Facilitating Humanitarian Access to Pharmaceutical and Agricultural Innovation

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ABSTRACT

Because certain patenting and licensing strategies can inhibit the development and dissemination of products for developing countries, intellectual property management strategies need to be developed that can help remove some of these obstacles. It is equally important to apply creative patent management strategies that actively promote access to needed products in developing countries. Care must be taken, however, to ensure that patents on research inputs do not discourage or unreasonably increase the cost for product development that targets needs in small or unprofitable markets. The American Association for the Advancement of Science project on Science and Intellectual Property in the Public Interest convened a working group to explore these issues in 2004. This chapter draws upon the expertise of that group to identify licensing strategies that are effective in promoting humanitarian access to health and agricultural product innovations and expanding their use among poor and disadvantaged groups, particularly in low-income countries. The chapter encourages more public sector IP managers to understand and employ strategies that will achieve these goals and seeks to help private sector licensees to understand the rationale behind and potential benefits of such strategies. Indeed, humanitarian licensing strategies should more and more become the norm by contributing to the development and dissemination of essential medicines and agricultural technologies for developing countries.

1. INTRODUCTION

1.1 *Patents and neglected markets*

Intellectual property (IP) rights play an increasingly important role in the development, manufacture, and distribution of products in agriculture and health. During the past 25 years, there has been an unprecedented increase in the scope, level, role, and geographic and subject-matter coverage of IP protection.[1] Strong patent protection is intended to contribute to increased research investments and a favorable climate for technology transfer. But it may not always produce these effects. In fact, IP licensing practices may inhibit access to IP-protected knowledge, research tools, and products.

The unmet medical and agricultural needs of developing countries are vast. Reflecting the technological and financial disparity between developed and developing countries, low- and middle-income countries account for less than 10% of worldwide research and development expenditures.[2] And despite increasing levels of investment in pharmaceutical R&D during the past 30 years, only 1% of new compounds marketed have been for developing-world diseases.[3] Recent research has identified some increase in innovative activity related to diseases specific to poor countries, though this activity "remains extremely low relative to pharmaceutical research overall,"[4] and has resulted, in large part, from increased public R&D funding for global health.[4, 5] Similarly, private sector agricultural research is more likely to focus on specialty crops of interest to developed countries than on staple crops that are important to resource-poor farmers in developing countries.[6]

Brewster AL, SA Hansen and AR Chapman. 2007. Facilitating Humanitarian Access to Pharmaceutical and Agricultural Innovation. In *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices* (eds. A Krattiger, RT Mahoney, L Nelsen, et al.). MIHR: Oxford, U.K., and PIPRA: Davis, U.S.A. Available online at www.ipHandbook.org.

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1.2 *Background and related initiatives*

Our discussion of strategies builds on the initiatives, experience, and proposals of other organizations for the management of IP. The United Nations Millennium Project Task Force on Science, Technology, and Innovation recommended expanding mechanisms for inventors to make their ideas available royalty free for uses that meet the needs of poor countries, noting in its final report that "only a handful of mechanisms are designed to promote such activities."[7] However, beginning in the 1980s, and expanding through the 1990s and the early years of the 21st century, an increasing number of organizations have been using IP management practices to promote the health and food security of underserved populations. These include the Program for Appropriate Technologies in Health (PATH) and the Population Council, as well as various other public and public/private partnerships, such as the International AIDS Vaccine Initiative, the Global Alliance for TB Drug Development, the Global Vaccine Initiative, the Diseases of the Most Impoverished Program of the International Vaccine Institute, and the Centre for the Management of Intellectual Property in Health Research and Development (MIHR). International entities (for example, the World Health Organization [WHO]) have undertaken humanitarian licensing, as have national entities such as the U.S. National Institutes of Health (NIH), which now includes humanitarian clauses in its licensing agreements as appropriate. Several governmental organizations in developing countries, such as the Council for Scientific and Industrial Research of India, are beginning to undertake humanitarian licensing. Agricultural organizations with relevant experience include the African Agricultural Technology Foundation[8] (AATF), the International Service for the Acquisition of Agri-biotech Applications (ISAAA), and the institutes of the Consultative Group on International Agricultural Research (CGIAR).

One of the most noted examples of humanitarian IP management involves vitamin-A-enriched Golden Rice. Although developed mainly with public sector funding and research, around 45 patents associated with Golden Rice are owned by approximately 30 companies and public institutions in the United States, and only a few patents are held in developing countries.[9] The inventors of Golden Rice licensed their inventions related to golden gice to Greenovation, a biotech spinout company from the University of Freiburg, which is owned by the inventors themselves. Greenovation then exclusively licensed its Golden-Rice-related patents to AstraZeneca, PLC (now Syngenta). Subsequently, Syngenta entered into a license agreement with the inventors that allowed them, and Syngenta, to license Golden Rice technologies to developing countries. Other companies holding Golden-Rice-related patents also agreed to the same arrangement. That arrangement allows both Syngenta and the inventors to grant licenses—with the right to sublicense—to any bona fide research organization for the development of Golden Rice. The rice can be used royalty free and allows farmers to earn as much as US$10,000 per year from its sale. Higher sales would require farmers to acquire a commercial license from Syngenta.[10] The example of Golden Rice illustrates that it is possible to make IP available for research and commercialization in developing countries.

