

**CO-DEVELOPING DRUGS WITH INDIGENOUS
COMMUNITIES: LESSONS FROM PERUVIAN LAW AND THE
AYAHUASCA PATENT DISPUTE**

Daniel S. Sem*

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I. INTRODUCTION

[1] This paper will examine the issues surrounding the co-development of drugs derived from traditional medicines used by indigenous peoples in Amazonia, with a focus on Peru. In particular, this paper will explore what national, regional and international legal structures are in place to protect the interests of indigenous peoples, while at the same time providing medical benefit to the world. This issue is explored in the context of Peruvian, U.S., and international treaties – especially the TRIPS agreement, the Andean Community, *sui generis* protections, and the US-Peru Trade Promotion Agreement.

[2] Commenters have noted that historically, drug development ventures based on traditional medical knowledge (TMK) from Amazonia had not been pursued in a manner that was fair and just to the indigenous peoples who owned this knowledge.¹ There are two pragmatic “fairness”

* The author is Dean and Professor of Business, and Professor of Pharmaceutical Sciences, at Concordia University Wisconsin. He would like to thank Dean Arneson, Pharm.D, Ph.D. (Professor and Dean of the CUW School of Pharmacy) for providing the pictures from his trips to Peru, and Professor Kali Murray at Marquette University for many helpful comments and guidance. This research was supported, in part, by National

considerations in the U.S.-Peruvian co-development of drugs derived from indigenous peoples in Amazonia, based on TMK.² First, any co-venture should identify the best legal structure(s) that protects the interests of researchers in both Peru and the United States, and the need to also protect the interests of indigenous peoples.³

[3] Second, any co-venture should consider whether international pharmaceutical patent protection is inherently biased to protect drugs as defined in western (U.S.) medical practice, versus the traditional and historically-based practices of indigenous peoples.⁴ There are potential problems for intellectual property (IP) protection, since medical treatments in traditional cultures are typically developed by groups over long periods

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¹ See, Manuel Ruiz, Isabel Lapeña, and Susanna E. Clark, *The Protection of Traditional Knowledge in Peru: A Comparative Perspective*, 3 WASH. U. GLOB. STUD. L. REV. 755, 760 (2004).

² See Ley N° 27811 [Law No. 27811], art. 5, Aug. 10, 2002, El Peruano, <http://www.wipo.int/edocs/lexdocs/laws/es/pe/pe011es.pdf>, archived at <https://perma.cc/28J9-VW3L> (trans. at <http://www.wipo.int/edocs/lexdocs/laws/en/pe/pe011en.pdf>, archived at <https://perma.cc/99RJ-GWCM> (Peru) (Law Introducing a Protection Regime for the Collective Knowledge of Indigenous Peoples derived from Biological Resources).

³ See generally, Howard Mann, *Intellectual Property Rights, Biodiversity and Indigenous Knowledge: A Critical Analysis in the Canadian Context*, Report Submitted to the Canadian Working Group on Articles 8(j) of the Convention on Biological Diversity (Ottawa, 1997) (Analyzing intellectual property rights of Aboriginal people in Canada with regard to today's laws, and addressing the correlating barriers and opportunities for the use of intellectual property rights in relation to indigenous knowledge and resources).

⁴ See, e.g., Heather A. Sapp, *Monopolizing Medicinal Methods: The Debate Over Patent Rights for Indigenous Peoples*, 25 TEMP. J. SCI. TECH. & ENVTL. L. 191, 196 (2006) (“...[W]estern patent systems appropriately exclude [Traditional Knowledge] from patent protection.”).

of time, as opposed to the more rapid discovery by individual researchers or companies in the pharmaceutical industry. In the former situation, it may be impossible to patent a medical treatment if it has been “in use” for many years since prior public use can create novelty or obviousness bars to patenting.⁵ Furthermore, most traditional medicines are mixtures of natural products (*i.e.*, chemical compounds that are “products of nature”), comprised of two or more active chemical ingredients; whereas, drug discovery and development in the U.S. focuses on *composition of matter* patent protection for single chemical compounds. Additionally, most pharmaceutical companies will not develop drugs in the U.S., unless they can obtain *composition of matter* patent protection on single chemical compounds.

[4] Given these differences in how medicines are developed and used in the U.S. versus Peru, coupled with different views of IP and TMK, what is the best IP protection and collaborative structure for co-development of medicines by pharmaceutical researchers in the U.S. and Peru, and traditional healers (shamans) in Amazonia? This paper explores the legal and cultural issues surrounding this question, then proposes solutions that build on existing legal structures and trends in the U.S. and Peru.

[5] Section I of this paper introduces challenges associated with co-development of drugs by researchers, defines key terms and concepts, and provides an example of one TMK-based medicine used by Amazonian shamans. Section II presents an attempted drug development initiative where indigenous rights were ignored. This involved the attempted patenting in the U.S. of a traditional medicine from Amazonia, ayahuasca. Section III of this paper explores the various legal structures and treaties in Peru, the Andean region, and the U.S., as well as international treaties that

⁵ See Gene Quinn, *The Impact of the America Invents Act on the Definition of Prior Art*, IP WATCHDOG (Oct. 3, 2012), <http://www.ipwatchdog.com/2012/10/03/the-impact-of-the-america-invents-act-on-the-definition-of-prior-art/id=28453/>, archived at <https://perma.cc/6RGD-KTJ7>.

pertain to intellectual property rights (IPR) of indigenous peoples, with respect to their general traditional knowledge (TK), and TMK in particular. Section IV builds on this background, and proposes a collaborative co-development research agreement that could be used by U.S. and Peruvian researchers who team up to discover and develop new medical treatments based on TMK. Such collaborations could be a tremendous new source of medicines.

