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Introduction

In order for agricultural biotechnology (agri-biotech)[1] to play a larger role in the development of sustainable agricultural systems,[2] intellectual property (IP) rights management must be addressed. These issues are not limited to developing countries. With increased globalization, the management of agri-biotech IP rights affects both developing and industrialized countries. In industrialized countries, for example, IP rights risk management entails protection of inventions via strong patent portfolios. For developing countries, IP rights risk management includes the acquisition of rights requisite for the use of inventions essential to the basic welfare of the population. Strategies are needed to bridge these disparate IP management paradigms to facilitate the successful transfer of the agri-biotech from an industrialized country source to a developing country recipient.

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Nothing in this paper constitutes a legal opinion and the authors recommend that the advice of a qualified attorney be obtained to assure appropriate counsel in completing a freedom to operate review.

1 Agri-biotech, as used in this article, includes the use of biotechnology for the development of genetically modified plants and microorganisms, associated molecular biology (i.e., manipulation of DNA and proteins), cell, tissue, and organ culture. *See* Robert P. Tengerdy & George Szakacs, *Perspectives in Agrobiotechnology*, 66 J. Biotechnology 91 (1998).

2 The World Commission on Environment and Development has defined sustainable development as "development that meets the needs of the present without compromising the ability of future generations to meet those of the future." *See* Cai Yunlong & Barry Smit, *Sustainability in Agriculture: A General Review*, 49 J. Agric., Ecosystems & Env. 299 (1994).

This paper examines IP management linked to agri-biotech products. Further, this paper examines Golden Rice, a genetically engineered rice strain that accumulates beta-carotene (i.e., pro-vitamin A) in the endosperm tissue of grain, as a case study for IP management, with emphasis on the international movement of agri-biotech from industrialized to developing countries.[3] Topics discussed include: the application of agri-biotech to international development; the challenge of transferring this technology from industrialized to developing countries; a method for evaluating the IP constraints impinging on the deployment of Golden Rice; industrialized/developing country perspectives vis-à-vis IP rights management; six shorter-term options for the management of IP connected to Golden Rice; and a longer-term proposed path to sustainable transfers of agri-biotech products.

Background

Six factors continue to pressure global agricultural production capacity: a rapidly expanding global population; an increasing demand for water resources; the depletion of quality water resources; the decline in arable land resources; pressure on crop production by diseases, pests and unfavorable climatic conditions; and the ever-increasing demand for quality food products. In developing countries the situation is especially critical.[4]

Historically, the "Green Revolution"[5] of the 1960s and 1970s effectively addressed pressing food concerns of that time. This was

3 For a definition of "developing countries," see *World Economic and Financial Surveys*, World Economic Outlook (May 1999) (available at <http://www.imf.org/external/pubs/ft/weo/1999/01/>).

4 Yeshwant L. Nene, *Sustainable Agriculture: Future Hope for Developing Countries*, 18 Canadian J. Plant Pathology 133 (1996) (The global population is projected to be 6.3 billion in the year 2000, 8.3 billion in 2020, and 12 billion in 2050, with disproportionate growth in developing nations. As applied to arable land, resources are estimated at seven million hectares annually, due to non-sustainable farming practices. A large part of this is linked to the building of roads, parking lots, buildings, etc., that is, the "development" of cropland into paved surfaces.); John C. Rodda, *Guessing or Assessing the World's Resources?*, 9 J. Chartered Instn. Water and Envtl. Mgt. 360 (1995) (Globally, irrigated lands have increased 7.5-fold since 1900. An accurate assessment regarding the depletion of quality water resources, however, remains problematic); David Pimental et al., *Environmental and Economic Costs of Soil Erosion and Conservation Benefits*, 267 Sci. 1117 (1995) (As applied to the decline in arable land resources, an estimated twelve million hectares are lost annually).

5 Dave Hoisington et al., *Plant Genetic Resources: What Can They Contribute Toward Increased Crop Productivity?*, 96 Proc. Natl. Acad. Sci. U.S. 5937 (1999).

accomplished primarily via conventional plant breeding and improved crop management practices. Of particular importance to the Green Revolution were the activities of the Consultative Group on International Agricultural Research (CGIAR).[6] The CGIAR has traditionally been a primary source/conduit of agricultural science and technology for the developing world.[7] However, since many agri-biotech discoveries and applications are protected by their industrialized country owners, it is difficult for CGIAR to legally distribute these to its developing world clients. Indeed, CGIAR has only recently begun major agri-biotech research.[8]

Agri-biotech has considerable potential for contributing to sustainable agricultural systems in developing countries.[9] Therefore, it is seen as an innovative approach to circumvent starvation, i.e., a "Second Green Revolution."[10] However, unlike the agronomic approach of the "First Green Revolution," agri-biotech is very expensive. Millions of scientific research hours and dollars go into the production and release of agri-biotech products. Therefore, organizations[11] that produce and own agri-biotech products have surrounded their discoveries with IP protection (patent portfolios).

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6 Dennis T. Avery, *Food Production: The Success of the International Agricultural Research Centres*, Assessments and Research Report, Bureau of Intelligence and Research, U.S. Department of State (No. 751-AR). Established in 1971, the Consultative Group on International Agricultural Research (CGIAR) is an informal association of 52 public and private sector members that supports a network of sixteen international agricultural research centers. These are distributed around the globe, in the centers of genetic diversity for their respective mandated crops, for example, International Potato Center in Peru for potatoes, International Rice Research Institute in the Philippines for rice, Centro Internacional de Agricultura Tropical in Colombia for beans. The World Bank, United Nations Food and Agriculture Organization, United Nations Development Program, and United Nations Environment Program are co-sponsors of the CGIAR. The mission of the CGIAR is to contribute, and promote through its research, sustainable agriculture for food security in developing countries. *See* <http://www.cgiar.org/>.