Yale University offers another example of humanitarian IP management. It holds a key patent on stavudine (d4T), a widely used HIV/AIDS antiretroviral drug. Yale renegotiated its exclusive license with Bristol-Myers Squibb Co. to incorporate renegotiated humanitarian terms, allowing the drug to be subsequently licensed for generic production in South Africa. The university also negotiated a price cut, immediately reducing the price of d4T in Africa to 1/30th of the price in the United States. When the generic product came on the market, it further reduced the price by as much as 40%.

Other examples of humanitarian IP management include Cornell University's transfer of ring-spot-virus-resistant papaya to Thailand, as well as several projects brokered by the International Service for the Acquisition of Agri-biotech Applications (ISAAA). The latter include local varieties of potato transferred from Monsanto Co. to Mexico, as well as ring-spot-virus-resistant

and delayed-ripening papayas transferred from Monsanto and Syngenta, respectively, to Southeast Asia.[11] Finally, a recent agreement between Gilead Sciences and the South African drugmaker Aspen Pharmacare is another example of humanitarian IP management for health products. Gilead will allow Aspen to produce generic versions of the HIV/AIDS antiretrovirals Truvada® and Viread®, and university inventors who own foundational patents for both drugs have agreed to waive royalties in the developing countries served by Aspen.[12]

1.3 *Intended audience*

This paper is written primarily for licensors, particularly university-based technology transfer managers and public sector intellectual property managers and, secondarily, for the staff of intellectual property departments in corporations with which these entities may enter into agreements or who may themselves decide to adopt some of the following strategies. Foundations or agencies that fund research and that may wish to encourage or require their grantees to engage in humanitarian IP management are another important audience.

1.3.1 *Public sector*

Universities and public sector institutions play key roles in the development of medicines and agricultural products. Their roles are generally early in the process, and because university-based research is most often upstream, final products based on their research often involve significant development by others. The manner in which public sector researchers make their "upstream" technologies and research tools available can influence whether populations in developing countries have access to the end products of this research.[13]

In recent years a number of nonprofit public/private partnerships (PPPs) have formed with the mission of developing health and agricultural products for markets that are neglected by traditional for-profit R&D companies. These PPPs are typically funded by foundations or public sources and may receive in-kind support, or in some cases direct funding, from private companies.

Like typical drug companies, health-focused PPPs often develop a portfolio of candidate products, hoping that a few will be safe and effective enough to treat their focal condition. Examples of PPPs that develop pharmaceuticals are listed in Box 1.

If a university has already licensed IP to a company, renegotiating to provide access for a PPP can be costly and difficult—even if the PPP seeks to develop the invention into a noncompeting product. However, the university can take steps at the beginning of the technology transfer process to facilitate the use of its invention for developing products that serve the poor. If a technology does not interest commercial licensees, university IP managers can seek PPPs or other nontraditional license partners to develop it for neglected markets. To be able to take advantage of these opportunities, it is very important for universities to establish policies and guidelines to manage university-generated IP for humanitarian use and applications.

Why should universities and public sector institutions take advantage of these opportunities to promote humanitarian use? Most universities and public sector research institutions seek to contribute to the wellbeing of humankind through their patenting and licensing activities. For example, each of the top four university recipients of U.S patents in 2004[16] states public benefit as an explicit goal in its patent policy:

- University of California (424 patents). "*It is the intent of the President of the University of California, in administering intellectual property rights for the public benefit, to encourage and assist members of the faculty, staff, and others associated with the University in the use of the patent system with respect to their discoveries and inventions in a manner that is equitable to all parties involved.*"[17]
- California Institute of Technology (135 patents). "*It is the policy of the Institute that such patents be used for the public benefit. If there are innovations or discoveries that result in the filing of patent applications and the acquisition of patents, the Institute intends to serve the public interest by prudent and ap-*

Box 1: PPPs That Develop Pharmaceuticals

Aeras (Aeras Global TB Vaccine Foundation)
www.aeras.org

Children's Vaccine Programme at PATH
www.childrensvaccine.org

CONRAD
www.conrad.org

DNDi (Drugs for Neglected Diseases Initiative)
www.dndi.org

FIND (Foundation for Innovative New Diagnostics)
www.finddiagnostics.org

Gates Foundation/University of North Carolina Partnership for the Development of New Drugs
www.ippph.org/index.cfm?page=/ippph/partnerships/name&thechoice=show&id=85&typobj=0

Global Microbicide Project
www.gmp.org

Global Vaccines Inc.
www.globalvaccines.org

Human Hookworm Vaccine Initiative at Sabin Vaccine Institute
www.sabin.org/hookworm_slides.htm

IAVI: International AIDS Vaccine Initiative
www.iavi.org

Infectious Disease Research Institute
www.idri.org

iOWH (Institute for OneWorld Health)
www.oneworldhealth.org

IPM (International Partnership for Microbicides)
www.ipm-microbicides.org

MMV (Medicines for Malaria Venture)
www.mmv.org

MVI (Malaria Vaccine Initiative)
www.malariavaccine.org

PATH (Program for Appropriate Technology in Health)
www.path.org

PDVI (Pediatric Dengue Vaccine Initiative)
www.pdvi.org

PneumoADIP (Pneumococcal Vaccines Accelerated Development and Introduction Plan)
www.pneumoADIP.org

TB Alliance (Global Alliance for TB Drug Development)
www.tballiance.org

Source: Compiled from Gardner and Garner[14] and Merz.[15]

propriate efforts to transfer the technology to those who will facilitate public use."[18]