[6] As the pipeline of new medicines coming from the U.S. pharmaceutical industry is dwindling, research and development costs are increasing and productivity of the industry is decreasing.⁶ These forces are converging to create intense market pressures, and perhaps more openness to explore new solutions to address the world's medical needs.⁷ These solutions will likely include academic researchers in the U.S. (and Europe) teaming up with researchers in Amazonia, to learn from their indigenous peoples.⁸ Together, they can co-develop new medical treatments based on the TMK possessed by Amazonian shamans; but, this can only work efficiently and fairly if the interests of the collaborating research teams and of the indigenous peoples from which the TMK originates, are

⁶ See Ish Khanna, *Drug Discovery in the Pharmaceutical Industry: Productivity Challenges and Trends*, 17 DRUG DISCOVERY TODAY 1055, 1088 (2012), http://ac.els-cdn.com/S1359644612001833/1-s2.0-S1359644612001833-main.pdf?_tid=4b6731ea-7ede-11e6-ab65-00000aab0f01&acdnat=1474340569_16e7ca651037b847bcc9a375343d47de, archived at <https://perma.cc/Y7QN-4ZQG>.

⁷ *Id.* at 1095-96.

⁸ See e.g., Carolyn Gregoire, *Scientists Put Shamanic Medicine Under the Microscope*, HUFFINGTON POST (Oct. 16, 2015), http://www.huffingtonpost.com/entry/shaman-medicine-autoimmune-disease_us_55f8737be4b0d6492d633c23, archived at <https://perma.cc/K3XP-W3S8>.

considered upfront and with equal weight.⁹ This paper aims to facilitate that process.

A. What are Traditional Knowledge (TK) and Traditional Medical Knowledge (TMK)?

[7] Traditional knowledge (TK) is defined by the World Intellectual Property Organization (WIPO) as “knowledge, know-how, skills and practices that are developed, sustained and passed on from generation to generation within a community, often forming part of its cultural or spiritual identity.”¹⁰ Negotiations on an international legal instrument, developed by the WIPO Intergovernmental Committee (IGC), are focused on developing protections for TK, along with protections for Traditional Cultural Expressions and Genetic Resources. This paper will focus on identifying protective strategies for a subset of TK, with a focus on TMK.

[8] Traditional Environmental Knowledge (TEK) is a subset of TK and the focus of western scientific fields such as ethnobotany and ethnomedicine.¹¹ Martha Johnson defined TEK as “...a body of knowledge built by a group of people through generations, living in close contact with nature. It includes a system of classification, a set of empirical observations about the local environment, and a system of self-management that governs resource use.”¹² TEK can be distinguished from

⁹ *See id.*

¹⁰ WORLD INTELLECTUAL PROP. ORG. (WIPO), *Traditional Knowledge*, <http://www.wipo.int/tk/en/tk/>, archived at <https://perma.cc/96MH-S43M> (last visited Sept. 21, 2016).

¹¹ Joe McCarter & Michael C. Gavin, *Perceptions of the Value of Traditional Ecological Knowledge to Formal School Curricula: Opportunities and Challenges From Malekula Island, Vanuatu*, 7 J. ETHNOBIOLOGY & ETHNOMEDICINE, no. 38, 2011, <https://ethnobiomed.biomedcentral.com/articles/10.1186/1746-4269-7-38>, archived at <https://perma.cc/S8UF-FUQG>.

western science in a number of ways, including that: (a) it is transmitted via oral tradition, (b) is holistic (versus reductionist), (c) is based on a view of social and spiritual connections between life forms, (d) views the natural elements as having a life force (infused with spirit), and (e) explains natural phenomena based on cumulative and collective experiences that are regularly validated and revised over time.¹³ Thus, while TEK bears some resemblance to western scientific knowledge, it is also distinct in many ways.¹⁴ TEK is especially relevant for this paper, since it is a source of TMK.

[9] Traditional medical knowledge (TMK) is a type of TK that centers specifically on the knowledge of traditional healers in their use of plant-based medicines.¹⁵ The World Health Organization (WHO) defines TMK as “the sum total of the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health, as well as in the prevention, diagnosis, improvement or treatment of physical and mental illnesses.”¹⁶ This paper focuses on the use and protection of TMK in

¹² See Martha Johnson, Research on *Traditional Environmental Knowledge: Its Development and Its Role*, in LORE: CAPTURING TRADITIONAL ENVIRONMENTAL KNOWLEDGE 3, 4 (Martha Johnson ed., 1992).

¹³ See Fulvio Mazzocchi, *Western Science and Traditional Knowledge: Despite Their Variations, Different Forms of Knowledge Can Learn From Each Other*, 7 EUROPEAN MOLECULAR BIOLOGY ORGANIZATION REPORTS 463, 463–466 (2006).

¹⁴ See Graham Dutfield, *TRIPS-Related Aspects of Traditional Knowledge*, 33 CASE W. RES. J. INT'L L. 233, 242 (2001).

¹⁵ See Ryan Abbott, *Documenting Traditional Medical Knowledge*, WIPO, 3 (Mar. 2014) http://www.wipo.int/export/sites/www/tk/en/resources/pdf/medical_tk.pdf, archived at <https://perma.cc/2F3G-55CT> citing *Fact Sheet No. 134: Traditional Medicine* WORLD HEALTH ORG. (WHO) <http://www.who.int/mediacentre/factsheets/2003/fs134/en/>, archived at <https://perma.cc/7Q4N-E7Z2>.

