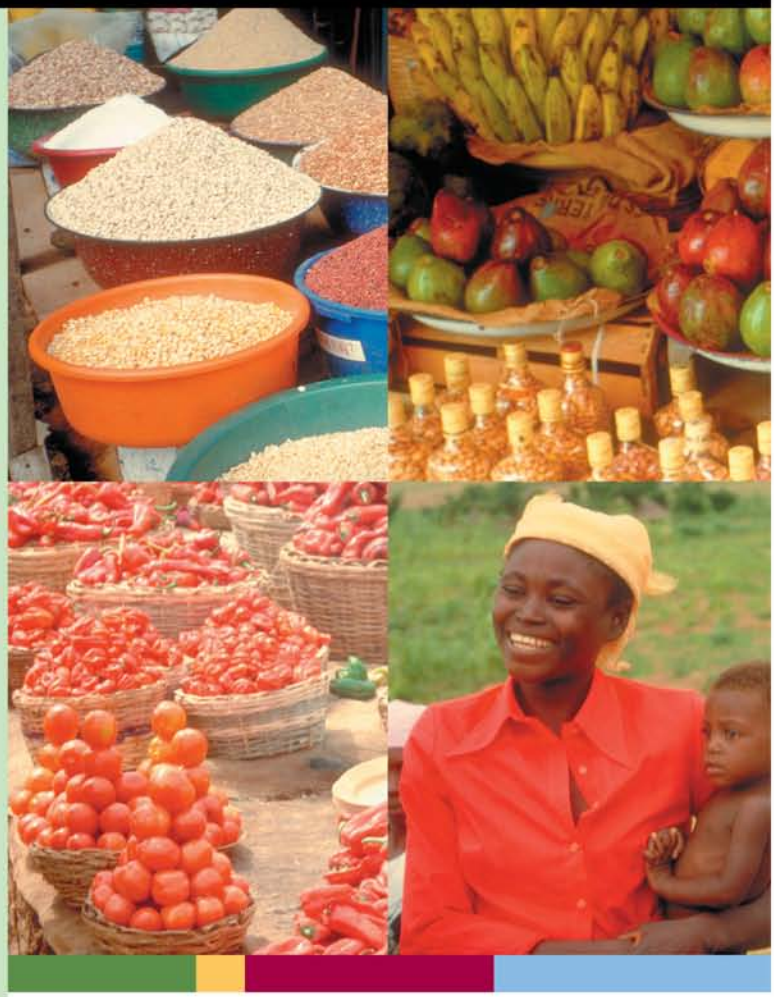
Innovation Strategy Today

eJournal • Volume 1 • Number 3 • 2005

Inside This Issue:



Special issue published in partnership with

AAAS

ADVANCING SCIENCE, SERVING SOCIETY

eJournal

An eJournal Sharing Creative and Innovative Ideas and Experiences about Global Issues in Agriculture, Health, and the Environment Facing Developing Countries

Innovation Strategy Today is published by ***bio*Developments-International Institute** in collaboration with **AAAS, Cornell University** and the **Biodesign Institute at Arizona State University**

bioDevelopments International Institute

Cornell University

THE biodesign INSTITUTE AT ARIZONA STATE UNIVERSITY

*Facilitating Humanitarian Access to Pharmaceutical and Agricultural Innovation**

Amanda L. Brewster, Audrey R. Chapman, Stephen A. Hansen
Science & Intellectual Property in the Public Interest (SIPPI), American Association for the Advancement of Science
1200 New York Ave., NW, Washington, DC 20005, USA, achapman@aaas.org or shansen@aaas.org

Executive Summary

This paper seeks to raise awareness about the importance of managing IP to facilitate humanitarian use and applications. Our goal is to identify intellectual property approaches that can promote access to and use of health and agricultural product innovations by poor and disadvantaged groups, particularly in low-income countries. The paper encourages more public-sector IP managers to understand and employ strategies that will accomplish these goals. Humanitarian use approaches should become the norm, and we seek to help private-sector licensees understand the rationale and potential benefits behind such strategies. This paper focuses on the pharmaceutical and agricultural sectors, but the principles noted could potentially be applied to other areas as well.