- Massachusetts Institute of Technology (132 patents): "*It has long been acknowledged that the primary functions of a university are education, research, and public service. It is in the context of public service that M.I.T. supports efforts directed toward bringing the fruits of M.I.T. research to public use and benefit.*"[19]
- University of Texas (101 patents): "*It is the objective of this policy to encourage the development of inventions and other intellectual creations for the best interest of the public, the creator, and the research sponsor, if any, and to permit the timely protection and disclosure of such intellectual property by development, commercialization after securing available protection for the creation, by publication, or both.*"[20]

Public funding agencies also seek to promote public benefit. The mission of NIH, for example, is to support biomedical research to extend healthy life by reducing illness worldwide. NIH therefore seeks to understand and overcome the obstacles hindering the public availability of inventions made by NIH scientists. To this end, NIH engages in a variety of forms of humanitarian licensing and humanitarian-use agreements.[21] Many other public sector actors and universities are also interested in "doing the right thing" in terms of promoting access, but they often do not know how to proceed.[22]

We anticipate that at least some types of humanitarian IP strategies will have little or no impact on licensing revenues for the technology creators. Whether that will be the case may depend on whether humanitarian licensing becomes commonly practiced and accepted. It may be important for a university or research institute's administration to commit to humanitarian

Box 2: Developing a Low-Cost Malaria Treatment

Strategy employed: *Agreeing on IP management conditions in advance*

A research group sponsored by the Medicines for Malaria Venture (MMV) has developed a promising, low-cost malaria treatment known as OZ277 /RBx11160. MMV supported collaboration between scientists at the University of Nebraska, Swiss Tropical Research Institute, Monash University, and the F. Hoffman-La Roche, Ltd. to develop OZ. The drug incorporates some chemical features of the plant-derived antimalarial artemesin, but can be produced through synthetic chemical processes, making it significantly cheaper. Patents covering OZ have been assigned to MMV, and MMV has engaged the Indian drug manufacturer Ranbaxy to further develop it. Upon regulatory approval, Ranbaxy Laboratories, Ltd. will distribute OZ at low cost in malaria endemic countries. MMV facilitated arrangements for patent, royalty, and pricing structures to benefit those in need by establishing an IP management plan with its collaborators in advance. Below are excerpts from the Statement of MMV Collaborative Principles:

> *MMV's central objective is to ensure the sustainable and continuous generation of appropriate new malaria medicines that are accessible to all of those in need in developing countries at the lowest prices practicable.*
>
> *MMV requires intellectual property rights on a royalty-free basis to the relevant intellectual property, in the field of malaria, and developed through the collaboration.*
>
> *MMV will seek the right to the relevant background intellectual property necessary to achieve the objectives identified herein.*
>
> *MMV would not normally have a desire to retain any interest in relevant intellectual property rights for use outside the field of malaria or to constrain such use by its collaborators.*

Source: MMV and JC CraftMedicines for Malaria Ventures. Statement of MMV Collaboration Principles. Personal communication, J. Carl Craft, Chief Scientific Officer, MMV.[23]

IP management as an extension of the institution's public mission (Box 2). This might enable technology licensing officers to risk sacrificing small amounts of licensing revenue when there is an opportunity to enhance product development initiatives for the poor. In addition, institutional administrations can foster approaches among technology licensing officers that would enhance such product development initiatives when financial promise is low.

1.3.2 *Private Sector*

Why address intellectual property managers in the commercial sector? Most technologies developed by universities and public sector institutions are at early stages of development and require private companies to invest more in research and development to create practical applications. Universities generally license these early-stage technologies to the private sector. The success of humanitarian licensing therefore depends on the willingness of private sector actors to accept certain conditions and requirements that would increase access later in the product development and marketing stages.

We think there are two reasons that commercial licensees may support humanitarian licensing. First, commercial entities usually expect major financial returns in developed world markets, but developing country markets are often considered unprofitable. Hence, many types of humanitarian licensing may not harm the financial interest of the commercial licensee. Moreover, a corporation may advance its reputation for social responsibility and win greater esteem from the public by accepting humanitarian licensing.

Multinational companies have already shown a willingness to segment their markets and offer concessionary terms to facilitate access to their products in poor countries. A number of examples have been highlighted already, including AstraZeneca, Bristol-Myers, Gilead, Monsanto, and Syngenta. Activities by Chiron Corp., GlaxoSmithKline, Pioneer International, Inc. (affiliate of E. I. du Pont de Nemours and Company), and Roche are mentioned later.

2. HUMANITARIAN LICENSING STRATEGIES

In this section we discuss some successful strategies and some new proposals for managing IP to facilitate humanitarian use and applications. These include case studies in which IP owners have used nontraditional IP management techniques to promote the development of products for neglected markets. In this section, we describe general approaches to licensing and some specific license features that a patent owner can use when transferring technology to a commercial entity.

2.1 *Identifying the intended beneficiaries*

Rights reserved or obligations set out to facilitate access in developing countries will need to specify the intended beneficiaries. In the end, all humanitarian licensing efforts should strive to benefit underserved people in developing countries by providing greater access to needed technologies. However, defining this population or identifying the institutions that could serve this population with the licensed technology may require different approaches, depending on the particular technology and requirements of the primary licensee. Below are some options for defining the beneficiaries of humanitarian license terms.