7 Deborah A. Rose, *Changing Relationships in Technology Transfer to the Third World: Case Study of Biotechnology in Agriculture*, 11 Rutgers Computer & Tech. L.J. 531 (1985).

8 Janet Bell, *A Greener Than Green Revolution?*, 15 Seedling 8 (1998).

9 Ismail Serageldin, *Biotechnology and Food Security in the 21st Century*, 285 Sci. 387 (1999).

10 Gordon Conway, *Green Revolutionary*, Bus. Week 191 (Nov. 16, 1998).

11 Multi-national corporations, university laboratories, private foundations, and government laboratories (e.g., USDA).

Increasingly, agri-biotech is owned by private sector corporations.[12] The proportion of global agri-biotech research and development expenditures by the private sector has grown from approximately 65% in 1994-1995 to 80-85% in 1999.[13] Hence, with so many agri-biotech products subject to IP protection, their commercial distribution to the developing world poses significant challenges. Corporations with substantial agri-biotech property portfolios are understandably reluctant to donate these products to developing countries which frequently lack enforceable IP protection and management capability. Corporations justifiably fear that such humanitarian acts might establish, or at least strengthen a competitor.

Developing countries would likely benefit from cutting-edge agri-biotech applications, most of which are the property of industrialized country-based corporations. However, many of these same developing countries are currently incapable of protecting or managing such property rights. Therefore, to develop and maintain international agri-biotech transfer, industrialized and developing countries need to cooperatively implement manageable systems of IP protection. As a critical component of this strategy, developing countries need to implement appropriate IP policies and effective enforcement procedures.

Golden Rice

Genetic engineering of crops has predominantly been in the production side (e.g., herbicide tolerance, insect resistance, virus resistance, fungi resistance), and less on the consumer side.[14] These first generation transgenic crops, targeted more towards the farmer,[15]

12 Clive James, *Agricultural Research and Development: The Need for Public-Private Sector Partnerships*, Issues in Agriculture 9 (The Consultative Group on International Agricultural Research, World Bank 1996).

13 Kandukuri V. Raman & David W. Altman, *Biotechnology Initiative to Achieve Plant Pest and Disease Resistance*, 13 Crop Protection 591 (1994); Steven P. Briggs, *Plant Genomics: More than Food for Thought*, 95 Proc. Natl. Acad. Sci. 1986 (1998); Gabrielle J. Persley, *Agricultural Biotechnology and the Poor: Promethean Science,* Agricultural Biotechnology and the Poor: Proceedings of an International Conference 3 (CGIAR 2000).

14 Adriana Cristina Alves et al., *Plant Transformation: Advances and Perspectives*, 56 Scientia Agricola 1 (1999).

15 Jim M. Dunwell, *Transgenic Crops: The Next Generation, or an Example of 20/20 Vision*, 84 Annals Botany 269 (1999).

represent attempts to reduce input costs. However, second generation transgenic crops embody "value-added innovations."[16] Golden Rice, as a second generation transgenic, is a pioneering step in the use of agri-biotech to produce a significant impact at the consumer level, more specifically in developing countries.[17]

In Golden Rice, the successful engineering of the carotenoid biosynthetic pathway (i.e., genes) in the rice endosperm, with the subsequent expression of pro-vitamin A (i.e., beta-carotene), represents a remarkable technological accomplishment. Specifically, this is due to the utter complexity of the carotenogenic pathway, as well as the interrelated nature of plant metabolic systems.[18] This technical and scientific complexity clearly indicates the IP/technical property (TP)[19] complexity of Golden Rice, which, in turn, makes its transfer to the developing world such a challenge.

Golden Rice has significant potential for the alleviation of chronic vitamin A deficiency (VAD) throughout the developing world.[20] VAD is a serious public health problem,[21] with worldwide estimates

16 Gordon C. Rausser & Arthur A. Small, *The Economic Value of Patents, Licenses, and Plant Variety Protection*, The Giannini Foundation of Agricultural Economics, Working Paper (June 1996).

17 Xudong Ye et al., *Engineering the Provitamin A (beta-carotene) Biosynthetic Pathway Into (carotenoid-free) Rice Endosperm*, 287 Sci. 303 (2000).

18 Gerhard Sandmann, *Carotenoid Biosynthesis and Biotechnological Application*, 385 Archives Biochemistry Biophysics 4 (2001); Trevor Walworth Goodwin & Eric Ian Mercer, *Introduction to Plant Biochemistry* (2d ed., Pergamon Press 1983).

19 Proprietary property, or proprietary science, as used throughout this paper, is comprised of intellectual property (IP) and technical property (TP), sometimes referred to as "tangible property." IP is taken to mean, without limitation, IP rights, including patent rights, plant variety protection certificates, unpublished patent applications, and any inventions, improvements, and/or discoveries that may or may not be legally protectable, including know-how, trade secrets, research plans and priorities, research results and related reports, statistical models, computer programs, related reports, market interests, and product ideas. TP is taken to mean, without limitation, tangible property such as computer software, germplasm and the biological materials and derivatives thereof, and related materials. As a hypothetical example of TP and IP, a plasmid-vector construct transferred from laboratory A to laboratory B, under a Material Transfer Agreement (MTA), is owned as a TP by laboratory A, and the MTA may stipulate restrictions on usage by laboratory B. However, IP rights owned by third parties may be embedded in the construct (e.g., gene promoters, selectable markers).

