sup> 467 F.3d 1104 (7th Cir 2006).

<sup>34</sup> Id. at 1107.

<sup>35</sup> Id. at 1108, 1007.

<sup>36</sup> unpublished Order of Dismissal in *Wallace v. Free Software Foundation*, S.D. Indiana, 2006, Case 1:05-cv-00618-JDT-TAB. (2006). available online at <http://www.groklaw.net/pdf/WallaceFSFGrantingDismiss.pdf>.

<sup>37</sup> Antitrust Guidelines for the Licensing of Intellectual Property. US Department of Justice and the Federal Trade Commission. April 6, 1995. available online at <http://www.ftc.gov/bc/0558.pdf>.



university-specific technology transfer policies. Yale saw no change in its NIH funding after it dropped its patent rights for stavudine; UC Berkeley's use of double-bottom line metrics has similarly not impacted its NIH funding. The NIH, itself, is also subject to Bayh-Dole, and its licensing is subject to government oversight and marching-in rights.<sup>38</sup> The NIH is actually moving its grant recipients to publish their research in open-access repositories, among other efforts to revisit existing exclusive arrangements.

GALs also have a history of attracting funding. UC Berkeley Vice Chancellor Carol Mimura described the Gates Foundation's \$42.6 grant this way: "Gates would not fund until we could guarantee access," requiring that the technology be sold to developing nations at the cost of production.<sup>39</sup>

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<sup>38</sup> 35 U.S.C. § 202(e)(4)(2000).

<sup>39</sup> Ledford, Heidi. "IP: Ideas for Purchase?" *Berkeley Science Review*. Spring 2006. at 38.

# The Scientist's Story

By William Prusoff

NEW HAVEN

Once helped create a drug that could enable millions of people to lead better and longer lives. At Yale University's pharmacology laboratory, my late colleague Dr. Tai-shun Lin and I developed d4T, an antiretroviral drug that now forms part of a "cocktail" used by people with H.I.V. and AIDS. The patent was held by Yale, which licensed it to Bristol-Myers Squibb for development. At great expense, Bristol-Myers took d4T through the necessary trials, then brought the drug to market under the name Zerit.

More recently, it became apparent that the drug Dr. Lin and I had developed was not reaching millions of desperately suffering people because they lacked the money to purchase it. However, Yale did hold the patent.

## From a U.S. lab to Africa, the journey of an AIDS drug.

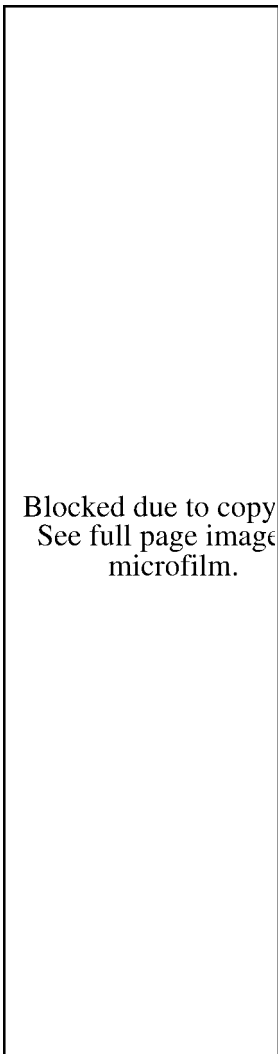
The medical aid group Doctors Without Borders learned this and approached the university late last month. At the same time, a group of law students at the university became interested in the issue. The campus newspaper published an article about it on March 2, mentioning my role in developing d4T. A New York Times reporter called, and I said I thought d4T should be either cheap or free in sub-Saharan Africa. I believe Dr. Lin, were he still here, would agree.

Within days, Bristol-Myers had announced that it would cut the cost of Zerit to 15 cents for a daily dose, or 1.5 percent of the cost to an American patient. This all happened so quickly. More than two-thirds of people with H.I.V. live in sub-Saharan Africa — about 26 million people. The numbers seem too great to understand. But they are not. In a way, they are as easy to understand as 15 cents. I suppose this has now occurred to Bristol-Myers Squibb.

What is a reasonable charge for d4T in industrialized countries, and to what extent can this charge be reduced in poorer nations? It is estimated that to bring a drug from conception to the marketplace costs from \$500 million to \$800 million. The investment by a university like Yale is probably less than 1 percent of this amount. The major expense is clinical studies required by the Food and Drug Administration. Millions may be spent on these studies — only to have unacceptable toxicities occur and the compound dropped like a hot potato.

Those lost millions become part of the cost of successful drugs. The patent enables pharmaceutical firms to

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Polly Becker

recoup such losses as well as the costs of clinical trials for successful drugs. If a patent did not exist, other companies that did not have the expenses of preclinical and clinical studies could obviously afford to sell these drugs at much reduced prices.

The d4T compound was first synthesized by Dr. J. P. Horwitz of the Detroit Cancer Center in 1966. He was also the first to synthesize AZT. These

were designed to be anticancer drugs, but they were not sufficiently potent. When AZT was reported to be a potent inhibitor of H.I.V.-1, Dr. Lin and I decided to look at similar compounds.

AZT is an analogue of thymidine, which is an essential component of DNA. I had worked on thymidine compounds for 40 years. Dr. Lin and I proceeded to synthesize d4T by modifying the process developed by Dr. Horwitz. We found that d4T was not toxic to human cells in cell cultures. Bristol-Myers became interested in d4T and received from Yale an exclusive license for further study and development. The company sent a sample to the National Institutes of Health for evaluation of its potential inhibition of H.I.V.-1. The institutes were slow in responding, so Dr. Lin and I sent a sample to Raymond F. Schinazi of Emory University School of Medicine and the Veterans Administration Medical Center in Decatur, Ga. I had known him since he was a postdoctoral fellow in my laboratory. He found d4T to be very potent against H.I.V.-1, as the N.I.H. eventually did as well.

Thus Bristol-Myers decided to do the clinical studies required by the F.D.A. to determine d4T's safety and efficacy in humans. Positive results were achieved after treating more than 13,000 patients, from Europe and the United States, infected with H.I.V.-1. Of course, d4T is not a cure, but it can help prolong a person's life and make that life better.

Now Bristol-Myers, encouraged by Yale, has begun the process of making d4T and its companion drug, Videx, available to millions of people for whom, just a week ago, these treatments seemed utterly remote. I imagine many of these suffering people thought they would die before seeing these drugs.