A developing country can be defined in a number of ways, for example, by reference to the United Nations list of least developed countries, by locale, or by reference to lists provided by the Organisation for Economic Co-operation and Development (OECD) countries, the World Bank, or the Food and Agriculture Organization (FAO). Beneficiary countries may also be mutually agreed to by the contracting parties, who may also need to decide whether the agreement will cover middle-income as well as low-income countries.

In addition to or in place of defining a list of countries covered by the reservations and/or exemptions in a humanitarian license, negotiators may wish to further define the population in those countries that would be covered. The intended population might be "the poor," "those in need," subsistence farmers, populations in geographically underserved regions, or a particular market segment.

A market segmentation, or dual market, approach is often used to target intended beneficiaries and is involved in many of the strategies discussed in this paper. With this approach, an exclusive license might give a private sector entity the sole right to use a technology in profitable markets, while allowing others to use the technology at no cost or reduced royalties to serve market segments that do not interest the private sector.

In the licensing arrangements for Golden Rice, a humanitarian-use clause was used to segment access to an agricultural technology, committing the owners of key proprietary components to donating their technology to the poor. Negotiations over how exactly to define and make operational such "donations" are ongoing. These negotiations focus on defining the humanitarian-use market and ultimately on the precise wording of the humanitarian-use clause. This humanitarian-use clause will determine who qualifies as a beneficiary of royalty-free access to Golden Rice and exactly how they would benefit.[24]

Although market segmentation strategies have been employed successfully,[25] certain challenges remain, namely the containment of the IP within the targeted markets. In addition to the humanitarian transfer of products to the intended populations, many developing countries may also have emerging private markets for the same goods. Markets that would not be attractive to large companies may nevertheless present niche opportunities for smaller companies. Market segmentation might be most successful where noncommercial markets can be sharply delineated by region, which makes it easier to exclude spillovers to nontargeted markets.[26] In addition, market segmentation often requires intense negotiation, the development of trust between partners, and the capacity to enforce agreements.

2.2 *Nonexclusive licensing*

In nonexclusive licensing, in addition to the primary license agreement, the licensor retains the freedom to license the technology to other parties. Some institutions (for example, NIH) seek to use nonexclusive licensing or to license to multiple companies whenever possible. If a university can accomplish technology transfer to a company using nonexclusive licensing, it is free to subsequently license the technology for humanitarian applications. Sometimes a commercial licensee insists upon an exclusive license, in which case public sector licensors may limit the exclusive license to developed-country markets (as discussed later) or for specific product applications.

2.3 *Transferring technology to public-private partnerships (PPPs)*

When it is clear that a technology could benefit neglected markets (for example, a low-cost HIV diagnostic or an agricultural trait important for subsistence agriculture), university technology managers may be able to transfer the technology to a nonprofit corporation for product development either on an exclusive or nonexclusive basis. The business models of PPPs vary. Some conduct in-house product development; others manage collaborative development by public and private sector labs (Box 3). The transfer of technology could take forms ranging from direct licensing or donation of a patented invention to contributions of know-how or scientific expertise.

Another possible model is an arrangement in which a commercial licensee focused on markets in affluent countries makes the technology available to a PPP on concessionary terms for marketing or development for poor countries. In order to minimize transaction costs for the PPP, it is highly preferable for the university to engage with the nonprofit developer before completing negotiations with the commercial licensee.

University technology managers can also facilitate nonprofit product-development efforts by offering PPPs ownership of patents that the university no longer wishes to maintain. Even when a technology does not appear to have a clear application for developing regions, it may prove useful for some aspect of the PPP's work to develop products for these regions.

2.4 *Transferring technology to companies in developing countries*

Technology managers may seek commercial partners in low- or middle-income countries to develop technologies that address conditions specific to

those regions. These companies are likely to have greater interest in developing products that meet the needs of these countries than commercial entities in wealthier countries. They may also be able to develop, produce, and distribute products at much lower cost than typical partners in the United States or other industrialized countries.

2.5 *Out-licensing*

Out-licensing is primarily executed by drug companies that are already producing name-brand versions of a patented drug, but universities could negotiate with corporate licensees to ensure that out-licensing to generic companies takes place. Under the out-licensing approach, drug patent holders award nonexclusive licenses to generics manufacturers, allowing them to produce cheap copies of drugs for sale exclusively in designated poor countries. The generic makers are prohibited from selling products in the patent holder's developed country markets, and they may be required to modify their packaging so as to discourage reimportation by making the generic versions easier for customs officials to identify. Generic producers pay a royalty to the patent holder, and are encouraged to compete on price. An advantage of this semicooperative approach is that generic makers in developing countries can get more information from the patent holder than just the patented technology itself, such as manufacturing expertise and regulatory data. In the rare case that a university holds IP that needs little additional development, it could essentially make the out-licensing arrangement itself by licensing the patent to a name-brand pharmaceutical company (as opposed to a company specializing in the production and marketing of generics) for wealthy markets and to generic manufacturers for production in developing countries. It may be more difficult, though not impossible, to encourage the sharing of manufacturing expertise and regulatory information.