20 Ingo Potrykus, *Golden Rice and Beyond*, 125 Plant Physiology 1157 (2001); *see* Ye et al., *supra* n. 17.

21 Alfred Sommer, *Vitamin A Deficiency and Its Consequences: A Field Guide to Detection and Control* (3d ed., World Health Organization 1995).

of 100 to 200 million children affected.[22] In 1989, up to 1.2 million deaths of preschoolers were attributed to VAD.[23] Five hundred thousand children are permanently blinded every year due to xerophthalmia (severe VAD).[24] These children die at nine times the rate of healthy children.[25] Between one and three million children die of infections every year, preventable if the children had not been deficient in vitamin A.[26]

Golden Rice represents the vanguard for a new class of agri-biotech products, and a model case study for the effective, efficient, and equitable distribution of an agri-biotech product from industrialized country sources to developing countries where such products are most needed. Unresolved IP/TP rights constraints present the risk of complicating international deployment of Golden Rice. This truly is a human dilemma in that restrictions on the distribution of beneficially appropriate, value-added, genetically engineered crops to developing countries may affect the welfare of millions of lives, and, in the case of Golden Rice, millions of children. For this reason, management of IP and TP issues associated with Golden Rice have potentially far-reaching ramifications.

Methodology

Pragmatic management of the international transfer of IP/TP rights associated with an agri-biotech product (e.g., Golden Rice), begins with a systematic product clearance (PC).[27] This is a para-legal document

22 Jean H. Humphrey et al., *Vitamin A Deficiency and Attributable Mortality Among Under 5-Year-Olds*, 70 Bull. of the World Health Org. 225 (1992).

23 Jenny Cervinskas & Mahshid Lofti, *Vitamin A Deficiency: Key Resources in Its Prevention and Elimination*, The Micronutrient Initiative Information Paper No. 1 (2d ed., 1996) (available at <http://www.micronutreint.org/publications/vadkey.shtml>).

24 Gerald F. Combs, *The Vitamins, Fundamental Aspects in Nutrition, and Health* (2d ed., Academic Press 1998).

25 *Id.*

26 Barbara A. Underwood, *Prevention of Vitamin A Deficiency, Prevention of Micronutrient Deficiencies, Tools for Policymakers and Public Health Workers* (C.P. Howson et al. eds., National Academy Press 1998).

27 *See* John H. Duesing, *Managing a Product Clearance Process Toward Freedom-to-Operate,* Proceedings of the American Seed Trade Association Annual Meeting (1996) (publicized with permission of J.H.D. and A.S.T.A.) (available at <http://www.amseed.com/index.html>). In order to manage the IP and TP attached to agri-biotechnological applications, a systematic PC process leading to freedom-to-operate (FTO), as clearly defined by John H.

produced in large measure by scientists who clearly understand the inherent technological complexities of the product. The PC involves a detailed listing and analysis of all aspects of the agri-biotech product. The PC is a detailed dissection, referred to in this paper as a "product deconstruction," into the product's essential components. The PC is based on, and developed from, a series of questions such as: what are the methods and procedures that went (will go) into producing the agri-biotech product; what are its principal components; what are the essential ingredients that constitute each principal component; what are the IP/TP rights that may be attached to each component and its ingredients; and who seems to own the IP/TP rights of each component and each of its ingredients?

Ideally, the PC describes and analyzes every essential aspect of the product. It must be as comprehensive as economically possible. Product deconstruction can take place either when the product is in the planning stage, when the research and product development is underway, or when the agri-biotech product, such as Golden Rice, is ready for distribution. Further, once the product is in the stream of commerce, it is prudent to produce an annual PC update because of the changing IP/TP rights landscape.

Duesing, is essential. According to Duesing, FTO is "the ability to undertake research projects and/or commercial development and sales activities involving a particular technology or product with minimal risk of infringing the unlicensed patent or tangible property ownership rights of another party." Duesing adds that "[a]n FTO opinion is prepared by patent counsel and reflects counsel's legal determination regarding FTO for a particular commercially-directed activity, including research." To reach an FTO opinion, a PC is necessary. As J. Duesing explains, "PC is a process that tracks FTO and other critical issues for a product under development and prior to and after commercial sale. It is undertaken at request of counsel as part of the total assessment of whole product FTO in order to support company decisions regarding product development and the sale of each product. All information pertaining to a given product (i.e., technical, patent, license, FTO options) is assembled to document the organization's full knowledge, completed and pending actions, and decisions relating to whole-product FTO." PC entails a detailed dissection of the product into the essential ingredients involved in its development. As defined by Duesing, PC "defines the technical content of the product or a potential product. A product or technology profile is prepared that includes 1) all "ingredients" incorporated into the product; 2) all processes used to achieve the product; 3) any specific combination of ingredients and processes used to achieve the whole product. The profile details every essential aspect of the product." This process of dissection is called "deconstruction." Although all of the relevant patents are searched, the TP also must be adequately monitored and assessed. The important point here is that (as per Duesing) "[e]ach company should monitor carefully its acquisition of tangible materials from other parties, to ensure that the material is obtained with the appropriate agreement to show that the company has legitimate control of the tangible material, and that there are no restrictions on its commercial use."

Generally, it is in any organization's strategic best interest to conduct a product deconstruction at the earliest possible phase in product development. When alternatives exist, this process can help research scientists focus only on those items where IP is most readily available. In some cases, the thrust of the scientific research may be to invent around a competitor's IP position. Producing a timely, proactive PC is a wise resource expenditure. It permits an early assessment of the IP landscape and allows management decisions to be made well in advance regarding which components, technologies, and processes are best to incorporate into the product under development, in order to avoid using those which are not owned or cannot be readily licensed.

A patent attorney can then draft a freedom to operate (FTO)[28] opinion. This is written on the basis of the para-legal PC, the attorney's thorough search of various patent databases, a review of the applicable patent claims, an understanding of the appropriate laws, and an analysis of all the pertinent documents such as Material Transfer Agreements (MTAs)[29] that might impact the product being developed. Finally, with all of this in place, the patent attorney renders an FTO opinion.