I am struck by all the steps that led us to today: the work of Dr. Horwitz on anticancer compounds, my own work and that of Dr. Lin, the timely tests performed by Dr. Schinazi, the inquiries made by Doctors Without Borders to Bristol-Myers, which then led to Yale and some Yale law students and the campus paper and then back to Bristol-Myers, whose executive vice president John L. McGoldrick said on March 14 that his company hoped to "energize a groundswell of action" to fight AIDS in Africa. I find it hard to see any pattern in all this, except perhaps that there is a moral urge among people that, however coincidentally, can sometimes bring results. □

# Leveraging University Research to Advance Global Health

Dave A. Chokshi, MSc

Rahul Rajkumar, MD, JD

**T**HE WORLD'S DESTITUTE SICK FACE A PERILOUS DISADVANTAGE in accessing essential medicines. The crisis stems from 2 related problems. First, for the billion people affected by neglected diseases such as trypanosomiasis and cholera, few safe and effective treatment options exist. Because these neglected diseases predominantly affect the poor, they attract little research and development funding, leading to a paucity of therapies.<sup>1</sup> Second, for other diseases, several interlinked factors impede access to medicines that do exist: high prices, underfunded and uncoordinated health care systems, and drug formulations ill-suited to resource-poor settings.

Generic competition has lowered the price of antiretroviral therapy for human immunodeficiency virus (HIV) from more than \$15 000 per patient-year 6 years ago to \$99 today.<sup>2</sup> Concomitant with this decrease in prices has been an increase in funding and political will to address the HIV/AIDS pandemic. This has shifted the debate from whether antiretroviral therapy is possible in resource-poor settings to how to strengthen health infrastructure to provide comprehensive care.<sup>3</sup>

Despite the progress demonstrated for antiretroviral therapy in poor countries, there is, as yet, neither a comprehensive nor a lasting solution to ensure that patients in poor countries pay less for medicines than patients in rich countries. Even antiretrovirals, generally heralded as a success story for differential pricing, show the evanescence of any progress that has been made. Implementing new first-line HIV treatment guidelines from the World Health Organization would cost 5 times more per patient-year than the older, first-line treatment regimen; second-line therapies are even more expensive.<sup>2</sup> Meanwhile, major generic-producing countries like India must now enforce product patents to comply with the World Trade Organization's Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement.<sup>4</sup> The US government is pushing further still for expanded intellectual property protection by systematically negotiating so-called TRIPS-plus provisions into bilateral free-trade agreements.<sup>5</sup> Taken together, these developments threaten to undermine gains for the health of the underserved that have been made by reforms to the international intellectual property system.

## The Role of Universities

Research universities have an opportunity to intervene in the access-to-medicines crisis in poor countries. By virtue of their

upstream contribution to the drug development pipeline—estimated at \$19.6 billion in 2002 for the United States alone—universities have considerable untapped influence.<sup>6</sup> Both the number of patents held and the number of license agreements executed by universities more than doubled between 1991 and 2005.<sup>7</sup> The case for university action becomes more tangible when considering actual medicines. For instance, the patent rights contributing to several currently marketed HIV drugs are held by universities: stavudine (Yale University), abacavir (University of Minnesota), lamivudine (Emory University), emtricitabine (Emory University), and enfuvirtide (Duke University). Overall, university patents are associated with 10 of the 30 HIV drugs approved by the US Food and Drug Administration between 1987 and 2007.<sup>8</sup>

Several institutions—both private and public—have demonstrated that it is possible to leverage ownership of intellectual property to improve access to medicines. For example, in 2001, Yale University negotiated price concessions from Bristol-Myers Squibb for stavudine in South Africa.<sup>9</sup> Similarly, the Bill and Melinda Gates Foundation, through its Grand Challenges in Global Health initiative, requires grantees to ensure that any health products created with Grand Challenges funds will be available at affordable prices in poor countries.<sup>10</sup> The grants call for principal investigators to outline *ex ante* intellectual property ownership issues, licensing strategies, and potential commercial partners. The US National Institutes of Health (NIH) has also pioneered proactive management of its intellectual property to benefit the developing world. For technologies with a worldwide market (such as new antiretrovirals), the NIH has adopted license terms that require companies in North America or Europe to provide a marketing plan for making products available in developing countries.<sup>11</sup>

Public-sector research and licensing practices have implications extending beyond HIV medicines. Of the 35 million deaths from chronic disease that occurred in 2005, 80% occurred in low- and middle-income countries.<sup>12</sup> Expanding access to primary care treatments for chronic illnesses like diabetes and cardiovascular disease could have an immediate effect, both for patients and for the structure of limited or unstable health care systems. Vaccine-preventable diseases also exemplify the magnitude of the opportunity. Human papillomavirus vaccine was originally developed at the Univer-

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sity of Rochester, Georgetown University, Queensland University, and the US National Cancer Institute. Research on rotavirus vaccine was originally conducted at the Wistar Institute and the Children's Hospital of Philadelphia. Both of these vaccines were recently licensed for use in the industrialized world without a clear strategy for access to the vaccines in poor countries, where the vast majority of deaths due to cervical cancer and diarrhea occur.

Ensuring access to university-derived medicines in poor countries would have a demonstrable effect on global health only if pro-access policies are adopted collectively by major research universities. An important step toward consensus was taken recently when the Association of American Medical Colleges (AAMC) and 18 research institutions called for ensuring access to university innovations in the developing world.<sup>13</sup> The AAMC and collaborating universities joined committees of the World Health Organization<sup>14</sup> and the American Association of Arts and Sciences<sup>15</sup> that previously espoused this same principle. What follows are policy recommendations for operationalizing that principle.

### Promoting Equal Access to Research

When university-owned intellectual property is necessary for the development of a potential health-related product such as a drug, a vaccine, or a diagnostic test, universities could either require the inclusion of licensing terms in exclusive technology transfer agreements that ensure low-cost access to health-related innovations in the developing world; or develop a transparent, case-by-case global access strategy to ensure access when licensing provisions will not serve access objectives.

The licensing transaction between a university, and, for example, a biotechnology company represents an important point of leverage for access considerations. A critical lesson learned from the first round of price reductions for antiretroviral agents was that generic competition is the most effective mechanism for lowering prices.<sup>4</sup> An effective licensing policy would engender such generic competition. One example of this type of policy is the equitable access license (EAL), developed by Universities Allied for Essential Medicines. The EAL is a nonexclusive, open licensing arrangement that provides a means to capture any downstream licensee improvements for the purpose of supplying developing-country markets.<sup>16,17</sup> The EAL applies to countries classified as low- or middle-income by the World Bank and permits multiple producers to compete in these countries simply by notifying the university and its licensee.

An advantage of the EAL is that, by relying on the market for generic production, the administrative burden on the university is minimized. However, this parsimony may not be well-suited to certain situations. For example, biologics (eg, vaccines and macromolecules such as monoclonal antibodies) and medical devices are subject to different scientific and technical constraints than are synthetic small molecules (eg, antiretrovirals such as stavudine) and may require different methods to ensure access. Universities ought to implement open licensing solutions like the EAL where possible but could pur-

sue alternative global access strategies for predefined situations in which open licensing may not be the best solution. While intellectual property ownership is an important and tangible point of influence, it is not the only leverage available to public institutions such as universities.