Amazonia, with a focus on Peru.

B. TMK as a Source of New Medicines

[10] The pharmaceutical industry benefits greatly from TMK. One estimate is that of the 119 plant-derived chemicals used in modern medicine, 74% have similar current uses as the medicinal plant from which the chemical was identified.¹⁷ The market value of plant-derived medicines was estimated at over \$15 billion in 1990, for United States pharmaceutical sales.¹⁸ Amazonia, and Peru in particular, is an especially rich source of traditional medicines.¹⁹ One of the most prominent and spiritually important traditional medicines to Peruvian shamans is ayahuasca.²⁰

C. Peruvian TMK – Ayahuasca

¹⁶ See WORLD HEALTH ORG. (WHO), GENERAL GUIDELINES FOR METHODOLOGIES ON RESEARCH AND EVALUATION OF TRADITIONAL MEDICINE (2000), http://apps.who.int/iris/bitstream/10665/66783/1/WHO_EDM_TRM_2000.1.pdf, archived at <https://perma.cc/4HZY-45KQ>.

¹⁷ See Norman R. Farnsworth, *Screening Plants for New Medicines*, in BIODIVERSITY 83, 95 (E. O. Wilson ed., 1988).

¹⁸ See Peter Principe, *Economics and Medicinal Plants*, in MEDICINAL PLANTS: THEIR ROLE IN HEALTH AND BIODIVERSITY 42, 44 (Timothy R. Tomlinson & Olayiwola Akerele eds., 1998).

¹⁹ See Rainer W. Bussmann & Douglas Sharon, *Traditional Medicinal Plant Use in Northern Peru: Tracking Two Thousand Years of Healing Culture*, 2 J. ETHNOBIOLOGY & ETHNOMEDICINE, no. 47, 2006, <http://ethnobiomed.biomedcentral.com/articles/10.1186/1746-4269-2-47>, archived at <https://perma.cc/H3E6-GKU8>.

²⁰ See *id.*

[11] Of particular fame and importance amongst shamans in Peru is the ayahuasca plant (*Banisteriopsis caapi*),²¹ of the plant family *Malpighiaceae*. Ayahuasca was discovered and introduced to the scientific community by Harvard biologist and “father of modern ethnobotany,” Richard Evans Schultes.²² In the native Quechua language of Amazonia, ayahuasca means “vine of the soul.”²³ Ayahuasca is used by indigenous peoples in religious and healing ceremonies.²⁴ Shamans have used ayahuasca for centuries to treat various psychiatric disorders, which indigenous peoples sometime believed were associated with witchcraft.²⁵



Fig. 1. Picture of a live ayahuasca root (left panel), and a piece of the root sold in a Peruvian market (right panel).²⁶

²¹ See *infra* Figure 1.

²² See Richard E. Schultes, *The Botanical and Chemical Distribution of Hallucinogens*, 9 J. PSYCHEDELIC DRUGS 247, 251 (1977).

²³ See Kenneth W. Tupper, *The Globalization of Ayahuasca: Harm Reduction or Benefit Maximization?*, 19 INT'L J. DRUG POL'Y 297, 297–303 (2006).

²⁴ See Marlene Dobkin De Ríos, *Banisteriopsis in Witchcraft and Healing Activities in Iquitos, Peru*, 24 ECON. BOTANY 296, 296 (1970).

²⁵ See *id.*

²⁶ E-mail attachment from Dr. Dean Arneson, Pharm.D, Ph.D., Dean of School of Pharmacy, Concordia University Wisconsin, to author (2013) (on file with author).

[12] While available for purchase in markets (**Fig. 1**),²⁷ the use of ayahuasca is generally restricted to shamans or *ayahuasqueros* who possess valuable TMK, since they know best how to prepare it in a way that is safe and effective.²⁸ The ayahuasca plant (*Banisteriopsis caapi*) vine is mixed in defined ratios and manners with plants such as *Psychotria viridis*, then boiled.²⁹ Chemicals from both of these plants work synergistically to produce the desired effect. Specifically, “harmala alkaloid” molecules (**Fig. 2**)³⁰ in ayahuasca inhibit an enzyme called monoamine oxidase (MOA) – preventing the chemical breakdown of the active chemical present in the *Psychotria viridis* plant, dimethyltryptamine (DMT).³¹ DMT produces the psychoactive effects of this traditional medicine by altering the activity in brain synapses of the serotonin receptors (**Fig. 2**).³²

²⁷ See *supra* Figure 1.

²⁸ See De Ríos, *supra* note 24, at 296.

²⁹ See *id.* (stating that the boiled ayahuasca infusion is sometimes mixed with additives like *chacrana*, a Quechua word describing the plant otherwise known as *Psychotria viridis*).

³⁰ See *infra* Figure 2.

³¹ See J.C. Callaway et al., *Pharmacokinetics of Hoasca Alkaloids in Healthy Humans*, 65 J. ETHNOPHARMACOLOGY 243, 244 (1999).

³² See *id.*; see also Dennis J. McKenna, J.C. Callaway & Charles S. Grob, *The Scientific Investigation of Ayahuasca: A Review of Past and Current Research*, 1 HEFFTER REV. OF PSYCHEDELIC RESEARCH 65, 67 (1998); see *infra* Figure 2.