Such an FTO opinion is ideally performed as early as economically feasible in the product development cycle as a pre-emptive "IP/TP rights hygiene" review. However, because of the significant resource

28 See the CAMBIA (Center for the Application of Molecular Biology to International Agriculture) website for useful information on IP issues in agriculture (available at <http://www.cambia.org. au/main/ip_primer_fto.htm>). Concerning FTO, "Determination of 'freedom to operate' – requires technical knowledge, a broad business overview, detailed understanding of patent claims in all relevant countries, understanding of markets and national jurisdictions, and knowledge of litigation and negotiation procedures in relevant jurisdictions. Our approach is for specialists with scientific and patent skills to work with researchers and business people to analyze relevant intellectual property and to develop appropriate strategies that will allow innovations to be implemented effectively." *See generally* Eran Binenbaum et al., *South-North Trade, Intellectual Property Jurisdictions and Freedom to Operate in Agricultural Research on Staple Crops*, International Food Policy Research Institute, Environment and Production Technology Division (2000).

29 An MTA is a type of contractual agreement that offers a variety of proprietary protection, frequently for materials (e.g., TP) not covered by patents. In agricultural research, MTAs are used in the transfer of plant genetic resources, plasmid constructs, transformation vectors, etc. *See* Michael Blakeney et al., *Intellectual Property Rights and Agricultural Biotechnology,* in *Managing Agricultural Biotechnology: Addressing Research Program Needs and Policy Implications* 209 (Joel I. Cohen ed., CABI Publishing 1999); *see also* Tai-Sen Soong, *Industrial Research and Business Development: Experiences From the Singapore Institute of Molecular Agrobiology,* in *Managing Agricultural Biotechnology: Addressing Research Program Needs and Policy Implications* 272 (Joel I. Cohen ed., CABI Publishing 1999).

requirement for such a FTO review, every agri-biotech R&D organization will be limited in the number of FTO opinions that it is willing to initiate. Further, because nearly all statutory protection is based on national law rather than international law, a separate FTO review is required for each country where a product will be made, used, imported, or sold. In addition, because new patents are continually issuing while others are expiring, the IP landscape is in continual flux. An FTO opinion is therefore a snapshot, and thus, is a risk management opinion regarding a particular product at a particular time for a particular country.

In a product deconstruction, it is vitally important to distinguish between IP rights and TP rights. This cannot be overemphasized. All IP issues need to be searched and all TP concerns must also be accurately identified and assessed. The sources of TP from other parties must be clearly documented to ensure that such TP has been obtained under an appropriate MTA. It is similarly important to assure that the source of the TP had a legitimate right to distribute that TP. A review of the MTAs will clarify the legitimate ownership of such TP as was used to produce the new agri-biotech product and will lay the groundwork for knowing if the developing country scientists will have commercial use and/or distribution rights.

As a part of IP/TP rights analysis attached to a new agri-biotech product, germplasm rights must be thoroughly investigated. This entails reviewing the source of all germplasm that is used to produce the new product. It must be determined if germplasm is protected, for example, by plant variety protection, a plant patent, or a utility patent.[30] The germplasm variety, inbred, or breeding population used to develop a transgenic product represents the foundation of that

30 Janice A. Kimpel, *Freedom to Operate: Intellectual Property Protection in Plant Biology and its Implications for the Conduct of Research*, 37 Annual Rev. Phytopathology 29 (1999) (A form of protection for plant varieties, similar to a patent, but with some significant exemptions. The U.S. Plant Variety Protection Act of 1970, amended in 1994, provides plant variety protection certificates for sexually and clonally, i.e., tuber-bearing, crops) (Expansion of the U.S. patent law in 1930, which provided provisions for the patenting of asexually propagated plants excluding uncultivated and tuber-propagated species); Frederic H. Erbisch & Carlos Velazquez, *Introduction to Intellectual Properties,* in *Intellectual Property Rights in Agricultural Biotechnology* 3 (Frederic Erbisch & Karim Maredia eds., CABI Publishing 1998) (An exclusive right given to an inventor to exclude all others from making, using, and/or selling the invention. The right the inventor possesses depends on which country issued the patent. Claims on utility patents relating to plants may extend to germplasm).

product. A detailed tracing of plant pedigrees with a determination of any rights or licenses attached to the germplasm (e.g., "bag tags"),[31] that impose any limitation on the use of and/or distribution of seeds and their progeny, must be duly carried out far in advance of product introduction. This analysis of the source of all germplasm must be included in the FTO opinion.

A product deconstruction of Golden Rice is presented in the following section.

Summary of Analyses

The overall product deconstruction of Golden Rice[32] tentatively identified 15 TP components and 70 patents (with 31 assignees)[33] of potential relevance. A great deal of this complexity stemmed from Golden Rice being a multi-transformant. Genes (enzymes/enzymatic activities/steps) required to catalyze four steps in the carotenogenic biosynthetic pathway were successfully engineered into rice seed endosperm.[34] Each of these, in turn, was assembled into a genetic transformation construct, complete with plant transcription promoter and termination sequences, as well as appropriate selectable markers. In the product deconstruction of Golden Rice, four major components were examined:

1. Plant/seed source, the rice race japonica (TP309), which is a tropical variety adapted to Taiwan;[35]

31 Peter J. Goss, *Guiding the Hand That Feeds: Toward Socially Optimal Appropriability in Agricultural Biotechnology Innovation*, 84 Cal. L. Rev. 1395 (1996).

32 For a detailed description of the product deconstruction and IP/TP analysis of pro-vitamin A rice (i.e., Golden Rice), see R. David Kryder et al., *The Intellectual and Technical Property Components of pro-Vitamin A Rice (GoldenRiceTM): A Preliminary Freedom-To-Operate Review,* ISAAA Briefs No. 20, at 56 (2000).