There are key moments when technology managers can improve the likelihood that their IP will benefit people in need: when they decide 1) who will receive a license, 2) whether the license will be exclusive, 3) what types of applications will be covered, and 4) how long the duration of the license will be. In addition, if and when technology managers reach the stage of negotiating license terms, particularly in an exclusive license, they may be able to include legally enforceable provisions to protect in advance the possibility of sharing their IP with third parties for the benefit of people in need. These humanitarian license provisions may define beneficiaries by the field in which the IP would be applied, by geographic region, by national income level, or by market (e.g., "subsistence farmers"). License terms may also require the licensee to meet specific milestones related to availability or price in order to ensure that the IP benefits the target populations. The license agreement can further increase access through specific terms that govern the use of the technology for research, the licensee's freedom to grant sublicenses, and the treatment of follow-on innovations developed by the licensee.

We acknowledge that improved IP management cannot by itself solve the access crisis. Even if technology managers adopt humanitarian IP management strategies, they will need to connect with development partners who can utilize the protected technologies. In some cases, these partners may not yet exist. But when partners are found, 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 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.

* 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, University of Iowa; John Barton, Stanford Law School; Alan Bennett, University of California, Davis and PIPRA; Cathy Garner, MIHR; Robert Horsch, Monsanto Company; Amy Kapczynski, Yale University; Anatole Krattiger, Arizona State University, MIHR and Cornell University; Richard Mahoney, Arizona State University and MIHR; 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, 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, Arizona State University; Duncan Matthews, Queen Mary Intellectual Property Institute, University of London; Jake Werksman, Rockefeller Foundation; and Katherine Woo, Institute for OneWorld Health.

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

Available online at www.bioDevelopments.org • ISSN 1555-6328 (online) • ISSN 1555-631X (print)

Introduction

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, geographical, 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]

Objectives of this paper

Because certain patent arrangements can inhibit the development and dissemination of products for developing countries, we need to explore intellectual property management strategies 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 AAAS project on Science and Intellectual Property in the Public Interest convened a working group to explore these topics in 2004. Working group members contributed experience from the public and private sectors, representing both the agricultural and health fields. This paper draws upon expertise provided by all group members, but it is not necessarily endorsed by them.

The goal of this paper is to identify licensing strategies that promote humanitarian access to health and agricultural product innovations and their use by poor and disadvantaged groups, particularly in low-income countries. The paper encourages more public-sector IP managers to understand and employ strategies that will achieve these goals. We also seek to help private-sector licensees understand the rationale and potential benefits behind such strategies. Indeed, humanitarian licensing strategies should more and more become the norm.

Of course, improved IP management cannot by itself solve the access crisis. Increased investments in providing basic needs (food, clean water, and adequate sanitation), sound national policies, and improved health care and agricultural infrastructures are all essential components of greater global development and equity. Nevertheless, better IP management practices can contribute to the development and dissemination of essential medicines and agricultural technologies for developing countries.

This paper deals with voluntary strategies, but this is not meant to exclude other approaches, such as incorporating some of the suggested changes in IP management into public policies, laws, or treaty reform. The advantage of voluntary strategies is that they can be implemented immediately, without the complexities involved in changing regulations and legal requirements.

Background and related initiatives

Our discussion of strategies builds on the initiatives, experience, and proposals of other organizations for the management of IP. The UN 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 (e.g., the World Health Organization) have undertaken humanitarian licensing, as have national entities such as the U.S. National Institutes of Health, which now includes humanitarian clauses in their 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, 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 US, and only a few patents are held in developing countries.[8] The inventors of golden rice licensed their inventions related to golden rice to Greenovation, a biotech spin-off company from the University of Freiburg, that is owned by the inventors themselves. Greenovation then exclusively licensed its golden rice-related patents to AstraZeneca (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 sub-license—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 $10,000 per year from its sale. Higher sales would require farmers to acquire a commercial license from Syngenta.[9] 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. After Yale licensed this patent to Bristol-Myers Squibb 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 by thirty-fold. 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 ringspot 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 to Mexico, as well as ringspot virus resistant and delayed ripening papayas transferred from Monsanto and Syngenta, respectively, to Southeast Asia.[10] Finally, a recent agreement between Gilead Sciences and the South African drug maker 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.[11]

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.

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.[12]

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 below. Entries were compiled from Gardner and Garner (2004)[13] and Merz (2005).[14]

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 non-competing 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 non-traditional 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 well-being of humankind through their patenting and licensing activities. For example, each of the top four university recipients of U.S patents in 2004[15] states public benefit as an explicit goal in its patent policy:

- **University of California** (#1 with 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."[16]
- **California Institute of Technology** (#2 with 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 appropriate efforts to transfer the technology to those who will facilitate public use."[17]
- **Massachusetts Institute of Technology** (#3 with 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."[18]
- **University of Texas** (#4 with 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."[19]

Public funding agencies also seek to promote public benefit. The mission of the U.S. National Institutes of Health (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.[20] 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.[21]

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 IP management as an extension of the institution's public mission. 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.