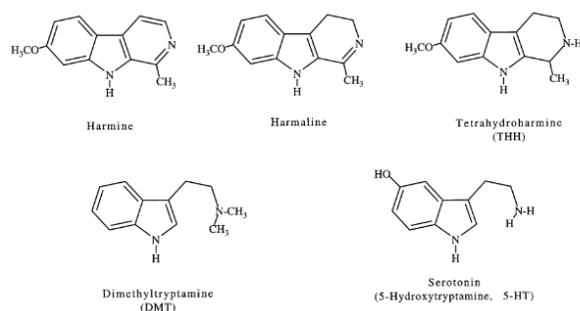


Fig. 2. Active chemical components in ayahuasca teas used by shamans, with serotonin comparison.³³

[13] In cases where shamans develop and administer medical treatments based on TMK, and scientists later explain the molecular basis for that medical effect and identify the active chemical components, who is the inventor? This question, exemplified in the case of ayahuasca, is complicated.³⁴ While the shamans, as TMK practitioners, knew how these plants needed to be mixed to achieve the desired effect, scientists ultimately discovered the molecular reason for needing the mixture.³⁵ Indeed, scientists could extract the active chemical components, mix them in the correct ratio, and develop this as a drug – taken perhaps as a pill. Which is the greater discovery? Both are important, and certainly the shaman’s TMK is a “but for” cause of the scientific (*i.e.* molecular)

³³ See Callaway et al., *supra* note 31, at 245.

³⁴ See, e.g., Andrea Rinaldi & Pryia Shetty, *Traditional Medicine for Modern Times: Facts and Figures*, SCIDEV.NET (June 6, 2015), <http://www.scidev.net/global/medicine/feature/traditional-medicine-modern-times-facts-figures.html>, archived at <https://perma.cc/9A3E-BUSS>.

³⁵ See generally Bussman & Sharon, *supra* note 19 (discussing Chiappe and Millones as the first scientists to study the Shaman’s use of ayahuasca).

discovery. It seems self-evident that the scientific discovery cannot and should not proceed to the benefit of others, without first considering the rights of the indigenous peoples who made the initial discovery.

[14] By using TMK, Amazonian shamans uncovered a pharmacologically useful and valuable medical treatment from ayahuasca. This treatment exists only because of specific molecular level interactions. While these molecules might not be patentable subject matter (as products of nature)³⁶, combinations of molecules might be considered patentable subject matter, as composition of matter. Pharmaceutical companies will typically only develop a drug if composition of matter protection can be obtained. Thus, co-development of TMK-derived drugs poses a challenge to the IP community, in terms of how a useful medical treatment can be patented. It is possible to patent at the level of the plants used, the active chemical components extracted from the plants, or mixtures of those active chemical components.

[15] TMK-derived drug development also challenges the international community to consider whether it is ethically permissible to allow this type of patenting. Is it right to allow researchers who discover the active molecular components, used in traditional medicines, to patent and then profit from their scientific discoveries, without returning benefit to the shamans? Can they patent them, or are there 35 U.S.C. §102 novelty (prior art) bars that prevent patenting, since shamans have been treating with traditional medicines, like ayahuasca, for centuries? These questions are addressed in Section III. While the scientists who discovered the active chemical components in ayahuasca made no attempt to patent their discovery, there was a significant controversy over an attempt to patent the

³⁶ See Richard Seth Gipstein, Note, *The Isolation and Purification Exception to the General Unpatentability of Products of Nature*, 4 COLUM. SCI. & TECH. L. REV. 2 (2003).

ayahuasca plant itself.³⁷ It was after this ayahuasca patent dispute that significant changes to protect TK and TMK were implemented in Peru.

II. A CASE STUDY IN BIOPROSPECTING OF TMK: LESSONS FROM AYAHUASCA

[16] Despite the fact that ayahuasca use was in the shaman's TMK toolbox for centuries, Loren Miller obtained a U.S. patent, Plant Patent No. 5,751 on the ayahuasca plant (*Banisteriopsis caapi*), which issued on June 17th, 1986 (**Fig. 3**).³⁸

United States Patent [19]		[11] Patent Number: Plant 5,751
Miller		[45] Date of Patent: Jun. 17, 1986
[54] <i>BANISTERIOPSIS CAAPI</i> (cv) 'DA VINE'	[56] References Cited	
[76] Inventor: Loren S. Miller, 1788 Oak Creek Dr., Apt. 407, Palo Alto, Calif. 94303	U.S. PATENT DOCUMENTS	
[21] Appl. No.: 669,745	P.P. 3,008 12/1970 Magnuson Pl./88	
[22] Filed: Nov. 7, 1984	P.P. 4,253 5/1978 Arnold Pl./88	
	OTHER PUBLICATIONS	
	Gates, Bronwen <i>Flora Neotropica</i> Monograph No. 30, <i>Banisteriopsis</i> , Dipteroxy (Malpighiaceae) Published for Organization for Neotropica by the New York Botanical Garden, N.Y. Feb. 18, 1982.	
	<i>Primary Examiner</i> —James R. Feyrer	
	ABSTRACT	
[63] Continuation of Ser. No. 266,114, May 21, 1981, abandoned.	[57] A new and distinct <i>Banisteriopsis caapi</i> plant named 'Da Vine' which is particularly characterized by the rose color of its flower petals which fade with age to near white, and its medicinal properties.	
[51] Int. Cl. ⁴ A01H 5/00		
[52] U.S. Cl. Pl./84		
[58] Field of Search Pl./54		2 Drawing Figures

Fig. 3. Patent on ayahuasca (*Banisteriopsis caapi*).³⁹

[17] Recognizing this as an exploitation of TK and TMK, in what is referred to as “bioprospecting,” David Downes and Glenn Wiser filed a

³⁷ See Leanne M. Fecteau, Note, *The Ayahuasca Patent Revocation Questions About Current U.S. Patent System*, 21 B.C. THIRD WORLD L.J. 69, 70 (2001).