33 It is of interest to note that every primary assignee was situated in an industrialized country (i.e., Belgium, France, Germany, Israel, Japan, Netherlands, Switzerland, U.K., and the U.S.).

34 *See* Ye et al., *supra* n. 17. Phytoene synthase (enzyme) = psy (daffodil gene); Phytoene desaturase (enzyme) = crtI (bacterial gene); Zeta-carotene desaturase (enzyme) = crtI (bacterial gene); Lycopene cyclase (enzyme) = lcy-b (daffodil gene).

35 For a discussion of the IP issues currently being debated with regard to the CGIAR germplasm collections, see Susan H. Bragdon, *Recent Intellectual Property Rights Controversies and Issues at the CGIAR,* in *Agriculture and Intellectual Property Rights, Economic, Institutional and Implementation Issues in Biotechnology* 77 (Vittorio Santaniello et al. eds., CABI Publishing 2000).

2. Gene constructs, e.g., cloning vectors (pBluescriptKS);plant transformation vectors (pBin19hpc, pZPsC, pZLcyH);

3.Transformation (Agrobacterium-mediated), tissue culture (scutella culture), plantlet regeneration (NB medium), as well as other techniques; and

4. DNA amplification, the polymerase chain reaction (PCR), and the enzyme that catalyzes this reaction (Thermus aquaticus "Taq" polymerase).

In turn, each of these major component categories was further dissected to yield deeper layers of complexity in the product. For example, the plant transformation vector pBin19hpc is a complex construct, with numerous subcomponents and processes integral to its generation, among these: the plant gene promoter CaMV35S; the seed endosperm specific gene promoter Gt1; the selectable marker nptII (kanamycin resistance); the pea Rubisco small subunit transit peptide (DNA); the selectable marker aphIV (hygromycin resistance); the carotenoid biosynthetic gene psy (phytoene synthase); the carotenoid biosynthetic gene crtI (phytoene desaturase); Agrobacterium-mediated transformation; and co-transformation technology. Each of these components might have IP and/or TP rights attached to it, potentially affecting the eventual FTO opinion. IP and TP issues potentially constraining the distribution of Golden Rice will vary on a country-to-country basis.

The product deconstruction of Golden Rice, as well as any similarly complex product, is additionally challenging due to the added factor of uncertainty. Four types of uncertainty are considered here:

(1) *Complexity of assignees on patents.* In the case of Golden Rice, thirty-one were tentatively identified.[36] However, it is important to note that these are the original assignees as listed on the patent cover pages. Because the corporate world is in a constant state of change, determining precisely which entity has the right to grant licenses for a particular component or process is not always straightforward. Indeed, as companies re-structure, sell/assign patents, or grant licenses, with or without the right to sub-license, the degree of uncertainty increases.

36 *See* Kryder et al., *supra* n. 32.

(2) *Absence of MTAs for TP.* If a MTA for a specific TP component is not available, this does not mean that distribution of that component is without restrictions. On the contrary, such absence of a MTA probably signals the need for greater caution and deeper investigation due to the added uncertainty which this produces. Although most agri-biotech research facilities in industrialized countries have functioning technology transfer offices, it is not uncommon for researchers to bypass the procedures set up by these offices. For example, scientists, particularly those at public sector research facilities, have long exchanged TP components (e.g., plasmid constructs, gene promoters, antibodies) very casually. Therefore, the absence of a MTA for a particular TP component should be heeded as a warning sign and not some sort of "fortuitous convenience."

(3) *Import/export issues.* The potential impact of international movement (import/export) of Golden Rice adds an additional layer of complexity to the international IP landscape. For example, if a product is produced outside the U.S. using an unlicensed U.S. patented process, U.S. law prohibits the importation of such products back into the U.S.[37] Similar provisions are incorporated into the language of the Trade-Related Aspects in Intellectual Property Property Rights agreement.[38] As the IP landscape evolves, worldwide IP harmonization proceeds, and the globalization of biotechnology extends more and more to developing countries, this situation will require continual and careful attention.[39]

(4) *Static (narrow time-frame) vs. dynamic (broad time-frame) PC analysis.* There is uncertainty and attendant risk associated with static versus dynamic PC analysis. Binenbaum et al. have observed that since most of the IP present in Golden Rice is not protected in the majority of regions where it is to be distributed, the PC analysis (to the

37 *See* 35 U.S.C. § 271 (g), 287(b), 295; *see also* <http://www.uspto.gov/>.

38 *See* Trade-Related Aspects in Intellectual Property Rights, § 28(1)(b); *see also* <http://www.wto.org/>. Note: Trade-Related Aspects in Intellectual Property Rights obligations are binding on any WTO signatory country.

39 David K. Y. Tang & Mary K. Williamson, *Intellectual Property Rights,* in *The International Lawyer's Deskbook* 109 (ABA Sec. Intl. L. Prac. 1996); Edgar J. DaSilva, *Review: Biotechnology: Developing Countries and Globalization*, 14 World J. Microbiology Biotechnology 463 (1998).

extent performed for Golden Rice) is largely not applicable.[40] In a static time frame, this is a correct and coherent observation. However, when reconsidered within the context of the dynamic nature of the international IP landscape, the uncertainty of future changes and developments, whether it be five, ten, or twenty years ahead, predominates. This persistent level of uncertainty, therefore, gives good reason for a dynamic, comprehensive, and global PC analysis. Hence, having better knowledge of the global IP landscape facilitates informed risk assessment (i.e., a greater number of potentialities can be anticipated). The two paradigms (static and dynamic) are not mutually exclusive, rather, they are two legitimate viewpoints. The static paradigm is an analysis of a "snapshot," and the dynamic paradigm relates more to the complex and fluid realities of international development and the harmonization of global IP rights systems. Related to this is the viewpoint that the entities which produce/own the most advanced agri-biotech applications released in industrialized countries will not seek IP rights protection on these products in developing countries. As a result, due to this lack of strong IP rights protection, developing countries would have a distinct advantage to be able to access (i.e., "pirate") these new products. Indeed, in the short term this may be true. However, a longer-term perspective suggests that such an approach would bring developing countries the greater risk of only obtaining second-tier products, rather than those that are truly cutting-edge. Unfortunately, this limitation would principally impact the developing countries that can benefit most from products such as Golden Rice.