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

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/U. 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
International Partnership for Microbicides
www.ipm-microbicides.org
iOWH: Institute for One World 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

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 Squibb, Gilead, Monsanto, and Syngenta. Activities by Chiron, GlaxoSmithKline, Pioneer Hi-Bred, and Roche are mentioned later.

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 non-traditional 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.

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," geographically, or by reference to lists provided by OECD countries, the World Bank, or the Food and Agriculture Organization (FAO). 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 certain 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

AGERI and Pioneer Hi-Bred *bt* maize in Egypt
Strategy employed: *dual market agreement*

The public-sector Agricultural Genetic Engineering Institute (AGERI) in Egypt owns patents covering a technology for producing insect-resistant maize via the insect toxin *Bacillus thuringiensis* (*Bt*). AGERI allowed the US company Pioneer Hi-Bred to evaluate some of these patented proteins and genes, and in exchange Pioneer Hi-Bred trained AGERI scientists in methods for characterizing *Bt* and maize transformation technologies. The Agricultural Biotechnology Support Program of the US Agency for International Development supported the project. Now, AGERI is commercializing the technology in Egypt while Pioneer has commercial rights in the US.

Source: Margarita Escalar, "Public-private partnerships in modern biotechnology," 2002 SciDev.net Policy Brief. Available at: www.scidev.net/dossiers/index.cfm?fuseaction=policybrief&policy=32&section=112&dossier=6

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.[22]

Although market segmentation strategies have been employed successfully,[23] 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 (i.e., markets that may not necessarily be lucrative for large companies but nevertheless present niche opportunities for smaller companies), many developing countries may also have emerging private markets for the same goods. Market segmentation might be most successful where noncommercial markets can be sharply delineated by region, which makes it easier to exclude spillovers to non-targeted markets.[24] In addition, market segmentation often requires intense negotiation, the development of trust between partners, and the capacity to enforce agreements.

Non-exclusive licensing

In non-exclusive licensing, in addition to the primary license agreement, the licensor retains the freedom to license the technology to other parties. Some institutions (e.g., NIH) seek to use non-exclusive licensing or to license to multiple companies whenever possible. If a university can accomplish technology transfer to a company using non-exclusive 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.

Transferring technology to public-private partnerships (PPPs)

When it is clear that a technology could benefit neglected markets (e.g., 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 non-exclusive basis. The business models of PPPs vary. Some conduct in-house product development; others manage collaborative development by public and private sector labs. 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.

Finding New TB Treatments

Strategies employed: *licensing to PPPs and reduced royalties in developing countries*

Over the past 40 years, virtually no investments have been made to develop new products for TB, and the standard course of treatment remains very long and cumbersome. However, many new compounds have been discovered by drug researchers in the interim, and the TB Alliance is reviewing some of the most promising for potential use against TB. Half of the compounds have come from universities, and the others from industry—licensed on concessionary terms. For example, the TB Alliance obtained an exclusive worldwide license to PA-824 and related compounds from Chiron Corp. under an agreement that eliminates royalties for drugs marketed in impoverished countries.

Source: TB Alliance website. Available at: www.tballiance.org/3_1_2_AportfolioofDrugCandidates.asp

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.

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 the product at much lower cost than typical partners in the U.S. or other industrialized countries.

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 non-exclusive 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 re-importation 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 semi-cooperative 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 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.

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. 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 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."

CDA malaria treatment

Strategies 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 anti-malarial 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 UK Department for International Development. It was approved by the UK 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 No. 72. 2004. "Artesunate combinations are coming: partnership develops Lapdap plus artesunate." Available at: www.who.int/tdr/publications/tdrnews/news72/lapdap.htm

Developing a Low-Cost Malaria Treatment

Strategies 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 Roche Company 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 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: 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

Positive 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 (e.g., 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.

The US National Institutes of Health (NIH) often uses these clauses in its agreements to ensure that the licensee undertakes specific actions to benefit the public sector (e.g., 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.[25]

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 triggered, for example loss of exclusivity, sublicensing, exercise of march-in rights, and even termination of the agreement.

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 re-

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 inexpensive and practical means of diagnosing HIV in resource-poor settings.