The term "global access strategy" derives directly from the Gates Foundation's guidance on intellectual property management for the Grand Challenges in Global Health.<sup>10</sup> Among other provisions, the guidance requires that the grantee's intellectual property revert to the Gates Foundation if the patented innovation is found to be inaccessible in poor countries. The purpose of the global access strategy, however, is to prevent this situation from arising in the first place by negotiating in advance a feasible plan to ensure access to innovations where they are needed most. Potential components of a global access strategy include: (1) stipulations for voluntary licenses to generic manufacturers and mandatory sublicensing requirements to alternative manufacturers when access objectives are not being met; (2) clauses requiring the licensee to make products developed from a university innovation available at a reduced cost in developing countries; (3) actively seeking third-party organizations to participate in development and distribution for the developing-world market; and (4) participating in patent pools (ie, joining with other institutions and companies to cross-license patents) that are organized in the interest of public health.<sup>15</sup>

### Promoting Research and Development for Neglected Diseases

Neglected diseases are those for which treatment options are inadequate or do not exist and for which drug-market potential is insufficient to attract a private-sector response. To promote research and development in treatments for neglected diseases, universities could adopt needs-based medical research policies, such as promoting in-house neglected-disease research; engaging with nontraditional partners to create new opportunities for neglected-disease drug development; and carving out a neglected-disease research exemption for any patents held or licenses executed.

Internally, university decision makers setting the research agenda could purposefully include work on neglected diseases in their deliberations. While funding sources and faculty interests govern the research agenda to some degree, steps can be taken to cultivate neglected-disease research. Capital investments by universities such as the \$30 million committed to found the Duke Global Health Institute—an interdisciplinary initiative combining education, research, and service missions—are too few and far between.<sup>18</sup> Even simple structural changes, such as the creation of a Center for Neglected Diseases, and marketing of neglected-disease research capacity can help attract talented researchers and new sources of funding, as seen in the cases of the George Washington University and the University of California at Berkeley.<sup>19,20</sup> One way that all universities could start is by formalizing annual review practices aimed at identifying new or currently shelved technologies with promising potential for application to neglected diseases.

University policy makers might also take note of the external developments that have changed the landscape of neglected-disease drug development. Product-development partnerships like the Medicines for Malaria Venture and the Drugs for Neglected Diseases Initiative have attracted hundreds of millions of dollars in funding, the majority of which is contributed by the Gates Foundation.<sup>21</sup> Universities could actively seek privately funded but targeted partnerships—as well as partnerships with developing-country companies and research institutions—to develop technologies applicable to neglected diseases.

In addition, when patented innovations have not yet been licensed for further development, universities could allow, as a matter of policy, other nonprofit institutions to use them in research for neglected diseases. One way to operationalize this research freedom could be to contribute to a comprehensive molecular screening library for neglected diseases.<sup>22</sup> When innovations have been externally licensed, universities could include an exemption for neglected-disease research in their licensing agreements. These agreements can be structured as a “dual-market” opportunity, permitting the universities to partner with companies for markets in industrialized countries while a nonprofit entity retains the rights to develop the compounds for patients in developing countries.<sup>23</sup>

### Measuring Research Success According to Effect on Global Public Health

University technology transfer operations are usually evaluated using simple, quantifiable criteria such as patents applied for and received, licenses granted, and licensing revenue generated. The focus on these types of statistics may partly explain why technology transfer objectives are often misaligned with the broader public mission of universities.<sup>24</sup> Yet perhaps surprisingly, licensing revenue from academic research is, in the majority of cases, not a lucrative investment. For example, among US institutions, the ratio of licensing income to sponsored research funding was reported to be 5% or less in 2005.<sup>25</sup> Thus, the positive social effect of university innovations—particularly in poor countries—would go largely unnoticed if the success of technology transfer were measured in dollars alone. To rectify this situation, universities could collect and report data on university intellectual property practices related to global health access. Furthermore, universities could collaborate to develop more robust technology transfer metrics that better gauge access to public health goods and innovation in neglected-disease research.

Even though perfectly sound technology transfer metrics may not yet exist, universities can make the nonmonetary benefits of technologies for global health more transparent. For example, universities could disclose all health care–related products in which they hold intellectual property rights. Universities could also publish information on patents applied for or granted in all developing countries, the number and nature of licensing agreements that include access-minded provisions, and reports of nontraditional partnerships for neglected-disease research and development.

University mission statements typically include the noble idea of creating and disseminating knowledge in the public interest. Holding universities to these standards is a critical means to fulfilling an even loftier principle, codified in the Universal Declaration of Human Rights: providing access to medical care and treatment as a basic human right.

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Debate

Open Access

## Closing the access gap for health innovations: an open licensing proposal for universities

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### Abstract

**Background:** This article centers around a proposal outlining how research universities could leverage their intellectual property to help close the access gap for health innovations in poor countries. A recent deal between Emory University, Gilead Sciences, and Royalty Pharma is used as an example to illustrate how 'equitable access licensing' could be put into practice.

**Discussion:** While the crisis of access to medicines in poor countries has multiple determinants, intellectual property protection leading to high prices is well-established as one critical element of the access gap. Given the current international political climate, systemic, government-driven reform of intellectual property protection seems unlikely in the near term. Therefore, we propose that public sector institutions, universities chief among them, adopt a modest intervention – an Equitable Access License (EAL) – that works within existing trade-law and drug-development paradigms in order to proactively circumvent both national and international obstacles to generic medicine production. Our proposal has three key features: (1) it is prospective in scope, (2) it facilitates unfettered generic competition in poor countries, and (3) it centers around universities and their role in the biomedical research enterprise. Two characteristics make universities ideal agents of the type of open licensing proposal described. First, universities, because they are upstream in the development pipeline, are likely to hold rights to the key components of a wide variety of end products. Second, universities acting collectively have a strong negotiating position with respect to other players in the biomedical research arena. Finally, counterarguments are anticipated and addressed and conclusions are drawn based on how application of the Equitable Access License would have changed the effects of the licensing deal between Emory and Gilead.

### Background

Last year, Emory University, Gilead Sciences, and Royalty Pharma announced a deal in which Emory sold its 20% royalty interest in the antiretrovirals Emtriva (emtricitabine, FTC) and Truvada (emtricitabine+tenofovir, FTC+TDF) to Gilead and Royalty Pharma for an up-front

payment of \$525 million [1]. The deal – in essence, a renegotiation of an earlier licensing agreement – reflected the demonstrated value of emtricitabine, a compound discovered by Emory researchers and patented by the university. On the surface, this deal seems like a boon for all parties involved: the university receives a wealth of unre-

stricted funds, while Gilead extends its control over marketing and distributing the drugs.

A closer look suggests that the deal was a missed opportunity for the university to collaborate with its licensee to assure not only high licensing revenues, but global access to the products of its innovation as well. Emtricitabine and tenofovir are likely to be recommended for both first-line and second-line therapy in updated World Health Organization antiretroviral treatment guidelines, making access to these medications increasingly important for millions of people with HIV across the world, particularly in poor countries [2]. Yet the terms of the deal did not address access to these medicines.