Options

The preliminary PC analysis, as summarized in this paper, was conducted to better understand the current IP/TP rights situation so that options and alternative future strategies can be discussed and developed. Resource-poor farmers and rice consumers in developing

40 *See* Binenbaum et al., *supra* n. 28; Kryder et al., *supra* n. 32 (Of the approximately 70 patents and PCT applications tentatively identified as potentially related to Golden Rice, the number of PCT applications listing major rice producer developing countries as designated states represented a subset: China on eleven, India on five, Indonesia on six, Vietnam on eight, and Sri Lanka on eleven PCT applications, respectively).

countries where rice is a staple are intended to be the ultimate beneficiaries of the deployment of Golden Rice. This desired end result, of providing farmers and consumers with a superior product, is the same regardless of the type of donor/recipient entities (i.e., private corporate, public university, national agricultural research center, philanthropic) that may be involved. The means and acceptable level of risk will likely vary depending on the nature of these organizations.

Hence, as a risk management tool, this study can serve as a template for an organization's assessment and management of risk (i.e., the degree of risk that it is willing to assume). What we present here, therefore, is a framework within which an IP/TP risk management course of action can be mapped out, taking advantage of a maximum amount of data that can realistically be assembled, analyzed, and organized. Furthermore, since numerous types of organizations are potentially involved and the term "developing country" is a broad categorization for many different countries, each with unique circumstances, a blanket recommendation is not possible.

Capacity building in IP/TP risk assessment and management is also of critical importance.[41] In that respect, the authors present six alternative options regarding the IP/TP risk management of Golden Rice.[42] Then it is hoped that, as full partners, developing and industrialized countries can proceed with deliberation and the decision to find the most appropriate process for the development, distribution, and production of agri-biotech products such as Golden Rice.

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41 Karim M. Maredia & Frederic H. Erbisch, *Capacity Building in Intellectual Property Management in Agricultural Biotechnology*, *Intellectual Property Rights in Agricultural Biotechnology* 49 (Frederic H. Erbisch & Karim M. Maredia eds., CABI Publishing 1998). Capacity building is a phrase frequently used in international development literature, broadly meaning "the strengthening and/or development of human resources and their institutional support structures."

42 Six previously proposed strategies for an international plant breeder to obtain the processes and products needed for modern breeding, presented as potential alternatives for consideration, include: 1) purchasing the necessary licenses; 2) cross-licensing; 3) merging with a holder of necessary technology; 4) getting a research license; 5) ignoring the problem and hope it will go away; and 6) making a market segmentation deal. For further elaboration of these strategies, see Brian D. Wright, *International Crop Breeding in a World of Proprietary Technology*, in *Agriculture and Intellectual Property Rights, Economic, Institutional and Implementation Issues in Biotechnology* 127 (Vittorio Santaniello et al. eds., CABI Publishing 2000); *see* Kryder et al., *supra* n. 32.

Option 1: *Invent around the current patents.* This is an intensive science and research-based approach, which entails developing and inventing alternative ways to "regenerate" Golden Rice. This could involve using alternative biosynthetic genes to engineer rice that accumulates carotenoids in the seed endosperm, hence an entirely new invention. For example, genes from plant sources might replace the bacterial genes, which had been used to originally generate Golden Rice. However, because it attempts to reduce the reliance on patents owned by others, this option may, relatively speaking, be too time consuming or costly, and, for scientific reasons, may be extremely laborious or not even feasible.

Option 2: *Re-design the constructs.* This is a product-development based approach and involves the re-design and re-engineering of the molecular constructs to purposely avoid certain TP and/or IP constraints, depending on the language found in relevant patents or licenses. Redesigning the constructs might involve reassembling the various molecular pieces found in Golden Rice, with possible substitutions (e.g., different markers and/or promoters instead of attempting to obtain these as "pre-assembled" packages). This approach may be quite effective, but, at best, science is not easily predictable and, at worst, such an approach will require considerable time (possibly three to five years).

Option 3: *Approach all current IP/TP owners with a request that they relinquish their proprietary claims.*[43] This is a humanitarian approach focused on public perception. Public or private statements of rights abandonment by the certified owners/assignees for each IP/TP right would eliminate all FTO issues attached to commercial activities with Golden Rice. This approach, of course, would greatly simplify licensing negotiations. However, a royalty-free license might still be required due to various liability/indemnity reasons. Further, such an

43 *See e.g.* <http://www.cbsnews.com/now/story> (Aug. 4, 2000). Monsanto announced it will give away free licenses to use its patented technology for so-called "golden rice" and other genetically engineered rice varieties that advocates say could save millions of Third World children.

approach might work on high profile products like Golden Rice, but might not provide full freedom to operate for all new agri-biotech products.

Option 4: *Ignore all IP and TP rights claims and just produce and distribute the agri-biotech product.* This is a short-term perspective with the lowest initial cost. However, longer-term difficulties are likely to ensue if this option is followed. For example, lawsuits, delays of product distribution, limitations on importation capabilities, and poor relations with IP/TP owners are some of the unpleasant possibilities that might flow from this option.

