

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 medical care. Licenses are complex and each will be unique. Universities should therefore implement Global Access Policies that adhere to the following six principles:

Goals

1. Access to medicines and health-related technologies for all is the primary purpose of technology transfer of health-related innovations. This includes protecting access to the final end product needed by patients (e.g. formulated pills or vaccines).
2. Technology transfer should preserve future innovation by ensuring that intellectual property does not act as a barrier to further research.

Strategies

3. Generic competition is the most efficient method of facilitating affordable access to medicines in resource-limited 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 technology transfer programs should facilitate future innovation by patenting only when truly necessary to promote commercialization, utilizing non-exclusive licensing, creating streamlined processes for materials transfer, and reserving broad rights to use licensed technology in future research.

A global access licensing policy 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

Licenses for *all* drugs with actual or potential global health applications should contain global 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.¹ Over three times as many people die annually from cardiovascular diseases as from HIV/AIDS, tuberculosis, and malaria combined.² 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 is difficult to know at licensing time whether a product will have an essential medical use, even products that are originally licensed for lifestyle indications should have global 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, for example 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 decision to include or exclude particular countries in a license has grave human consequences. One key concern remains the treatment of lower-middle income countries like China, Brazil and India. More than a billion poor people live in those three countries. Although a small portion of these countries’ population may be technically able to afford to pay monopoly prices for medicines and vaccines, the vast majority cannot. Coverage is doubly important because these countries, particularly India, serve as the pharmacies for the rest of the world’s developing countries. China, India, and other countries in similar situations must be covered by universities’ global access licensing policies. Resource-limited countries should be defined to include those countries not ranked as high income on the World Bank's List of Economies (<http://go.worldbank.org/K2CKM78CC0>).

Generic provision is the best way to facilitate access.

Market competition generated by generic provision of drugs is recognized as the most effective means of driving down prices and increasing access.³ There are several reasons that generic provisions should

¹ *Preventing Chronic Disease: A Vital Investment*, World Health Organization (2005), http://www.who.int/chp/chronic_disease_report/en/.

² *The World Health Report 2003—Shaping the Future*, Geneva: WHO, 2003

³ *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>.

be required in all licenses:

1. Generic provision enlists competitive market forces to develop the most affordable, most efficient ways to get drugs to patients and providers. Generic companies sustainably supply large volumes of drugs as cheaply as possible. In contrast, pharmaceutical companies' drug donation programs do not provide an effective long-term solution—charitable providers have fewer incentives to drive down costs and are not sustainable options for meeting continuous demand.⁴
2. Generic provision eliminates the measurement and enforcement problems inherent in “at-cost” approaches.⁵
3. Approaches that foster generic access, such as open licensing, can also foster important innovations specific to the developing-world. For example, such approaches could allow generic companies to create pediatric and heat-stable formulations of new drugs.⁶

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 the global access license offers licensees revenues from reasonable royalties on the generics. Drugs with a global market generate only a tiny fraction of their revenue in resource-limited countries. The Pharmaceutical Research and Manufacturers of America (PhRMA) estimated that between 2002 and 2007, Africa accounted for only 0.4% of the global pharmaceutical market for PhRMA members, China accounted for only 0.4%, and India only 0.2%.⁷ Sales in the United States, European Union, and Japan accounted for 93.2% of all pharmaceutical revenues for PhRMA members during that same period.⁸

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.⁹ Differential appearance and packaging requirements can be used to ensure that products destined for developing world market are not illegally sold elsewhere.¹⁰

⁴ 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>.

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

⁶ *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>.

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

⁸ *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>.

⁹ *Ministerial Declaration*, World Trade Organization (Nov. 14, 2001), http://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_e.htm.

¹⁰ 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).

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,¹¹ and both Gilead and Johnson & Johnson announced at the 2008 World AIDS conference that they would be willing to put intellectual property into a new patent pool being created by UNITAID to allow further generic production of AIDS medications.¹² 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 that 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 modifications to, or new formulations of the original compound, such as those permitting increased solubility.
- *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,

¹¹ *Gilead Announces Licensing Agreements*, Gilead (Sep. 22, 2006), http://www.gilead.com/pr_908393.

¹² 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/>.

including non-assert clauses, sublicensing agreements, patent pools, data waivers, and grantback provisions.¹³

At-cost or other access provisions are sometimes necessary, but they should never 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.

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 biosimilar 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.

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.¹⁴ 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.

Intellectual property barriers to innovation should be minimized

While patents and other forms of intellectual property are commonly justified on the grounds that they promote innovation, such property rights can also have the unintended consequence of discouraging future innovation.¹⁵ Costly licensing fees, as well as “reach through” provisions that call for royalties on

¹³ 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>.

¹⁴ 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).

¹⁵ See generally, Anthony D. So, et. al, *Is Bayh-Dole Good for Developing Countries? Lessons from the US Experience*, *PLoS Biol* 6(10): e262.

products developed from upstream technologies, place taxes on downstream research that discourages commercialization and use of future technologies. Patenting also raises concerns about patent thickets, blockages that result when numerous patents on a product lead to bargaining breakdowns that can prevent downstream research and development from taking place. Exclusively held patents may also block useful follow-on innovation that can result in combination products that magnify the impact of a technology, or in products that are tailored to serve the needs of people in developing countries. Finally, the practices of patenting and licensing can have a negative impact on longstanding academic norms regarding the open, swift, and disinterested scientific exchange of knowledge.

To avoid these unnecessary barriers to innovation, universities should craft policies that allow for patenting only those inventions that would fail to be commercialized in absence of the patent incentive. For example, universities need not seek patents on research platforms, diagnostic tests, and other technologies that can be adapted for commercial use in a short period with little additional investment. Such patents hinder innovation while providing no social benefits beyond enrichment to the patent-holding institution. Where patents are acquired, such technologies should be licensed non-exclusively to encourage the broadest possible dissemination of university research. Universities should reserve rights to grant future researchers the right to work with products in order to make improvements and modify them for uses particular to developing countries. Finally, universities should work to foster the scientific exchange of knowledge by adopting streamlined processes for materials transfer and providing internal incentives for the exchange of knowledge among researchers.

Implementation requires effective governance: policies must be systematic, transparent, and utilize explicit access metrics

The dynamic nature of the technology transfer process means that no single set of mechanisms, policies, or commitments is likely to be sufficient to ensure the greatest possible access to university technologies in the long term. For this reason, universities must strive to continuously improve on existing licensing practices, evolving policies and practices in order to improve access to medicines for all people, regardless of income. Effective governance is essential to ensure the implementation of global access licensing policies and to help guide this evolution. Transparency and accountability are essential features to ensuring effective governance.

One way to ensure transparency and accountability is to make redacted licenses available through publication. Where such publication is not practicable, governance may be accomplished by committees that, like institutional review boards, have public stewardship and review responsibilities. Governance mechanisms should be accountable to the broader university community, for example by including faculty with expertise in medical research and global health, as well as students and administrators.

Each university should develop and implement metrics to account for their own access-oriented licensing strategies. These metrics should include operational or process measures of university licensing activities in order to support and further develop technology transfer strategies that prioritize access. Metrics should measure not only university implementation of access licensing strategies through concrete licensing terms and provisions, but also the frequency of implementation of such terms for all health-related invention disclosures. The indicators should be clear and publicly-available.