Source: Holly Foskett, Rebecca Menapace, Seema Shah Basu. "Developing Inventions for Neglected Diseases." Poster Presentation, 2003 AUTM Annual Meeting.

quirements concerning access.[26] This model could be expanded whereby licenses to companies include an appropriate 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.[27] To ensure that an appropriate price is reached and maintained, the licensor may also include contractual language that mandates the submission of manufacturing cost reports and product cost calculation details on a regular basis. [28]

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.

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 a research exemption clause into licensing agreements that exempts specified categories and types of research from patent infringement in using its proprietary technologies, (e.g., to develop products that broadly benefit the public or the population of poor countries). The University of California technology transfer office is beginning to insert such research exemption clauses into licensing agreements. Other universities already reserve research rights for academic institutions in their standard exclusive licensing agreements (e.g., Stanford, whose standard license language is reproduced here). 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.

Sublicenses for developing countries

Unless provided for in the agreement, a licensee generally does not have sublicensing rights. Should the parties agree to allow sublicensing, the main agreement should specify the rights and obligations of the licensee with respect to the sub-licensee(s). In

Yale d4T Treatment for HIV
Licensing to producers in developing countries, Amending existing agreements

Yale University, which holds a key patent on stavudine (d4T), a widely used antiretroviral drug, renegotiated an agreement with its licensee Bristol-Myers Squibb to incorporate humanitarian terms that allowed the drug to be licensed for generic production in South Africa. This reduced the price of d4T in Africa by thirty-fold.

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 sub-licensee fulfils all the requirements of the principal license. The best way to ensure that the sub-licensee 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.

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 (e.g., revoking a license or sub-licensing to third parties in order to assure access).

Treatment of future rights in license agreements

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, as subject to 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.

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 non-exclusive 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.

Amending existing agreements

While the goal of this document is to promote humanitarian licensing from the outset, when agreements already exist they can also 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 upfront wherever possible, the fact that an agreement has already been concluded should not discourage participants from revisiting the agreement when an unforeseen need arises.

Stanford Reservation of Academic Research Rights in Standard License Agreement

Strategy: *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 has the right to publish any information included in the Technology or a Licensed Patent.

Source: Stanford Office of Technology Licensing, Available at: otl.stanford.edu/industry/resources/exclusive.pdf

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.

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.[29]

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), for sale into low- or middle-income countries will be openly licensed to any company that meets Good Manufacturing Practice[30] standards. 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 in the U.S.[31]

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 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.

Notes and References *(all web pages have last been accessed on 2 November 2005)*

1 Commission on Intellectual Property, *Integrating Intellectual Property Rights and Development Policy* (London, 2002), p. 2. www.iprcommission.org/papers/pdfs/final_report/CIPRfullfinal.pdf

2 Ibid., p. 1

3 Priya Shetty, "More Creative thinking needed on Drug R&D," 3 May 2005 editorial, SciDev.net: www.scidev.net/content/editorials/eng/more-creative-thinking-needed-on-drug-rd.cfm

4 Jean Lanjouw and Margaret 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 are 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 Mary Moran. 2005. "A Breakthrough in R&D for Neglected Diseases: New Ways to Get the Drugs We Need." PLOS Medicine Vol. 2, Issue 9. The author reports an increase in neglected disease drug development projects since the year 2000, including activity by multinational companies, small companies, and PPPs. She observes that "commercial incentives were largely irrelevant to the decision by multi-national companies to re-enter 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 website of PIPRA: www.pipra.org/main/purpose.htm

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

8 Contrary to the often quoted 70-plus patents, Kryder, Kowalski and Krattiger (2000) 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, R.D., S. Kowalski and A.F. Krattiger. 2000. The intellectual and technical property components of pro-Vitamin A rice (GoldenRice™): A Preliminary Freedom-to-Operate Review. *ISAAA Briefs* 20. pp. 74. www.isaaa.org

9 A. Krattiger, Cornell University [2005], personal communication.

10 Travis J Lybbert, "Technology Transfer for Humanitarian Use: Economic Issues and Market Segmentation Approaches," *IP Strategy Today*, No. 5-2002, p. 18. www.biodevelopments.org/ip

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

12 Amy Kapcynski, "Access to Essential Medicines and University Research: Building Best Practices," Yale University Center for Interdisciplinary Research on AIDS, Fall 2003, p.3.