Option 5: *Seek licenses from all of the IP and TP rights owners.* This is the licensing approach. It would require the acquisition of an appropriate license for each individual IP/TP right connected to Golden Rice. The nature of the license negotiated would be determined by the needs of the potential licensee, as well as by what the licensee and licensor mutually determine to be required. This is the safest route to distribution, and ensures good, long-term relationships with the IP/TP rights holders. However, this option is complex, costly, and potentially very time consuming. Furthermore, given the relatively limited legal and governmental infrastructure in many developing countries, the owners of the IP/TP rights may be reluctant to consummate such licenses until the recipients exhibit additional IP rights management capacity.

Option 6: *A mix of all of the options 1 to 5.* This represents a pragmatic, realistic approach to obtaining full FTO for Golden Rice. Due to the flexibility imparted by taking advantage of the numerous available options, this is the most effective route for the distribution of Golden Rice. However, it still requires that both the recipients of Golden Rice and the donors understand and recognize the issues that are involved.

Discussion

Sustainable, Equitable, and International Agri-biotech Transfers: Managing Risks and Maximizing Opportunities

Despite current disagreements over the appropriateness of various proposed IP regimens and inconsistencies in enforcement of IP laws throughout the developing world, the inexorable movement towards global harmonization of IP rights systems appears highly likely.[44] This trend is linked to the continuing expansion of the global economy.[45] As the legal norms for IP rights protection become progressively more consistent at the international level (i.e., the international deployment of IP systems similar to those that have proven to be successful in industrialized countries) trans-national corporations are likely to increase operations in developing countries.[46] Worldwide recognition of, and adherence to, IP rights harmonization should facilitate the participation of many countries as full partners in the global economy.[47] For developing countries, agricultural improvement is a top priority.

When considering the global harmonization of IP rights protection, certain realities must be appreciated. Developing countries will change, but it is critical to recognize that such change is gradual, and proceeds

44 Lorna Brazell, *Strategies for Minimizing IP Risks*, 120 Patent World 19 (2000); *see* DaSilva, *supra* n. 39; *see* Tang & Williamson, *supra* n. 39.

45 John G. Fernald & Victoria Greenfield, *The Fall and Rise of the Global Economy*, 164 Chi. Fed Ltr. 1 (2001).

46 The Nuffield Council on BioEthics, May 1999, Genetically Modified Crops: The Ethical and Social Issues, The Nuffield Foundation, London.

47 This viewpoint represents an optimistic affirmation of the value of IP rights in international agricultural development. The polarity of viewpoints has been summarized by Lesser et al.: "One school of thought maintains that developing countries with effective IPRs will attract more research and development (R&D) spending, particularly from the private sector. A second widely held view disputes this conclusion, maintaining that, at the extreme, IPR amounts to economic colonialism." William Lesser et al., *Intellectual Property Rights, Agriculture, and the World Bank,* in *Intellectual Property Rights in Agriculture, The World Bank's Role in Assisting Borrower and Member Countries* 1-21 (Lele et al. eds., The World Bank 1999). In a similar manner, Ismail Serageldin states that: "Supporters of patenting point out that if the private sector is to mobilize and invest large sums of money in agrobiotechnology R&D, it must protect and recoup what it has put in. On the other side of the argument is fear that patenting will lead to monopolization of knowledge, restricted access to germplasm, controls over the research process, selectivity in research focus, and increasing marginalization of the majority of the world's population." *See* Serageldin, *supra* n. 9.

stepwise. In this context, a "three-stage model" of IP rights evolution in developing countries is useful:[48]

1. The first stage is in those countries with the lowest level of economic development. In such countries, IP rights protection is not an issue because the economic and technological infrastructure is below the basic requirement needed for utilization of technological advances.

2. The second stage is in those countries that can utilize advanced technologies, but the economic level of development, or the domestic supply of capital, is still low. In these circumstances, technology piracy routinely occurs.

3. The third stage is in those countries where public and private entities can generate world-class inventions. Here, IP rights protection becomes essential in order to credibly and productively participate in the international economic community, with reciprocal recognition and enforcement of IP rights.

Coupled with the global harmonization of IP rights is the inexorable international spread of biotechnology into agricultural systems.[49] The global planting of transgenic crops continues to increase. In industrial countries where the total transgenic acreage is currently concentrated, the rate of deployment of transgenic crops currently appears to be leveling off. However, in developing countries, the planting of transgenic crops is increasing significantly.[50] In both industrialized and developing countries where transgenic crops have, until recently, been primarily agronomic (crop-protection) based, value-added products with broad application such as Golden Rice are on the horizon.[51]

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48 Stefan Kirchanski, *Protection of U.S. Patent Rights in Developing Countries: U.S. Efforts to Enforce Pharmaceutical Patents in Thailand*, 16 Loy. L.A. Intl. & Comp. L.J. 569 (1994); *see also* Lesser et al., *supra* n. 58. (a somewhat parallel model is discussed: "Sherwood (1997) distinguishes between three levels of IPR protection: (1) nonrobust, (2) TRIPs-compatible, and (3) investment stimulating/robust.").

49 *See* Rausser & Small, *supra* n. 16.

50 Clive James, *Global Status of Commercialized Transgenic Crops: 2000*, ISAAA Briefs No. 21 (ISAAA 2000). The global increase of transgenic crops between 1999 and 2000 was 11%, equivalent to 4.3 million hectares. Of this increase, 84% was in developing countries.

51 *See* Dunwell, *supra* n. 15; Potrykus, *supra* n. 20.