Gilead is among the most advanced among pharmaceutical companies in implementing efforts to address questions of access in poor countries, known in particular for its Access Program. But even this well-intentioned approach is not free of limitations. For example, those administering antiretroviral treatment on the ground in poor countries have pointed out endemic problems with the Access Program, such as failure to register the drugs in the countries purportedly eligible to receive a discount on the drugs [3]. Moreover, Emtriva is not currently included in Gilead's Access Program [4]. The \$525 million deal with Emory University raises the question of whether Emory, as a university dedicated to serving the public interest, could have acted further to improve access to the products of its innovation. This article centers around a proposal outlining how Emory, and other universities in its position, could engage their licensees in an effort to close the access gap for health innovations, such as Gilead's antiretrovirals, based on discoveries at those universities.

## Discussion

### 1. Intellectual property rights and access to medicines

Barriers impeding access to Truvada and Viread (and Emtriva) are indicative of a larger problem that impedes access to other medicines as well. Approximately ten million people die needlessly each year because they lack access to existing essential medicines and vaccines [5]. This "access gap" stems from several factors, including unreliable health care delivery systems, lack of political will for public financing of health care, and high prices for medicines [6]. These factors are mutually reinforcing, particularly in poor countries, as patients in poor countries pay on average more than seventy percent of medicine costs themselves [7].

High prices result in large part from the temporary monopolies granted to pharmaceutical companies through patent and regulatory systems [8]. In fact, generic competition may be the most important factor in lower-

ing prices in a given country [9]. Importantly, increased generic competition in poor countries is unlikely to significantly impact the revenues of patent-based pharmaceutical companies and thereby impede future innovation. The branded pharmaceutical industry in the United States derives only five to seven percent of its profits from all low- and middle-income (LMI) countries [10].

Some authors have argued that pharmaceutical companies rarely patent in poor countries and that intellectual property protection has little relation to access [11]. Yet there is widespread evidence that pharmaceutical companies do seek patents in poor countries [12]. For instance, many of the most important antiretrovirals for HIV treatment are widely patented in Africa [13]. Moreover, patents in key source countries for generics – for example, India – may affect access to generics in countries where no patents exist, because many developing countries have little or no capacity to produce medicines locally.

It appears that things will get worse before they get better [14]. India passed legislation in March of 2005 to comply with the World Trade Organization's Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement, jeopardizing the world's most important supply of generic medicines. Additionally, the United States continues to pressure developing countries to adopt so-called "TRIPS-plus" standards in its bilateral free trade agreements. These standards extend monopoly rights for medicines, impede generic competition, and make importing generic drugs from other countries even more difficult.

There have been some positive developments in the arena of intellectual property and health. Most notably, in May 2006, the World Health Assembly passed resolution WHA59.24, which created an intergovernmental working group to develop a global plan of action on intellectual property, innovation, and public health. While this is undoubtedly a useful initial step, true reform of intellectual property protection can only be achieved through domestic, government-driven reform or binding international agreements along the lines of the TRIPS regime. Difficulties implementing the public health protections under TRIPS – as well as the United States' stance toward intellectual property and health in bilateral trade negotiations – indicate that such reforms will be halting at best in the current political climate [14]. Moreover, given the pharmaceutical industry's dependence on university research, universities will likely continue to license their patent stakes in medical products for cash payments and royalties. Therefore, we propose that public sector institutions, universities chief among them, adopt a modest intervention – an Equitable Access License (EAL) – that works within existing trade-law and drug-development paradigms in order to proactively circumvent both

national and international obstacles to generic medicine production.

Our proposal has three key features: (1) it is prospective in scope, (2) it facilitates unfettered generic competition in poor countries, and (3) it centers around universities and their role in the biomedical research enterprise. The open licensing mechanism we propose complements more systematic efforts to reform the international intellectual property regime. It is a policy change that can be implemented in the near term by a different set of leaders – university administrators rather than political representatives. Indeed, we believe part of the utility of implementing our proposal will be the united voice of universities signaling to governments that they have not sufficiently addressed a humanitarian crisis. The details of this proposal have been laid out elsewhere [15]; the purpose of this paper is to describe the key components of a university licensing structure that would facilitate access to medicines in developing countries.

## **2. The case for university action**

University research is integral to the biomedical research and development pipeline. This gives universities the power to act to improve the lives of patients – and also to collectively persuade their private sector partners of the mutual benefits of an open licensing approach. Further, the institutional principles of universities – to create and disseminate knowledge that improves people's lives – are well-aligned with the objectives of our proposal. Each of the top four recipients of US patents in 2004, including two private universities, the California Institute of Technology and the Massachusetts Institute of Technology, cites public benefit as an explicit goal in its patent policy [16].

Multiple studies have confirmed that public sector research, including research done at universities, is vital to the development of new medicines [17-19]. A US Senate Joint Economic Committee study concluded that the contribution of universities and other public research institutions was instrumental in developing fifteen of the twenty-one drugs considered by experts to have had the highest therapeutic impact [20]. Universities have held US patent rights in a wide array of key pharmaceuticals, including the cancer drugs cisplatin and carboplatin, pemetrexed (Alimta), cetuximab (Erbix); the anemia treatment epoetin alfa (Epogen); the AIDS drugs stavudine (Zerit), 3TC (Epivir), abacavir (Ziagen), and T20 (Fuzeon); and the best-selling glaucoma medicine latanoprost (Xalatan) [15].

The Bayh-Dole Act of 1980 gave US universities control over intellectual property resulting from federally-funded research. Typically, universities license biomedical tech-

nologies to private sector companies for further development. Therefore, while universities often hold intellectual property rights to key components of many end products on the market – licensees, usually biotechnology or pharmaceutical companies, generally acquire secondary patents and generate the safety and efficacy data needed to market the drug. Nevertheless, two characteristics make universities ideal agents of an open licensing proposal. First, universities, because they are upstream in the development pipeline, are likely to hold rights to the key components of a wide variety of end products. Second, universities acting collectively have a strong negotiating position with respect to other players in the biomedical research arena.

## **3. The equitable access license**

### *The open licensing approach*

The ultimate goal of our proposal is to achieve marginal cost pricing for health-related end products, including medicines and medical devices, in low- and middle-income countries [21]. To achieve this, we propose that universities' technology transfer agreements facilitate generic competition by providing open licenses guaranteeing third-party manufacturers the right to compete in LMI markets, regardless of patents or other forms of exclusive rights.

While a 'fair pricing' approach – obliging the original manufacturer to make a medicine available at a low markup on marginal cost of production – might seem like a plausible (or even preferable) alternative to an open licensing approach, it would require a credible threat of enforcement for breach of contract. The open licensing approach, on the other hand, does not require universities to take an active role in monitoring or enforcement. It achieves this by introducing third parties (generics companies) with market incentives to narrow the access gap by offering low-priced, but still profitable, products. Additionally, the balance of the evidence – most clearly seen in the case of HIV antiretrovirals – indicates that competition has been more reliable as a method of lowering prices than voluntary "at cost" pricing [22,23].