2.6 *Conditions in funding agreements*

Foundations, government agencies, and other organizations can require that funded work be licensed under humanitarian terms by inserting conditions into funding agreements. Establishing humanitarian IP management conditions in advance can simplify later negotiations, help researchers and IP managers plan ahead, and increase the prospects of success (Box 4). The Rockefeller Foundation has crafted language to include in research agreements for this purpose, offering a model for ways that funders can increase humanitarian access to the research supported by their grants. The Rockefeller Foundation requires grantees, whether or not they claim or obtain

Box 3: CDA Malaria Treatment

Strategy employed:
PPP-sponsored product development and preferential pricing requirement

The WHO Tropical Disease Research program, the Medicines for Malaria Venture (MMV), and GlaxoSmithKline have formed a partnership to build upon the two-drug antimalarial LapDap™ by adding artesunate to the combination. The new therapy will be called CDA, for its ingredients chloroproguanil, dapsone, and artesunate. The original LapDap was conceived by scientists from the Wellcome Trust Laboratory in Nairobi and the University of Liverpool, then brought to market by a public/private partnership involving MMV, British universities, the Wellcome Trust, GlaxoSmithKline, and the U.K. Department for International Development. It was approved by the U.K. Medicines and Healthcare Products Regulatory Agency in 2003. Under the agreement for developing the new triple-drug combination, it will be made available at preferential prices to the public sector in malaria endemic countries.

Source: TDR News.[27]

patents or other proprietary rights in their discoveries, "*to license or otherwise make available the Discoveries to third parties in the commercial and public sectors (to the extent permitted under the MTAs) for the purpose of furthering the creation, reproduction, modification, and/or sale of the improved end product.*"

2.7 *Humanitarian conditionality in licensing agreements*

Licensing conditions may require the licensee to do specific good things to benefit disadvantaged populations. These conditions are sometimes referred to as white knight clauses. These may include marketing a product in developing nations at a reduced royalty or price, donating materials for clinical trials, or cooperating with a humanitarian licensee in a specified way (for example, by providing clinical or field trial results). A licensor could also insert language requiring the licensee to make products developed from improvements to the technology available in low- and middle-income countries at a reduced cost.

NIH often uses these clauses in its agreements to ensure that the licensee undertakes specific actions to benefit the public sector (for example, mandating the supply-back of licensed products or services, health education programs, indigent access programs, reduced royalties for developing countries, biodiversity compliance for natural products, and other means of ensuring developing country access for licensed products). NIH also requires licensees to create a worldwide development and marketing plan to facilitate developing country access to licensed products, the implementation of which it monitors through agreed-upon benchmarks.[29]

2.8 *Performance milestones*

A *milestone* is a performance requirement on the part of the licensee. Milestones are often used in public/private partnerships and sponsored research agreements to measure a project's progress and success. An example of a humanitarian licensing milestone might be a requirement that on or before the date of the first phase of a clinical trial for a new drug, the licensee will have identified a generic manufacturer in a middle-income country to produce the licensed technology at a reasonable price for developing countries. Subsequently, if this milestone is not met, other provisions and reservations in the agreement would be activated, for example, loss of exclusivity, sublicensing, exercise of march-in rights, and even termination of the agreement.

2.9 *Ensuring accessibility through pricing*

To help ensure access to products, the licensor may require that any product developed and brought to the market be distributed at a reasonable price. Despite the inherent difficulties in defining what is reasonable, price is a readily measurable condition that is easier to monitor than more broadly defined requirements concerning access.[30] This model could be expanded, whereby licenses to companies include an appro-

Box 4: Developing a Portable HIV Diagnostic

Strategy employed: *Condition in funding agreement*

When technology transfer officers at Massachusetts General Hospital and the University of Texas were licensing a prototype HIV diagnostic device to a start-up company, the requirements of the foundation funders allowed the foundations to grant additional licenses to entities capable of meeting charitable objectives in LDCs. Since it is a portable device, the technology could provide an inexpensive, practical means of diagnosing HIV in resource-poor settings.

Source: Foskett, Menapace and Basu.[28]

priate balance of incentives to the licensee and market access for the poor. Licensees might be required to meet certain milestones, such as government procurement targets in defined countries, and at prices that are deemed appropriate for that market. Here, an appropriate price may be defined as the cost of production plus a small profit, usually in the 5%–10% range prior to being allowed to commercialize the product in more lucrative markets.[31] To ensure that an appropriate price is reached and maintained, the licensor may include contractual language that mandates the submission of manufacturing cost reports and product cost calculation details on a regular basis.[32]

2.10 ***Reserving rights in license agreements***

It is important to think through how the humanitarian-purpose licensee will actually use the technology and to reserve an appropriate set of rights and exemptions. For example, the negotiators will certainly want to consider the scope of research rights and, depending on the particular technology and application, the scope of international trade rights. The humanitarian licensee might need the right to carry out research or manufacture within the commercial licensee's territory, so long as the research is done only for developing nation needs or the manufacture for export to developing nations. The commercial licensee may then wish to be protected against re-export into its primary commercial market. As noted earlier, the humanitarian licensee may also need rights for commercial use in low- and middle-income regions. Although the reservation may be defined as humanitarian use, licensors may wish to consider additional, more specific reservations as described below.

2.11 ***Research exemption***

One of the several goals of humanitarian IP management is to encourage research to develop products appropriate to the needs of the developing world. To this end, licensors could opt to insert into licensing agreements a research exemption clause that exempts specified categories and types of research from patent infringement in using its proprietary technologies, (for example, to develop products that broadly benefit the public or the population of poor countries). The University of California technology transfer office has begun to insert such research exemption clauses into licensing agreements.[33] Other universities already reserve research rights for academic institutions in their standard exclusive licensing agreements (for example, Stanford, whose standard license language is reproduced in Box 5). Such a clause could facilitate humanitarian use of the technology if it also reserved rights for nonprofit research institutions developing products for use in developing countries.