³⁸ See U.S. Patent No. Plant 5,751 (filed Nov. 7, 1984); see *infra* Figure 3.

³⁹ *Id.*

request for re-examination.⁴⁰ Downs and Wisner were with the Center for International Environmental Law (CIEL), working on behalf of the Coordinating Body of Indigenous Organizations of the Amazon Basin (COICA) and the Amazon Coalition, on March 30, 1999.⁴¹

[18] The Miller patent had a single claim, for “a new and distinct (cultivar) of the species *Banisteriopsis caapi*,” which Miller called “Da Vine.”⁴² Downs and Wisner argued this claim was invalid on a number of legal theories, but especially based on prior art that included publications and plant specimen sheets, such as one listed as: “Plants of Cultivation: *Banisteriopsis caapi*, Accessioned Specimen Sheet, The University of Michigan Herbarium (mounted Jan. 5, 1981).”⁴³

[19] Wisner and Downes raised five arguments before the U.S. Patent

⁴⁰ See David R. Downes & Glenn M. Wisner, Center for Int’l Env’tl. Law, *Comments on Improving Identification of Prior Art: Recommendations on Traditional Knowledge Relating to Biological Diversity Submitted to the United States Patent and Trademark Office*, Aug. 2, 1999, at 15, www.ciel.org/Publications/IdentificationofPriorArt.pdf, archived at <https://perma.cc/R26N-LSRW> [hereinafter *Comments on Improving Identifications of Prior Art*]; see also David R. Downes & Glenn M. Wisner, *The Legal Elements of the “Ayahuasca” Patent Case*, Center For International Environmental Law (Mar. 30, 1999), <http://ciel.org/Publications/ayahuascalegalelements.pdf>, archived at <https://perma.cc/F7JE-BFPX> [hereinafter *Legal Elements*].

⁴¹ See Downes & Wisner, *Legal Elements*, *supra* note 40.

⁴² U.S. Patent No. Plant 5,751 (filed Nov. 7, 1984).

⁴³ David R. Downes, et al., Request for Reexamination of U.S. Patent No. Plant 5,751 (Mar. 30, 1999), at 1, <http://www.ciel.org/wp-content/uploads/2015/06/ReexaminationofUSPlantPatent5751.pdf>, archived at <https://perma.cc/L6JE-N6YV>; Downes & Wisner, *Comments on Improving Identifications of Prior Art*, *supra* note 40, at 15.

and Trademark Office (PTO) as to why the Miller patent was not valid.⁴⁴ First, they claimed the existence of significant prior art, which should produce 35 U.S.C. §102 rejections.⁴⁵ Specifically, they argue that the plant Miller is patenting is not new and distinct, because it is “well described in the scientific literature and in the ‘traditional knowledge of indigenous peoples throughout Amazon.’”⁴⁶ *Banisteriopsis caapi* was described in herbarium specimens, as well as a number of more typical printed publications that discuss the medicinal and ceremonial use of ayahuasca.⁴⁷

[20] Second, Wisner and Downes argued that under the U.S. Patent Act one cannot patent plants if they “[are] found in an uncultivated state,” in the wild.⁴⁸ There is a statutory bar in 35 U.S.C. §161 that prevents patenting of plants found in the wild, and this should prevent patenting of Miller’s “Da Vine.” While Miller argues that “Da Vine” was only found in a garden (*i.e.* in a cultivated state), this was apparently not true. *Banisteriopsis caapi* is actually found throughout the Peruvian Amazon region.⁴⁹

⁴⁴ See generally Downes & Wisner, *Comments on Improving Identifications of Prior Art*, *supra* note 40, at 13–16 (discussing arguments against the validity of Miller’s patent).

⁴⁵ See *id.* at 4.

⁴⁶ Daniel S. Sem, *Legal, Ethical and Business Consideration in Developing Drugs Derived from Traditional Medicine*, in Conference Report, UNIV. OF APPLIED SCIENCES UPPER AUSTRIA SCH. OF MGMT. CROSS-CULTURAL BUSINESS CONFERENCE 2016 96, 98 (May 19-20, 2016), https://www.fh-ooe.at/fileadmin/user_upload/fhooe/ueber-uns/kongresswesen/2016/ccbc/allgemein/docs/fhooe-ccbc2016-proceedings-final.pdf, archived at <https://perma.cc/AJN8-PSSK>.

⁴⁷ See Downes, et al., *supra* note 43, at 1–2.

⁴⁸ Downes & Wisner, *Comments on Improving Identifications of Prior Art*, *supra* note 40, at 13 n. 39.

⁴⁹ See *id.* at 13; see also, *supra* note 35.

[21] Downes and Wiser then make a third argument – one that has significant implications, since it also suggests a mechanism by which indigenous peoples might protect their plant-based TMK.⁵⁰ They argue that accession sheets of plants from herbarium collections can be categorized as prior art within the meaning of 35 U.S.C. §§ 102 and 103.⁵¹



Fig. 4. Sample of a herbarium sheet from Cayetano University in Peru.⁵²

[22] The existence of such herbarium sheets should bar any future patenting of the plant that was preserved on the sheet.⁵³ While there may only be a single copy of the herbarium sheet, if it is accessible to the public, it may be considered prior art. In the same way that “a single catalogued thesis in one university library [constitutes] sufficient accessibility to those interested in the art exercising reasonable diligence,”

⁵⁰ See Downes & Wiser, *Comments on Improving Identifications of Prior Art*, *supra* note 40, at 14–15.