Due to the differing perspectives and circumstances of industrialized and developing countries, establishing a foundation for fair and equitable negotiations vis-à-vis IP rights is not simple. Many developing countries may not consider the legal recognition of foreign patents to be important.[52] When negotiating license terms, developing countries are usually at a disadvantage because key personnel are inadequately trained[53] and most developing countries have an insufficient number of licensing officials and IP managers.[54] Therefore, in such developing countries, since agriculture is considered integral to national sovereignty, piracy of agri-biotech is more likely to be considered justifiable.[55] The unfortunate legacy of colonialism complicates the situation even more.[56] From the industrialized country perspective, investors view the IP portfolio of a company as an absolutely essential component.[57] The system of IP rights protection of a potential partner influences technology transfer and investment decisions.[58] Therefore, industrialized countries firmly believe that a healthy patent system encourages invention/investment in a sustainable fashion.[59] Notwithstanding the different viewpoints between developing and industrialized countries, improved IP rights harmonization appears to be integral to the economic development of all countries.[60] Hence, if IP issues are adequately addressed,

52 *See* Kirchanski, *supra* n. 48.

53 *See* Lesser et al., *supra* n. 47.

54 *See* Nuffield Council on BioEthics, *supra* n. 46.

55 *See* Kirchanski, *supra* n. 48.

56 *Id.*

57 Cliff D. Weston, *Chilling of the Corn: Agricultural Biotechnology in the Face of U.S. Patent Law and the Cartagena Protocol*, 4 J. Small Emerging Bus. L. 377 (2000).

58 *See* Lesser et al., *supra* n. 47.

59 David G. Scalise & Daniel Nugent, *International Intellectual Property Protections for Living Matter: Biotechnology, Multinational Conventions and the Exception for Agriculture*, 27 Case W. Res. J. Intl. L. 83 (1995).

60 *Id.* In addition, Lesser states that "Adequate (IPR) protection is credited with three benefits: (i) encourages investment and creativity; which in turn (ii) enhances technological progress, a critical aspect of U.S. competitiveness; and (iii) attract(s) needed foreign know-how and investment to developing countries." *See* William Lesser, *Intellectual Property Rights Under the Convention on Biological Diversity*, in *Agriculture and Intellectual Property Rights, Economic, Institutional and Implementation Issues in Biotechnology* 35 (Santaniello et al. eds., CABI Publishing 2000). For two studies (using economic models) on the potential benefits of strengthened IP rights to developing countries, see Robert E. Evenson, *Intellectual*

globalization presents opportunities to move agri-biotech internationally, thereby fostering the technological and legal infrastructure conducive to domestic R&D activities (that is, "home-grown product development") within developing countries.

Within the context of these disparate positions, momentum for constructive change is essential. Industrialized countries need to understand the evolutionary process of IP protection in developing countries and to provide incentives to facilitate accelerated progression from Stage 1 (i.e., minimal technology infrastructure) to Stage 3 (i.e., technology infrastructure with IP protection).[61] Correspondingly, developing countries need to fully recognize the necessity of stable and enforceable IP systems, which will support the sustainable movement of advanced agri-biotech into their countries. Under the best of circumstances, this is a win-win scenario.[62] The long-term benefits to the technology providers (most likely industrialized countries) include: protection of IP portfolios; protection and expansion of commercial markets, while providing technology to those who need it most; improved public perception of trans-national corporations; and new, sustainable partnerships. The long-term benefits to technology recipients (mostly developing countries) include: increased agricultural outputs; improved agricultural products (e.g., Golden Rice); opening of export markets; access to "hands-on" knowledge and skill of practitioners of the art; legal access to patented technologies at a more fundamental level;[63] fostering of a national infrastructure for

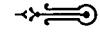
Property Rights, Access to Plant Germplasm, and Crop Protection Scenarios in 2020, 39 Crop Sci. 1630 (1999); James R. Markusen, *Contracts, Intellectual Property Rights, and Multinational Investment in Developing Countries*, 53 J. Intl. Econ. 189 (2001). For empirical data supporting the potential benefits of strengthened IP rights to developing countries, see Keith E. Maskus & Guifang Yang, *Intellectual Property Rights, Foreign Direct Investment and Competition Issues in Developing Countries*, 19 Intl. J. Tech. Mgt. 22 (2000); Carlos A. Primo Braga & Carsten Fink, *International Transactions in Intellectual Property and Developing Countries*, 19 Intl. J. Tech. Mgt. 35 (2000). The potential short and long-term economic impact (e.g., foreign direct investment) of IP rights protection in developing countries is complex, whereas benefits may be of a primarily dynamic nature, there might also be some benefit to developing nations in the static perspective.

61 *See* Kirchanski, *supra* n. 48.

62 Mary Arends-Kuenning & Flora Makundi, *Agricultural Biotechnology for Developing Countries*, 44 Am. Behavioral Scientist 318 (2000) (discussing the benefits to both technology donors and recipients in the specific case study involving the transfer of viral resistance technology in potatoes from Monsanto Corp. to Mexico).

sustainable technology development; fostering of a legal infrastructure;[64] and new, sustainable partnerships.

Golden Rice represents a specific case study/model system of an agri-biotech product that can be transferred to the developing world. The genetic engineering of value-added nutritional quality into Golden Rice is a turning point both scientifically and in terms of international technology transfer. Scientifically, the engineering of plant (in this case rice) metabolism to enhance accumulation of carotene is a complex and pioneering advance. To transfer this promising technology from the industrialized sources who own it to the developing countries of the world, where it is most needed, is equally complex. This paper proposes six short-term strategies for management of IP risk potentially associated with the international movement of Golden Rice. However, over the longer term, increased international harmonization of IP laws and management might serve to ameliorate many of these risks, and hence facilitate the sustained transfer of Golden Rice as well as future advances in agri-biotech.



63 David R. Purnell, *International Implications of New Agricultural Biotechnology*, 25 U. Mem. L. Rev. 1189 (1995)

64 For a broad discussion on the importance of property rights to the overall betterment of developing countries and their societies, see *Poverty and Property Rights*, Economist 20 (Mar. 31, 2001).