2.12 ***Sublicenses for developing countries***

Unless provided for in the agreement, a licensee generally does not have sublicensing rights.

Box 5: Stanford Reservation of Academic Research Rights in Standard License Agreement

Strategy employed: ***Reservation of research rights***

3.4 Retained Rights. Stanford retains the right, on behalf of itself and all other nonprofit academic research institutions, to practice the Licensed Patent and use Technology for any purpose, including sponsored research and collaborations. Licensee agrees that, notwithstanding any other provision of this Agreement, it has no right to enforce the Licensed Patent against any such institution. Stanford and any such other institution have the right to publish any information included in the Technology or a Licensed Patent.

Source: Stanford Office of Technology Licensing.[34]

Should the parties agree to allow sublicensing, the main agreement should specify the rights and obligations of the licensee with respect to the sublicensee(s). In allowing for sublicenses, consideration should be given to the possibility of the original licensee entering into sublicenses inconsistent with the humanitarian goals of the agreement. This should be restricted. It is general practice for the licensor to hold the licensee responsible for assuring that the sublicensee fulfills all the requirements of the principal license. The best way to ensure that the sublicensee has obligations comparable to the licensee's is for the licensor to draft the sublicense terms. The licensor can thus be certain that all the humanitarian requirements within the primary agreement are included.

2.13 *March-in rights*

A licensor may wish to reserve march-in rights if the humanitarian purposes or milestones embodied in the agreement are not met (for example, revoking a license or sublicensing to third parties in order to ensure access).

2.14 *Treatment of future rights in license agreements*

2.14.1 *Reach-through clauses*

Reach-through clauses attempt to reach beyond the licensed technology and to ensure that the licensee treats new technologies, developed through use of the licensed technology or under a cooperative agreement, honoring the same kinds of development obligations covered by the original license. This type of clause is often used by public–private partnerships to encourage the development of specific technologies that benefit developing nations while allowing the private sector partner to benefit in the developed world.

Licensors can also help make inventions more available to populations in need by insisting on certain terms when licensing inventions to commercial partners. Opportunities to transfer technologies to be developed by public–private partnerships or by other organizations can also be pursued.

2.14.2 *Grant-back clauses*

If it is likely that the commercial licensee will develop improvements to the technology, it would be wise to require that the licensee grant back nonexclusive rights to those improvements. This would ensure that they would be available later for a humanitarian purpose licensee. The same might go for access to test results or regulatory data. If either party is concerned about liability issues, there might be, for example, requirements for any humanitarian licensee to be adequately insured or to be operating in compliance with relevant regulations.

2.14.3 *Amending existing agreements*

While the goal of this document is to promote humanitarian licensing from the outset, when agreements already exist they can be amended or revised to meet humanitarian needs. There are several examples of successful renegotiations. For example, the humanitarian license mentioned earlier between Yale University and Bristol-Myers Squibb was actually the result of a renegotiation of their license for the AIDS drug d4T, which permitted generic d4T to be made and used in South Africa. There are also examples from the agricultural sector in which parties successfully addressed barriers posed by a worldwide exclusive license between a university and a company. In one case, a company insisted that no license was required to use the licensed technology in a certain country. It stated this in a letter that permitted the university to transfer a gene construct directly to the country. In general, renegotiating license terms is not desirable because it increases transaction costs, delays projects, and may not always succeed. However, while there are clear benefits to addressing these issues up front wherever possible, the fact that an agreement has already been concluded should not discourage participants from revisiting the agreement when an unforeseen need arises.

3. PROPOSALS FOR NEW APPROACHES FOR HUMANITARIAN LICENSING OF IP

Two new proposals conclude our discussion of specific strategies for humanitarian licensing: (1)

considering a shorter length for an exclusive license and (2) equitable access licensing.

3.1 *Shorter lengths of license exclusivity*

Instead of granting exclusive licenses that match the term of the patent, the licensor can grant licenses for shorter periods, allowing access by multiple licensors over the life of the patent. There may be practical complications to this approach, since universities often receive patent-cost reimbursements from licensees, which in turn require exclusivity until expiration of the patent term. Granting short-term exclusive licenses would likely require the university to bear all the costs related to maintaining and enforcing the patent, which it could only afford to do if the patent itself was bringing in significant licensing revenues. In that case, the university may be reluctant to end its licensing relationship with the high-revenue licensor.[35]

3.2 *Equitable access licensing*

Universities can also make use of an equitable access license to create enabling conditions for competition in low- and middle-income countries. An equitable access license (1) ensures freedom to operate for any party that manufactures and distributes the licensed technology and any derivative products in low- and middle-income countries and (2) minimizes administrative overhead and political contingency by initiating a self-enforcing open licensing regime. In such a license, a university and licensee agree that any licensed technology, as well as licensee improvements (including improvement patents and registration data), to be sold in low- or middle-income countries will be openly licensed to any company that meets Good Manufacturing Practice standards.[36] This arrangement allows multiple producers (including producers in high-income countries) to compete to produce low-price products for sale only in low- and middle-income countries simply after notifying the parties to the license.

The Equitable Access License developed by Universities Allied for Essential Medicines (UAEM) includes a humanitarian research clause to encourage research on neglected diseases. It provides that any party may pursue research anywhere in the world using the university technology and licensee improvements without paying a royalty, if the research targets a neglected disease.[37]

4. NEXT STEPS FOR AAAS HUMANITARIAN IP MANAGEMENT INITIATIVE

This document emphasizes the importance of managing public sector IP to facilitate humanitarian use and applications. It seeks to raise awareness about some of the techniques that have been pursued so far, and we are optimistic that additional approaches will emerge as more institutions undertake IP management with humanitarian use and applications in mind. We certainly do not mean to preclude other options.