⁵¹ See *id.* at 15.

⁵² See E-mail from author, to Dr. Dean Arneson, Pharm.D, Ph.D., Dean of School of Pharmacy, Concordia University Wisconsin (2013) (on file with author).

⁵³ See Downes & Wiser, *Comments on Improving Identifications of Prior Art*, *supra* note 40, at 15.

is considered a printed publication, for purposes of a prior art rejection under 35 U.S.C. §102.⁵⁴ To serve as prior art, the herbarium sheets must be accessible and available to persons interested in the subject matter—in this case medicinal plants associated with the TMK of Amazonian shamans. If this is true, then one way for indigenous peoples to prevent patenting of their medicinal plants is to make herbarium sheets containing dried plant specimens with written entries (*e.g.* describing the plant, where collected, date collected), such as that shown in **Fig. 4** from the University of Cayetano in Peru.⁵⁵

[23] Downs and Wisner make a fourth argument, based more on a sense of social justice than on patent law.⁵⁶ They argue that the patent should be canceled because the plant (ayahuasca) has been used by indigenous peoples for hundreds of years, long before Miller considered patenting “Da Vine.”⁵⁷ Of course, the challenge from a patent perspective is that this use – part of an oral tradition – may not have been documented in any printed publication and U.S. patent law does not prevent patenting of subject matter that was simply “in use” in a foreign country (at least not

⁵⁴ *In re Hall*, 781 F.2d 897, 900 (Fed. Cir. 1986) (“...we reject appellant’s legal argument that a single cataloged thesis in one university library does not constitute sufficient accessibility to those interested in the art exercising reasonable diligence.”).

⁵⁵ *See supra* Figure 4.

⁵⁶ *See generally* Downes & Wisner, *Comments on Improving Identifications of Prior Art*, *supra* note 40, at 3, 5–6, 16 (discussing the social implications on the traditional knowledge of indigenous communities).

⁵⁷ *See id.*; *see also* Glenn Wisner, Center for Int’l Env’tl. Law, *U.S. Patent and Trademark Office Reinstates Ayahuasca Patent: Flawed Decision Declares Open Season on Resources of Indigenous Peoples*, (June 25, 2001) at 1, <http://www.ciel.org/wp-content/uploads/2015/06/PTODecisionAnalysis.pdf>, *archived at* <https://perma.cc/PY75-MJZG>.

before the 2013 America Invents Act [AIA]).⁵⁸ In an analogous situation, a U.S. patent for use of turmeric in wound healing (based on Indian TMK) was issued in 1995.⁵⁹ This patent was canceled because turmeric had actually been used for many generations by indigenous peoples in India for this same purpose, so the invention was not considered novel.⁶⁰

[24] Finally, Downs and Will argued that the Miller patent should not be allowed on moral and public policy grounds:

“... issuance of the Patent does not meet the public policy and morality aspects of the Patent Act, which preclude awarding a patent on a plant ... that is sacred to indigenous peoples ... and revered in their cultures for many generations ... the PTO should not provide patent protection to a plant based on supposed medicinal characteristics that are well known in the systems of traditional knowledge of indigenous peoples ... the PTO may and should decline to award intellectual property rights where their imposition would violate established moral, religious and cultural values.”⁶¹

⁵⁸ See *infra* Section III (E).

⁵⁹ Use of Turmeric in Wound Healing, U.S. Patent No. 5,401,504 (filed Dec. 28, 1993).

⁶⁰ Sanjay Kumar, *India Wins Battle with USA Over Turmeric Patent*, 350 THE LANCET 675, 724 (1997); Use of Turmeric in Wound Healing, U.S. Patent and Trade Office Reexamination Certificate B1 5,401,504 (Apr. 21, 1998).

⁶¹ *Detailed Statement in Support of Request for Reexamination of U.S. Plant Patent No. 5,751* from David R. Downs & Glenn Wiser to the Commissioner of Patents and Trademarks (filed Nov. 7, 1984), <http://www.ciel.org/wp-content/uploads/2015/06/ReexaminationofUSPlantPatent5751.pdf>, archived at <https://perma.cc/5XJ9-YQMN> [hereinafter *Detailed Statement*].

[25] While this moral argument is attractive, there is little support in U.S. patent law for an argument based on protection of “moral, religious and cultural values.”⁶² U.S. patent law has no equivalent to the moral rights doctrine of copyright law. Although, a PTO Media Advisory statement⁶³ offers a glimmer of hope for moral grounds arguments – noting that courts had excluded inventions that are “injurious to the well-being, good policy, or good morals of society.”⁶⁴ Downs and Wisner argue that patenting plants like ayahuasca, which are used widely in religious ceremonies as part of indigenous peoples’ TMK, “offends religious and moral sensibilities” and “wrongly appropriates traditional knowledge of indigenous and local communities [and] may deprive its creators and conservators of incentives to preserve, develop and improve upon it.”⁶⁵ Perhaps because this *moral sensibilities* argument is not supported by U.S. patent law and associated legal precedent, the PTO ultimately based its decision to reject the Miller patent on other arguments presented by Downs and Wisner.⁶⁶

[26] After considering the request for reexamination and the various arguments presented by Downs and Wisner, the PTO responded by

⁶² *Id.* at 4.

⁶³ *See generally* Press Release 98-6, USPTO, Facts on Patenting Life Forms Having a Relationship to Humans, (April 1, 1998) (on file with author), <http://www.uspto.gov/about-us/news-updates/facts-patenting-life-forms-having-relationship-humans>, *archived at* <https://perma.cc/7MDZ-SSLJ>.