Finally, an open licensing approach fosters more sustainable and locally appropriate supplies of low-cost medicines in developing countries. A small but meaningful market would attract the investment by low-margin generic companies. Similarly, our proposal seeks to allow third parties to modify products for the particular needs of target populations via fixed dose combinations or pediatric dosing.

### *Appropriate technologies and territories*

To be appropriate for an Equitable Access License, a technology must be health-related. However, universities

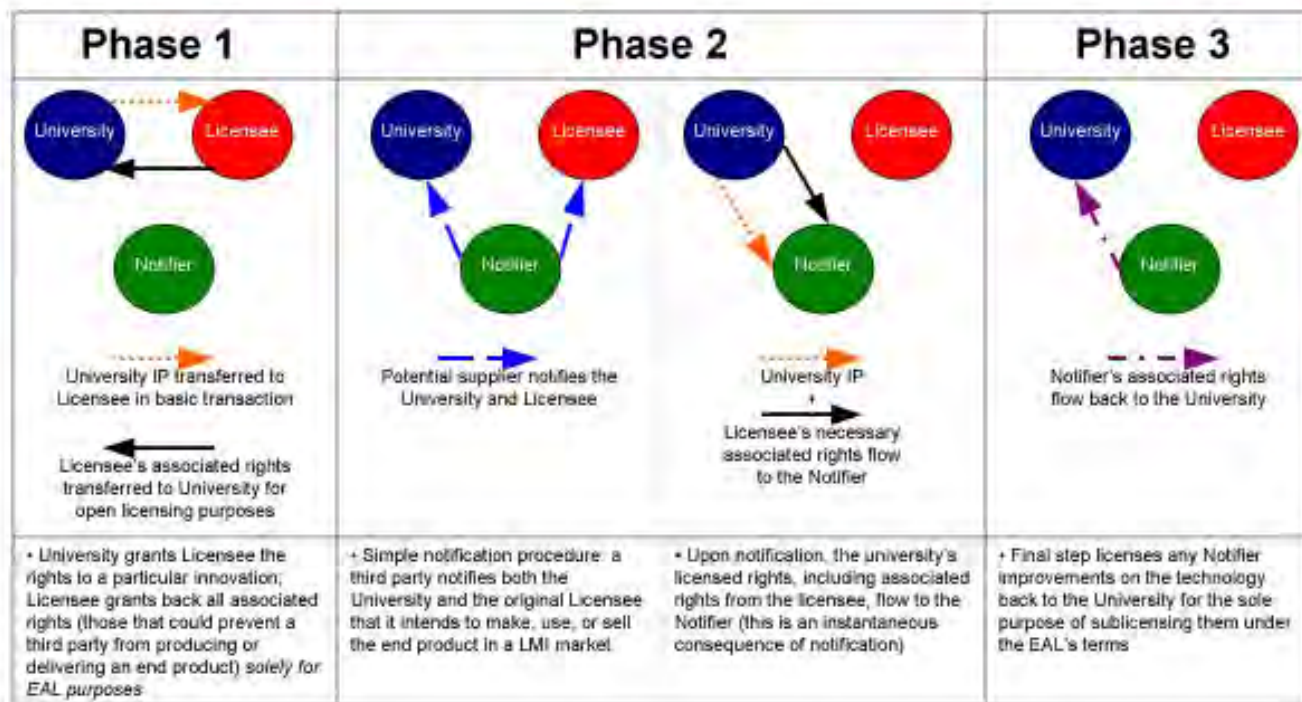
should resist the pervasive assumption that access concerns in developing countries are limited to drugs for infectious diseases. The burden of chronic non-communicable disease is primarily borne by those living in developing countries [24]. Meanwhile, the equitable access approach should be well-suited to a wide variety of technologies, from small-molecule drugs and macromolecules to diagnostic and manufacturing tools. The most obvious candidates are potential pharmaceutical products, both small-molecule drugs and biologic therapies.

We contend that, in order to meet the health needs of patients in developing countries, EAL provisions must apply to all low- and middle-income (LMI) countries (as defined by the World Bank) and must include the right to supply the private sector in these countries [25]. Middle-income countries (e.g., Brazil, Mexico, and South Africa) are included for their highly unequal income distributions and large poor populations that must obtain their own care in the private sector [26]. Moreover, middle-income countries are critical as incentives to sustain the generic manufacturers. Finally, any entity that wishes to supply a LMI market – even a company based in a high-income country – would be able to do so under the EAL.

**Mechanism of the EAL**

The mechanism of operation for the EAL can be summarized in three steps: (1) cross-licensing and grant back of rights between the university and a licensee; (2) notification by a third party of intent to supply an LMI market, triggering the provisions of the EAL; and (3) grant back of rights for any subsequent developments made by the third party to the university. These steps are described in Figure 1 below.

The first step is essentially an exchange of licenses. Just as with a normal exclusive licensing transaction, the university grants the licensee rights to a particular innovation. This grant will likely include, at a minimum, rights to practice the university's technology in some or all high-income countries. In exchange, the licensee will "grant back" to the university a set of rights referred to as "associated rights"; this would include all of the potentially exclusive rights the company holds or acquires that could prevent a third party from producing or delivering an end product. The EAL's provisions must apply to any technologies necessary to the production of the end product even if those technologies are not directly related to the university's innovation.



**Figure 1**  
**Schematic diagram of the mechanism of the Equitable Access License.** The three phases of the Equitable Access License.

However, the grant back would not include any material property – such as cell lines – possessed by the original licensee or sub-licensees. Importantly, the EAL's provisions are designed to apply not only to the initial licensee but also to any subsequent sub-licensees. The university obtains these rights solely for the purpose of granting an automatic sub-license to any third-party manufacturer, thereby ensuring freedom to operate in LMI countries.

The second transactional element of the EAL is a simple notification procedure: a third party notifies both the university and the original licensee that it intends to make, use, or sell the end product in a LMI market. We anticipate three main types of third-party notifiers: (1) generics companies wishing to produce or sell in an LMI country; (2) government agencies or NGOs wishing to import generics from a third party; or (3) researchers wishing to adapt an end product to developing-country use. In order to foster an open and competitive environment, the EAL permits multiple notifiers. Upon notification, the university's licensed rights, including associated rights from the licensee, flow to the third-party manufacturer. Through this contractual flow of rights, patent, regulatory, and manufacturing barriers are lifted for the notifying entity.

In keeping with the spirit of the Bayh-Dole Act, the EAL requires notifiers to pay a small royalty to both the university and the biotechnology company. This has the added benefit of offering a revenue stream to all parties implementing the EAL. For low-income countries, we propose that the royalty be set at a rate within the lower part of the range recommended by the United Nations Development Programme of zero to six percent of sales [26]. For middle-income countries, we propose a slightly higher flat rate (e.g., five percent). The license will have to establish an equitable division of royalties between the university and the licensee.