Even if technology managers adopt humanitarian IP management strategies in the construction, negotiation, and formalization of legal agreements, they will also need to connect with development partners who can utilize the protected technologies to serve unmet needs in developing countries. In some cases, these partners may not yet exist. But when they do, it will be important to establish simple, efficient ways for them to identify technologies that public sector institutions are willing to share.

We believe that the number and variety of technologies being managed with humanitarian goals in mind will continue to increase, and so the Science and Intellectual Property in the Public Interest (SIPPI) project plans to explore ways to increase the transparency of license terms covering these technologies, thus making this information more widely available to potential beneficiaries.

In continuing its work on humanitarian licensing, the SIPPI project will identify ways to encourage the use of humanitarian licensing practices and increase the transparency of license terms covering technologies in health and agricultural innovation, thus making that information more widely available to potential beneficiaries. It is pursuing the following interrelated activities as a means to advance the use of humanitarian licensing strategies.

Promoting the use of humanitarian licensing practices. In collaboration with the Centre for the Management of Intellectual Property in Health Research and Development (MIHR), SIPPI plans to identify and develop approaches for encouraging technology managers to adopt humanitarian licensing models. That will be accomplished through a wide range of outreach activities that will include holding workshops to coincide with meetings of the Association of University Technology Managers and the Association of American Universities, and hosting a series of meetings on this topic at the AAAS headquarters in Washington, D.C., as well as at SIPPI's annual meeting.

Developing a Web-based clearinghouse. We will develop and implement a Web-based clearinghouse of technologies that are available for humanitarian licensing for product development. The clearinghouse will be designed as an openly accessible database listing technologies available for humanitarian use. It will identify the owner of the technology and provide information as to the specific licensing terms for each listed technology, including type of license, field of use, and the intended beneficiaries for the use of the technology. In addition to facilitating access to technologies, the clearinghouse will allow technology transfer managers to submit detailed information about new technologies and, similar to the *creative commons* model, will supply online tools to build specific humanitarian licenses for those technologies. This model will allow the clearinghouse to continue serving its intended purpose over the long term. ■

ACKNOWLEDGEMENTS

This work was supported by grants from the MacArthur and Rockefeller foundations. The authors would like to thank all members of the SIPPI Working Group on Humanitarian Licensing for input on earlier drafts of this paper. Members of the working group included: Nalini Anand, Fogarty International Center, NIH; Usha Balakrishnan, then at University of Iowa; John Barton, Stanford Law School; Alan Bennett, University of California, Davis, and PIPRA; Cathy Garner, Manchester: Knowledge Capital; Robert Horsch, then at Monsanto Company; Amy Kapczynski, Yale University; Anatole Krattiger, Arizona State University and Cornell University; Richard Mahoney, IVI; Duncan Matthews, Queen Mary Intellectual Property Institute, University of London; Luis Salicrup, Office of Technology Transfer, NIH; Joelle Tanguy, Global Alliance for TB Drug Development; and Jacob Werksman, then at The Rockefeller Foundation; AAAS Staff: Audrey Chapman, Stephen Hansen, and Amanda Brewster. A staff member from Eli Lilly and Co. attended the first meeting of the working group. We also appreciate the inputs of the following people for their comments in later stages of its drafting: Nalini Anand, NIH; Usha Balakrishnan, University of Iowa; J. Carl Craft, Medicines for Malaria Venture; Amy Kapczynski, Yale University; Richard Mahoney, IVI; Duncan Matthews, Queen Mary Intellectual Property Institute, University of London; Jake Werksman, The Rockefeller Foundation; and Katherine Woo, Institute for OneWorld Health.

An extended version of this paper was published by Brewster AL, AR Chapman and SA Hansen. 2005. Facilitating Humanitarian Access to Pharmaceutical and Agricultural Innovation. *Innovation Strategy Today* 1(3):203–216. www.biodevelopments.org/innovation/index.htm

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1 CIPR. 2002. Commission on Intellectual Property Rights. Integrating Intellectual Property Rights and Development Policy. Final Report of the Commission on Intellectual Property Rights, p. 2. DFID: London. www.iprcommission.org.

2 Ibid.

3 Shetty P. More Creative Thinking Needed on Drug R&D. (editorial) 3 May 2005 *SciDev.net*. www.scidev.net/content/editorials/eng/more-creative-thinking-needed-on-drug-rd.cfm.

4 Lanjouw J and M MacLeod. 2005. Statistical Trends in Pharmaceutical Research for Poor Countries. Commissioned by the WHO Commission on Intellectual Property, Innovation, and Public Health. www.who.int/intellectualproperty/studies/stats/en/index.html. The authors found an increase in indicators of innovative

activity (patenting and bibliometric citation) related to some diseases specific to developing countries between 1980 and 2002, but only the subset still in need of better, low-cost treatments. The authors found a downtrend in innovative activity among the subset for which treatments already exist. The authors suggest that although the increase in innovation coincides in part with the introduction of stronger patent protection in developing countries, increased public R&D funding for global health and political developments is likely to have made significant contributions over the same interval. Still, drug innovation targeting developing countries remains a tiny fraction of drug innovation overall.