⁶⁴ *Tol-O-Matic, Inc. v. Proma Produkt-Und Marketing Gesellschaft m.b.H.*, 945 F.2d 1546, 1553 (Fed. Cir. 1991) (citing *Lowell v. Lewis*, Fed. Case No. 8568 (C.C. Mass. 1817)).

⁶⁵ Downs & Wisner, *Detailed Statement*, *supra* note 61, at 24.

⁶⁶ *See infra* Section III (E).

rejecting the Miller patent in a November 3, 1999 office action.⁶⁷ They did this in part based on a consideration of the herbarium specimen sheets as being “printed matter” that could serve as prior art, under §102(b).⁶⁸ One particular herbarium specimen that was identified as prior art was: “Plants of Cultivation: *Banisteriopsis caapi*, The University of Michigan Herbarium (mounted Jan. 5, 1981).”⁶⁹ This is significant precedent because it is the first such consideration of herbarium sheets as prior art. Thus, herbarium sheets like those in **Fig. 4** could be used as a bar to prevent patenting of plants that are part of TMK, and a potential source of new drugs.⁷⁰ This result suggests one mechanism by which countries with indigenous populations might protect their plant-based TMK – by creating herbarium collections documenting the plants they use in traditional medicine. By rejecting the patent based on this narrow view only (*i.e.* §102, prior art), the PTO avoided the broader question of rejection based on public policy and morality grounds, which could potentially be associated with the Patent Act’s utility requirement, as noted in the Media Advisory statement.⁷¹

⁶⁷ See Glen M. Wiser, *U.S. Patent and Trademark Office Reinstates Ayahuasca Patent, Flawed Decision Declares Open Season on Resources of Indigenous Peoples* CIEL 2 (June 25, 2001).

⁶⁸ See *Ex parte* Nehls, No. 2007-1823 (B.P.A.I. Jan. 28, 2008).

⁶⁹ Downes & Wiser, *Detailed Statement*, *supra* note 61, at 1.

⁷⁰ See generally Glen M. Wiser & David R. Downes, CENTER FOR INTN’L ENVTL. LAW, *Comments on Improving Identification of Prior Art: Recommendations on Traditional Knowledge Relating to Biological Diversity Submitted to the United States Patent and Trademark Office*, (Aug. 2, 1999), <http://www.ciel.org/wp-content/uploads/2015/03/IdentificationofPriorArt.pdf>, archived at <https://perma.cc/7P9U-QTSN>.

⁷¹ See Press Release 98-6, USPTO, *supra* note 63.

[27] The “Da Vine” patent reexamination teaches three important lessons. First, one way to prevent biopiracy is to create “printed documents” that could serve as prior art, and therefore block the patenting of plant-based TMK. Second, one effective type of “printed document” that can be used for this purpose are collections of herbarium sheets that document the plants that are part of shamanic TMK. If indigenous peoples take this defensive move of creating herbarium sheets as prior art, they should be aware that this may also prevent them from patenting as well, either alone or as part of a collaborative drug co-development effort. Prior art creation is a protective tool that cuts both ways; so, it should be used with caution. Third, an argument based on the moral and social harm caused to indigenous peoples, while intuitively attractive, may not carry weight with the PTO due to lack of supporting legal precedent and statutory language.

III. LEGAL PROTECTIONS OF TMK FOR DRUG CO-DEVELOPMENT IN PERU

A. Peruvian, Bolivian and Ecuadoran Law

a. Constitutional Protections in Peru, Bolivia and Ecuador

[28] While Peru does not directly protect indigenous rights, Chapter II, Article 68 of the Peruvian Constitution provides a related protection: “The State is obliged to promote the conservation of biological diversity, and protected natural areas.”⁷² So, to the extent that TMK is associated with biological diversity (*i.e.* plant-based medicines), Peru has some relevant constitutional protection. In contrast, Bolivia and Ecuador’s more recent constitutions have more explicit protections for indigenous people’s TK,

⁷² Constitución Política Del Perú [C.P.] art. 68.

with several articles of the Bolivian Constitution excerpted below:

Article 42: The promotion of traditional medicine shall incorporate a registry of natural medicines and their active substances, as well as the protection of the associated knowledge as intellectual, historical and cultural property, and as patrimony of indigenous nations and peoples.

Article 100. The State shall protect knowledge by means of a registry of intellectual property that safeguards the intangible rights of indigenous nations and peoples...

Article 304. Indigenous autonomies have the following competences: ... safeguard and register collective intellectual rights related to knowledge on genetic resources, traditional medicine and germplasm ...⁷³

[29] The Bolivian Constitution is relatively new, having been approved only in 2009; and, it is a result of the 2005 election of Evo Morales, an Aymara coca peasant who fought for the rights of indigenous peoples.⁷⁴ Given its origins in a political movement focused on indigenous peoples, it can be viewed as a model for national protection of TK IP rights. While Bolivia and Ecuador are unique in having these protections at the constitutional level, their Constitutions may have value as persuasive legal authority for other Andean Community countries like Peru, and for any country that seeks to protect the TK and TMK of its indigenous peoples.

b. Sui Generis Protections in Peru: Law No. 27811

[30] While Peru does not protect TMK at the constitutional level, it

⁷³ See GRAIN, *The Struggle Against IPR in the Andes*, SEEDLING, July 12, 2009, at 21.