The EAL also permits notifiers in any country to engage in research to improve an end product, for example, to adapt a technology to local circumstances. The final step of the EAL licenses any such improvements back to the university for the sole purpose of sublicensing them under the EAL's terms. In other words, any improvements made by a notifier would themselves be subject to the terms of the EAL, entitling them to royalties for the use of its improvements in LMI markets, but restricting them from preventing others from exploiting these improvements.

#### **4. Feasibility**

The unique appeal of the Equitable Access License is that it promotes true generic competition in LMI countries while requiring minimal oversight. Nevertheless, we anticipate that the feasibility of our proposal will raise a

number of doubts, three of which we attempt to address here.

#### *Diversion*

It may be argued that generic end products resulting from EAL pricing regimes could find their way into high-income countries, threatening pharmaceutical companies' sales there. However, our approach actually reduces the risk that generic medicines would be diverted to markets in high-income countries compared to a drug-donation or fair-pricing approach. Differentially priced products sold by the original, branded company may be susceptible to parallel trade, though regulatory barriers prevent these medicines from entering high-income markets easily. Generic versions of the same medicines must overcome a second barrier governed by patent law and enforced through customs procedures. Licensees may express disquiet about the possibility of generic products entering high-income markets illegally. However, there is no empirical evidence of any substantial flows of medicine from LMI countries to high-income countries [12]. Insofar as this is a concern, EAL signatories can address it as the WTO has – by requiring different packaging, pill color, and pill shape in different countries to facilitate identification of illegal imports [27].

#### *Diverse technologies*

With some technologies, such as biologics, materials (e.g., cell lines for producing monoclonal antibodies) may be essential to the production of an end product. These cannot be transferred in our simple open licensing approach. In principle, an EAL license could seek to bind a licensee to provide the necessary materials; however, such arrangements would require the university to provide credible threat of legal enforcement in case a licensee violated the agreement, sacrificing much of the EAL's ease of use. The EAL might instead require negotiations between all parties if transfer of materials is requested. If some enforcement mechanism becomes inevitable, one solution might be to create a standing inter-university body charged with monitoring equitable access licenses. Such a body might be modeled on a similar initiative in agriculture known as the Public Intellectual Property Resource for Agriculture (PIPRA), a multi-university collaboration for the management of intellectual property associated with agricultural development [28]. Additionally, governments are still deciding how to regulate bioequivalence and generic production of biologics. Since the EAL relies upon generic competition for efficient price reduction, its applicability remains dependent upon the regulatory framework surrounding the approval of generics.

#### *Effect on universities*

University administrators and directors of technology transfer may doubt the financial viability of the EAL. The

data not only suggests its viability, but that it could yield a net gain for universities. Licensing revenues typically account for only four percent of university research funds – and this figure decreases significantly when the costs of patenting, license management and the inventors' share of royalty income are subtracted [29]. Further, university revenue from developing country markets, even on a blockbuster drug, would be vanishingly small. Under the EAL, however, universities stand to gain a small but significant revenue stream from its share on royalties from end products that would otherwise not be sold in LMI countries.

The pharmaceutical industry's increasing dependence on external research, suggests that universities can promote access without abandoning their partnerships with pharmaceutical companies, reducing their income, or jeopardizing the viability of technology transfer operations [30]. This is particularly true if universities act collectively. While pharmaceutical companies will likely resist any changes to the status quo, if major research institutions act together, potential licensees will be more amenable to the EAL. While an individual university may be dispensable to the pharmaceutical industry, universities as a whole are not. Such collective action on the part of universities has a precedent in the PIPRA project, showing that when the need arises, universities can be quite willing to work cooperatively to ensure access to intellectual property.

### 5. Conclusion

It is worth summarizing how the EAL's provisions differ from potential alternative solutions. First, a contractual obligation that would require pharmaceuticals or biotechnologies to be sold at marginal cost means little if there is no mechanism that defines marginal cost, monitors prices, and enforces breaches in the contract. Neither universities nor pharmaceutical companies are likely to volunteer the infrastructure needed to enforce such an agreement. The EAL surmounts this problem through a self-implementing mechanism that requires little monitoring or administrative oversight.

Second, access provisions could specify an agreement not to enforce a university's patents in a pre-determined set of developing countries. Such access provisions would not require that the company with the license give up its rights in those countries; therefore, the company would still be able to use any of its own patents (e.g., on formulations, processes, dosages) or its rights to clinical trial data to exclude generics companies. The EAL sidesteps this difficulty by capturing any "improvements" in a licensed technology within the purview of its terms.

Finally, if access provisions were to be negotiated on a case by case basis, licensees would likely veto inclusion of

those provisions in cases where they might be most useful in improving access. This problem can only be solved by making certain access provisions uniform across numerous universities, and, except in extreme circumstances, non-negotiable.

Emory could have included EAL-like provisions in its original license with Gilead to ensure access beyond the company's Access Program. It missed a second chance in the royalty buyout negotiated with Gilead and Royalty Pharma earlier this year. While the administration celebrated the royalty transaction as an unparalleled boon for Emory, the truth is that the university signed a raw deal. Emory could have received the same \$525 million payment *and* ensured access to Emtriva and Truvada to millions of patients in developing countries. The reason for this is simple: those patients are not currently able to afford the drugs that they so desperately need and therefore factor into neither Gilead's revenue nor (by extension) Emory's royalties.

Universities will undoubtedly put their royalty payments to good use; most likely at least some of these funds will be reinvested in health sciences research. This should be applauded wholeheartedly. But for universities to truly consider themselves leaders in global health, and to be true to their mission, they should look also to how effectively their research agenda is translated to innovations useful to society.

### Competing interests

SC, DC, RR, and DS are members of the nonprofit organization Universities Allied for Essential Medicines, which was funded by the Ford Foundation during 2004–05.

### Authors' contributions

SC and YB originally conceived of the Equitable Access License with other collaborators. DC, RR, and DS were responsible for coordinating the preparation of this manuscript. All authors read and approved the final manuscript.

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# Improving Access to Medicines in Poor Countries: The Role of Universities

Dave A. Chokshi

According to the World Health Organization, about 10 million people—most of them in low- and middle-income countries—die needlessly every year because they do not have access to existing medicines and vaccines [1]. Countless others suffer from neglected tropical diseases, such as sleeping sickness, lymphatic filariasis, and blinding trachoma, for which there are still too few safe or effective medicines [2]. Drug companies have traditionally been reluctant to develop drugs for neglected diseases because the patients are too poor to pay for them, so there is no financial incentive for drug development.

Comprehensive solutions are thus needed to increase both access to existing medicines and research on neglected diseases. These solutions must involve strengthening health-care systems in poor countries, increasing financial flows for the most pressing public health crises, and better matching our research and development efforts to the needs of the poor. The challenges of making such wholesale changes are daunting [3]. Our organization, Universities Allied for Essential Medicines (UAEM) (Box 1), a coalition of students and faculty at about 25 universities across North America, focuses on the role of academic research institutions as a starting point for closing the access and research gaps. To be sure, much of the recent progress in global health research and awareness can be attributed to universities. Yet we must go further. As medical students, we have a unique ability to “turn the spotlight inward” by calling attention to our universities’ responsibilities when it comes to essential medicines.