13 Charles Gardner and Cathy Garner. 2004. "Technology Licensing to Non-traditional Partners: Nonprofit Health Product Development Organizations for better Global Health." Available: www.mihr.org/?q=taxonomy_menu/1/6

14 Jon F. Merz. 2005. "Intellectual Property and Product Development Public/Private Partnerships." WHO CIPIH. www.who.int/intellectualproperty/studies/intellectual_property/en/

15 U.S. Patent and Trademark Office. "USPTO Releases List of Top 10 Universities Receiving Most Patents in 2004." www.uspto.gov/web/offices/com/speeches/05-18.htm

16 www.ucop.edu/ott/patentpolicy/patentpo.html

17 www.ogc.caltech.edu/Patent_Policy.htm

18 web.mit.edu/tlo/www/Inventors_Guide.pdf

19 www3.utsystem.edu/ogc/intellectualProperty/polguide.htm Series 90101, "General Rules for Intellectual Property"

20 Luis Salicrup, Rachelle F. Harris, and Mark L. Rohrbaugh, "Partnerships in Technology Transfer: An Innovative Program to Move Biomedical and Health Technologies from the Laboratory to Worldwide Application," *IP Strategy Today*, 12 (2005): 1-12. www.biodevelopments.org/ip/ipst12.pdf

21 Kapcynski, p.7.

22 Lybbert, p. 18.

23 For example, a Monsanto and Kenyan Agricultural Research Institute agreement for unrestricted use of a transgene for the control of sweet potato feathery mottle virus in African sweet potatoes, and insect resistant maize with proprietary technologies is being transferred from Syngetna to Africa but cannot be used outside of the region; IRRI negotiated the rights for use of a stem borer resistance gene for rice from Plantech for all developing countries as defined by the UN. (from Byerlee and Fischer 2001, p. 14).

24 Derek Byerlee & Ken Fischer, Accessing Modern Science: Policy and Institutional Options for Agricultural Biotechnology in Developing Countries, *IP Strategy Today*, No. 1-2001, p. 18. www.bioDevelopments.org/ip

25 Mark Rorbaugh, "Technology Transfer to Benefit Public Health in LDCs," presentation made at Global Health & Technology Transfer Meeting, NIH Office of Technology Transfer, March 15, 2005.

[26] Kapcynski, p.9.

[27] The Concept Foundation (CF) has been pioneering 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 manufactures 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

[28] Joachim Oehler, "The Role of Milestones in Licensing Deals to Assure Access to Health Products in Developing Countries," *IP Strategy Today*, No. 10-2004, p. 68. www.bioDevelopments.org/ip

[29] Personal Communication, Usha Balakrishnan, Director, MIHR-USA. www.mihr-usa.org

[30] WHO established a detailed set of Good Manufacturing Practice (GMP) standards, and many individual countries maintain their own GMP requirements for regulatory approval.

[31] A. Kapczynski, "An 'Equitable Access License' for Use by Universities," Universities Allied for Essential Medicines.

An *e*Journal Sharing Creative and Innovative Ideas and Experiences
about Global Issues in Agriculture, Health, and the Environment Facing Developing Countries.

Published by

in collaboration with Cornell University
and The Biodesign Institute of Arizona State University (ASU)

Available online at
www.bioDevelopments.org

Innovation Strategy Today
*bio*Developments-International Institute
Cornell Business and Technology Park
POBox 4235, Ithaca NY14852, USA.

Editorial Policy

Papers must have a problem solving orientation and demonstrate originality and innovation in thinking, analysis, methods or application. Issues related to research investments and management, bilateral and multilateral donor policies, extension, teaching, public-private partnerships are equally encouraged, as is interdisciplinary research with a significant innovation and international development component. Manuscripts, review articles and working papers that offer a comprehensive and insightful survey of a relevant subject, consistent with the scope of *Innovation Strategy Today*, are welcome. All articles published, regardless of their nature, will be reviewed anonymously by members of the editorial board.

Concept and Inside Design
*bio*Developments LLC, Interlaken, NY

Cover Design
Jacob Sahertian & Charles Kazilek
Arizona State University School of Life Sciences Visualization Laboratory, Tempe, AZ

Acknowledgements
We are grateful to the Rockefeller Foundation, to the Department of Plant Breeding and to the International Program of the College of Agriculture and Life Sciences (IP/CALS) at Cornell University, and to the Biodesign Institute at Arizona State University for support.

Disclaimer

The views expressed are those of the authors and do not necessarily reflect those of their respective institutions, nor of the publishers, editors and donors of *Innovation Strategy Today*.

ISSN 1555-6328 (online)
ISSN 1555-631X (print)

Free electronic distribution
US$45 for printed versions