5 Moran M. 2005. A Breakthrough in R&D for Neglected Diseases: New Ways to Get the Drugs We Need. *PLOS Medicine* 2 (9). The author reports an increase in neglected-disease drug development projects since the year 2000, including activity by multinational companies, small companies, and public-private partnerships (PPPs). She observes that "*commercial incentives were largely irrelevant to the decision by multinational companies to reenter the neglected disease field, while small companies involved in neglected disease R&D were indeed responding to commercial drivers. In most cases, the involvement or planned involvement of PPPs was crucial to company involvement, commercial or otherwise.*"

6 See the discussion of these issues on the Web site of PIPRA. www.pipra.org/purpose.htm.

7 UN Millennium Project. 2005. Innovation: Applying Knowledge in Development. Task Force on Science, Technology, and Innovation, p. 170.

8 See, also in this *Handbook*, chapter 17.18 by R Y Boadi and M Bokanga.

9 Contrary to the often-quoted 70-plus patents, Kryder, Kowalski and Krattiger (see below) clearly showed that the 70-plus patents included patent applications and patent families in different countries. Only 45 unique patents were identified at the time. Kryder RD, S Kowalski and AF Krattiger. 2000. The Intellectual and Technical Property Components of Pro-Vitamin A Rice (GoldenRice™): A Preliminary Freedom-to-Operate Review. *ISAAA Briefs* 20. p. 74. www.isaaa.org.

10 A Krattiger. 2006. Cornell University. Personal communication.

11 Lybbert TJ. 2002. Technology Transfer for Humanitarian Use: Economic Issues and Market Segmentation Approaches, *IP Strategy Today*, 5:18. www.biodevelopments.org/ip.

12 Gilead Press Release. 25 April, 2005. Gilead Sciences and Aspen Pharmacare Sign Letter of Intent to Establish Nonexclusive Licensing and Distribution Agreement for Antiretrovirals Truvada and Viread in Developing World Countries. www.gilead.com/wt/sec/pr_700521.

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17 ucop.edu/ott/patentpolicy/patentpo.html.

18 www.ogc.caltech.edu/patent Policy.htm.

19 web.mit.edu/tlo/www/guide.4.htm.

20 The University of Texas System: Rules and Regulations of the Board of Regents, Series: 90101. www.utsystem.edu/ogc/intellectualProperty/polguide.htm.

21 Salicrup L, RF Harris and ML Rohrbaugh. 2005. Partnerships in Technology Transfer: An Innovative Program to Move Biomedical and Health Technologies from the Laboratory to Worldwide Application. *IP Strategy Today*, 12:1–12. www.biodevelopments.org/ip/ipst12.pdf.

22 See *supra* note 13, at p.7.

23 Medicines for Malaria Ventures. "Statement of MMV Collaboration Principles." Personal communication, J. Carl Craft, Chief Scientific Officer, MMV. See also "Ranbaxy and MMV Achieve Potential Breakthrough in Malaria, Drug Enters Human Trials Phase." Ranbaxy Lab. Press Release, 18 August 2004. www.ranbaxy.com/newsroom/pressrelease_det.asp?sno=169.

24 See *supra* note 11, at p. 18.

25 For example, a license by Monsanto to the Kenya Agricultural Research Institute allows for unrestricted use of certain Monsanto technology and know-how for the development of virus-resistant sweet potatoes in Kenya and Africa. Other agreements allow for the use of insect resistance in maize transferred by Syngenta to Africa but cannot be used outside of the region; IRRI negotiated the rights for use of a stem-borer-resistant gene for rice from Plantech for all developing countries as defined by the UN. (Byerlee D and K Fischer 2001.Accessing Modern Science: Policy and Institutional Options for Agricultural Biotechnology in Developing Countries, *IP Strategy Today*, 1:14. www.biodevelopments.org/ip.

26 See Byerlee and Fischer at *supra* note 25.

27 TDR News No. 72. 2004. Artesunate combinations are coming: partnership develops LapDap plus artesunate. www.who.int/tdr/publications/tdrnews/news72/lapdap.htm.

28 Foskett H, R Menapace and S Shah Basu. 2003. Developing Inventions for Neglected Diseases. Poster Presentation, AUTM annual meeting.

29 Rorbaugh M. 2005. Technology Transfer to Benefit Public Health in LDCs. Global Health & Technology Transfer Meeting (presentation made 15 March), NIH Office of Technology Transfer.

30 See *supra* note 13, at 9.

31 The Concept Foundation (CF) has been a pioneer in licensing that helps to ensure access through appropriate pricing mechanisms. It has partnered with 10 different PPPs with pharmaceutical companies worldwide. It has licensed technology to nine manufacturer in five developing countries. CP has had products manufactured in eight countries and made available in more than 30 developing countries. Its first product, Cyclofem®, an injectable hormonal contraceptive, was made available to public sector health services in 1993. Since then, over 140 million doses of Cyclofem have been manufactured and distributed by CF licensees worldwide. Around 16 million HIV rapid tests have been distributed by CF licensees to public sector health services worldwide as well. www.conceptfoundation.org.

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33 See, also in this *Handbook*, chapter 2.1 by AB Bennett.

34 otl.stanford.edu/industry/resources/exclusive.pdf.

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36 The World Health Organization has established a detailed set of Good Manufacturing Practice (GMP) standards, and many individual countries maintain their own GMP requirements for regulatory approval.

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