## Why Universities?

University research is vital to the development of new medicines; total

biomedical research expenditures at universities were US\$19.6 billion in 2002 [4,5]. Meanwhile, the principles that guide universities—creating and disseminating knowledge for public benefit—are well aligned with the goal of improving access to medicines globally. In addition, many universities have offices responsible for transferring academic innovations (those arising from university research) to the commercial sector. Such transfer allows these innovations to

## University research is vital to the development of new medicines.

be further developed and marketed so that they can benefit the public; universities rarely have the resources to do such development and marketing themselves. University technology transfer offices aim to embody the same guiding principles as those of the university itself. For example, the Center for Technology Transfer at the University of Pennsylvania explicitly states that its chief objective is to “commercialize Penn research discoveries for the public good” (see <http://www.ctt.upenn.edu/>).

In most instances, the transfer of an innovation from a university to a for-profit company means that the university relinquishes control over the subsequent development and marketing of a medicine. This raises the possibility that the company will put the medicine out of reach of poor patients, either by charging prices that poor patients cannot afford or through legal maneuvers that otherwise restrict access in poor countries. However, two recent cases demonstrate that universities can influence access to such medicines.

First, in 2001, the humanitarian organization Médecins Sans Frontières sought the permission of Yale University to use a generic version of Zerit (stavudine), an antiretroviral

drug for HIV infection, to treat South African patients. Médecins Sans Frontières made this request because it had gathered evidence that generic stavudine could be purchased for a fraction of the cost of the expensive branded version available in South Africa; the cost savings would permit an expansion in the number of patients who could be treated for HIV. Yale University owned the patent for stavudine, but the university had granted an exclusive license that conferred intellectual property rights for the medicine to the drug company Bristol-Myers Squibb (New York, New York, United States of America). The request from Médecins Sans Frontières prompted global attention and intense discussions between the university and Bristol-Myers Squibb [6]. The result was the first patent concession on an HIV drug—that is, Bristol-Myers Squibb allowed generic stavudine to be bought and sold within South Africa—and a 30-fold reduction in the price of the patented drug in South Africa. The impact of this intervention from Médecins Sans Frontières, and from Yale’s negotiations with the drug

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**Abbreviations:** EAL, Equitable Access License; UAEM, Universities Allied for Essential Medicines

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The Student Forum is for medical students to give their perspective on any topic related to health or medicine

## Box 1. Universities Allied for Essential Medicines

### Who We Are

- UAEM is a coalition of students and faculty at about 25 research universities across North America.
- Our goal is to improve access to medicines in poor countries through university action.

### What We Do

- Our activities take place at both the chapter level and the international level.
- At the chapter level, we petition for changes in the policies and practices at the universities we attend. For example, at the University of California Berkeley, administrators announced a Socially Responsible Licensing Initiative (<http://ipira.berkeley.edu/docs/sociallyresponsible.pdf>) that arose in part through discussions with the Berkeley UAEM chapter.
- At the international level, we convene groups of students—in consultation with faculty members and other experts—to determine how best to

improve access to medicines in poor countries through research and policy analysis. For example, a consensus UAEM Policy Statement was released in October 2005 after a meeting at Georgetown University (Washington, D. C., United States of America) that brought together more than 75 students representing 28 universities (see <http://www.essentialmedicine.org/Oct2005PolicyStatement.pdf>).

### How You Can Get Involved

- Join UAEM through our Web site (<http://www.essentialmedicine.org>).
- Figure out what steps your university currently takes to ensure access to its innovations in poor countries by talking to faculty members, technology transfer officers, and administrators who set the university research agenda.
- Learn more about the access and research gaps through organizations such as Médecins Sans Frontières (<http://www.accessmed-msf.org>) and build awareness on your own campus.

company, was indisputable. Rapid expansion of HIV-treatment programs in sub-Saharan Africa would not have been possible without the widespread availability of generic stavudine, a treatment recommended by the World Health Organization as first-line therapy for HIV/AIDS [7].

A second example further demonstrates the leverage universities can have in improving access to medicines. Scientists at Emory University (Atlanta, Georgia, United States of America) had conducted research that contributed to the development of the antiretrovirals, Emtriva (emtricitabine) and Truvada (emtricitabine and tenofovir). These discoveries were transferred to industry through an intellectual property agreement that stipulated that the university would receive royalty payments for any drugs developed from the Emory research. Last year, in a deal with Gilead Sciences (Foster City, California, United States of America) and Royalty Pharma (New York City, New York, United States of America), Emory sold its rights to those royalties for a lump sum payment of US\$525 million [8].

The magnitude of the deal, which was the largest-ever transaction of its kind for an academic institution, caught the attention of student activists at Emory, who investigated Gilead's provisions for access to Emtriva and Truvada in poor countries and found them lacking [9]. Emory students are currently engaged in discussions with the university administration about Gilead's access practices, armed with a straightforward but cogent argument: Emory could have received the same royalty payment while advocating for greater access to Emtriva and Truvada for patients in poor countries. That is, expanding access does not require that universities sacrifice their bottom line. The reason for this is simple: the patients who aren't currently able to afford the drugs they so desperately need do not factor into either Gilead's revenue or (by extension) Emory's royalties.

### Closing the Access and Research Gaps: Policy Proposals for Universities

The case of Emory and the two medicines Emtriva and Truvada highlights the difficulty of crafting

retrospective solutions to problems that should have been foreseen. Ideas on how to prevent similar situations from arising in the future have been circulating in academic and policy circles over the past two years. For instance, in 2005 the American Academy of Arts and Sciences (Cambridge, Massachusetts, United States of America) published a report exploring how to license university discoveries to drug companies in a way that still ensures that the drugs can be accessed for humanitarian uses [10]. 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.” The Association of University Technology Managers (Northbrook, Illinois, United States of America) has convened a group known as Technology Managers for Global Health to look at how university research can be optimally exploited to advance global health outcomes (<http://www.tmgh.org>). Our own organization, UAEM, has drafted recommendations that we advocate for individual institutions through our university-based chapters [11].

UAEM proposes that universities make changes in both their principles and policies in order to improve access to medicines in poor countries. We recommend that universities adopt an official resolution that improving global human welfare is the most important goal of university technology transfer. To satisfy this principle, we put forward two specific policy proposals: (1) universities should adopt licensing provisions that facilitate access to their health-related innovations in poor countries, and (2) universities should promote research on neglected tropical diseases and find ways to work with nontraditional partners (such as developing-world research institutions and public-private partnerships) that seek to develop medicines for these diseases.

We advocate a set of humanitarian licensing provisions known as “equitable access licensing,” which is designed to do a number of things that traditional university licenses typically do not do. For example, under the Equitable Access License

(EAL), when certain conditions in the license are met (e.g., when a generic pharmaceutical company in a poor country notifies the university that a key medicine is overpriced there), patent barriers are lifted. Under the EAL, the intellectual property required to make that product is open to anyone that wants to use it to increase access in poor countries. And so a generic pharmaceutical company wanting to produce a medicine in a poor country won't get sued for doing so, as long as the conditions that trigger the license are met.

Beyond humanitarian licensing, we advocate the institution of policies to promote neglected-disease research. Specifically, we recommend that the universities facilitate participation in innovative research activities such as public-private partnerships (in which the public sector teams up with the commercial sector). We also recommend that universities promote projects that hold potential for neglected-disease drug development [12]. Such promotion includes removing any barriers that prevent university scientists from accepting research funding from public-private partnerships, proactively monitoring university innovations for potential neglected-disease applicability, and ensuring that university intellectual property does not serve as an impediment for scientists working on neglected diseases, either within universities or elsewhere. Full details of both the EAL and our neglected-disease policies have been laid out elsewhere [13].

### Addressing Counterarguments

The unique appeal of an EAL is that it promotes true generic competition in poor countries. We anticipate, however, that the feasibility of our proposal will raise a number of doubts, some of which we attempt to address here.

First, it is important to note that for any given product, a pharmaceutical company's bottom line would remain relatively intact. Equitable Access Licensing works by dividing the world pharmaceutical market between rich and poor countries. Consider, for example, any university innovation that has been developed into a drug. That drug can remain under patent protection in high-income countries, where the pharmaceutical industry



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### Logo of Universities Allied for Essential Medicines

(Image: UAEM)

earns the vast majority of its revenue. Generic competition is allowed only in markets where there is little access—and, therefore, little revenue—in the first place.

Licensees may express disquiet about cheaper generic products overcoming regulatory (customs) barriers and entering high-income markets illegally. However, there is no empirical evidence of any substantial flows of medicine from poorer countries to high-income countries [14]. Insofar as such diversion is a concern, EAL signatories can address it in the same manner that the World Trade Organization has—by requiring the use of different packaging, pill color, and pill shape in different countries to facilitate the identification of illegal imports [15].

Another concern universities may have is whether the EAL is financially viable for universities. This concern is not justified, because pharmaceutical companies would not lose a significant amount of revenue as a result of the EAL, and any decrease in licensing revenue at a given university would be vanishingly small. The fact that licensing revenues typically account for about 4% of university research funds underscores the point that universities would not suffer ill effects from implementing Equitable Access Licensing [16].

Finally, aside from any intangible benefits research institutions might derive from being leaders in responding to an important humanitarian issue, there are reasons to believe that pioneering universities

stand to gain financially by adopting our proposals. Combining access-oriented licensing policies with an augmented neglected-disease research agenda can help universities position themselves as research centers for foundation-sponsored partnerships. The burgeoning field of public-private partnerships for global health research has attracted over US\$1.2 billion in funding from sources such as the Gates Foundation, the vast majority of which is contracted out to research scientists [17]. The University of California Berkeley (Berkeley, California, United States of America) has recently begun marketing its “Socially Responsible Licensing Initiative” as a way to attract some of this nontraditional funding and has already signed a handful of deals with foundations and other nonprofits under that licensing rubric [18]. In our role as students, UAEM members have even loftier aspirations: to foment a collective movement that ensures that our universities' innovations reach those who need them the most. ■

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# EDITORIAL

## Global Health and University Patents

Universities have long been important in the development of life-saving medicines and technologies, and they once considered patenting to be antithetical to academic science and public health. Now a fierce debate rages about whether and when patents promote innovation, but in practice, the patenting worm has turned: Seeking revenues and ways to commercialize their inventions, U.S. universities are taking out patents in unprecedented numbers. In 2001, they were granted more than 3000 of them.

But patents bring more than revenues. They also bring controversy, when they ensure power over commodities that are the very currency of life itself. Today, universities hold important patents on many life-saving drugs, including the antiretroviral drugs stavudine (Yale University), abacavir (University of Minnesota), lamivudine (Emory University), and enfuvirtide (Duke University). As the AIDS pandemic has demonstrated, patents and exclusive licenses typically drive prices up and thereby impede access to life-saving medications. Low prices alone cannot solve the global crisis in access to medicines, but they are necessary, particularly for those in low- and middle-income (LMI) countries, where governments have limited resources and people often pay for part or all of their health care.

We have seen firsthand the effects of university patenting and licensing decisions. In February 2001, Doctors Without Borders sought Yale's permission to use a generic version of stavudine in South Africa. This prompted global attention and intense discussions between the university and Bristol-Myers Squibb (to whom it had exclusively licensed the drug). The result was the first patent concession on an AIDS drug and a 30-fold reduction in the price of the patented drug in South Africa. This action was taken without negative consequences to the university, financial or otherwise. Recently, a local company began selling generic stavudine in South Africa at up to 40% less than the reduced patented price.

A group of experts recently convened at Yale concluded that universities can improve and save lives by working collectively to adopt access-friendly intellectual property (IP) policies (see *Access to Essential Medicines and University Research: Building Best Practices* at <http://cira.med.yale.edu>). This will require developing specific licensing and patenting strategies that are applicable to LMI countries. Such strategies must be tailored to the technology and partner, but broadly speaking, they fall into two categories. First, universities could not patent their discoveries in LMI countries. This will promote generic competition as long as all the IP necessary to produce a generic version of a product stays in the public domain and no patent barriers exist in important source countries for generics (such as Brazil, India, and Thailand). Today, universities rarely patent in most developing countries because of the expense, but some will do so if a licensee requests it or if there is a market or potential generic competitor in the country. If universities already hold patents in LMI countries or want them for leverage (for example, over companies who might take out improvement patents), they can still promote competition by granting non-exclusive licenses to these patents. Second—and regardless of where they hold patents—universities should negotiate clauses in their licensing agreements that require the resulting products to be made available in LMI countries quickly, in sufficient quantities, and at an appropriate cost.

Such actions should not hurt universities' bottom line, diminish their ability to strike licensing deals, or discourage innovation for one simple reason: There is very little profit at stake. For 2002, Africa was projected to make up a mere 1.3% and Southeast Asia, China, and the Indian subcontinent only 6.7% of the world pharmaceutical market. These markets are too small to significantly influence revenues or, unfortunately, innovation. Universities can, however, seek creative ways to bridge the innovation gap; for example, by licensing compounds that may be useful against neglected diseases to new, nonprofit, drug development initiatives. A few have already done so.

Issues of access and IP will be with us for years to come. Some progress has been made in the past few years at the World Trade Organization and by governments, but this provides little comfort when so many people still lack essential medicines. Where lives and health are at stake, universities should not pass the buck. University research is intended to advance the common public good. It is time that it consistently do so globally, as well as locally.

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A makeshift clinic in Kampala, Uganda.