⁷⁴ *Id.* at 20.

does protect TK and TMK in its national legislation.⁷⁵ In particular, Peru passed Law No. 27811 in 2002, introducing a Protective Regime for the Collective Knowledge of Indigenous People Derived from Natural Resources. The objectives of Law No. 27811 are stated in Article 5:

(a) To promote respect for and the protection, preservation, wider application and development of the collective knowledge of indigenous peoples;

(b) To promote the fair and equitable distribution of the benefits derived from the use of that collective knowledge;

(c) To promote the use of the knowledge for the benefit of the indigenous peoples and mankind in general;

(d) To ensure that the use of the knowledge takes place with the prior informed consent of the indigenous peoples;

(e) To promote the strengthening and development of the potential of the indigenous peoples and of the machinery traditionally used by them to share and distribute collectively generated benefits under the terms of this regime;

(f) To avoid situations where patents are granted for inventions made or developed on the basis of collective knowledge of the indigenous peoples of Peru without any account being taken of that knowledge as prior art in the

⁷⁵ See Ley N° 27811 [Law N° 27811], Ley que Establece el Régimen de Protección de los Conocimientos Colectivos de los Pueblos Indígenas Vinculados a los Recursos Biológicos [Law Introducing a Protection Regime for the Collective Knowledge of Indigenous Peoples Derived from Biological Resources], Aug. 10, 2002, EL PERUANO, at 227953–54 (Peru).

examination of the novelty and inventiveness of the said inventions.⁷⁶

[31] Noteworthy is the emphasis on informed consent and equitable sharing of benefits, along with specific protections for patents and other protections.⁷⁷

[32] The “Protective Regime for the Collective Knowledge of Indigenous People Derived from Natural Resources” (Law No. 27811) goes beyond the general objectives outlined in Article 5, to describe in detail how TK (and TMK) is to be protected. It explains the key considerations when intellectual property is to be licensed from indigenous peoples. In particular, if a third party is going to commercialize traditional knowledge (Article 7) it requires outside parties to sign license agreements to “ensure due reward for said access and ... equitable distribution of the benefits”⁷⁸ A percentage of benefits (at least 10%) must go to the Fund for the Development of Indigenous Peoples (Article 8).⁷⁹ Thus, it ensures that the indigenous owners of TMK are duly rewarded, and benefits obtained in any drug co-development efforts are shared equitably. Furthermore, it explicitly points out that protected knowledge does not belong to individuals, but rather to groups of indigenous peoples.⁸⁰ That is, knowledge and discovery is “collective” (Article 10), in contrast to the individualistic approach that underlies U.S.

⁷⁶ *Id.* at art. 5.

⁷⁷ *See id.* at art. 5(d),(e).

⁷⁸ *Id.* at art. 7.

⁷⁹ *See* Ley N° 27811 [Law N° 27811], *supra* note 75 at art. 8.

⁸⁰ *See id.* at art. 10

patent law and, more generally, U.S. culture.⁸¹

[33] The law goes on to describe how national registers of TK and TMK are to be created. Title VI describes the formation of registers of collective knowledge, with Article 15 explicitly creating three types of registers: (a) Local Registers of Collective Knowledge of Indigenous Peoples, (b) Private National Registers of Collective Knowledge of Indigenous Peoples, and (c) Public National Registers of Collective Knowledge of Indigenous Peoples.⁸² Article 20 describes what type of information must be included in the registration of the TK and TMK into these registers.⁸³

[34] These three registers each serve unique and important purposes. The first, The Local Registers, are managed by indigenous peoples with assistance of the National Institute for the Protection of Competition and Intellectual Property (INDECOPI).⁸⁴ They serve the local needs of indigenous peoples, to enable sharing of their TMK with each other, and to provide a high level of access to and control of information by the local community. The second, the Private National Registers, are kept confidential, and contain what could be viewed as trade secrets.⁸⁵ These trade secrets could be licensed to third parties, if desired. The third, the Public National Registers, could serve the alternative purpose of providing prior art that will prevent the patenting of TMK by other countries (*e.g.*

⁸¹ *Id.*

⁸² *Id.* at art. 15.

⁸³ *See id.* at art. 20.

⁸⁴ *See* Ley N° 27811 [Law No. 27811], *supra* note 75 at art. 24.

⁸⁵ *See id.* at art. 18.

via 35 U.S.C. §102 in the U.S.).⁸⁶ Indeed, Article 23 specifically states that “INDECOPI shall send the information entered in the Public National Register to the main patent offices of the world in order that it may be treated as prior art in the examination of the novelty and inventiveness of patent applications.”⁸⁷ Thus, Peru has made a very explicit defensive move to prevent the patenting of its TK and TMK; this was a valuable lesson from the ayahuasca case above (section II), and is now institutionalized in national policy.⁸⁸ Interestingly, the recent passage of the U.S. AIA has obviated some of the need for this defensive strategy, since prior use (even if no printed publication exists) is now considered a bar in considering novelty or non-obviousness (inventiveness).⁸⁹ This is discussed in greater detail in section III(E).

[35] The Private National Register contains TK and TMK trade secrets which could be of significant value to the world as a source of new medicines. To enable dissemination of this TMK, if desired, indigenous peoples can license their TMK to third parties, such as pharmaceutical companies. But, they must register the license according to the Article 26 “Compulsory written form for license contracts” requirements.⁹⁰ The contents of this contract are designed to protect the intellectual property rights (IPRs) of the indigenous owner, and are specified in Article 27:

(c) A statement of the compensation that the indigenous

⁸⁶ *See id.* at art. 23.

⁸⁷ *Id.*

⁸⁸ *See* discussion *supra* Section II.

⁸⁹ *See infra* Section III(E).

⁹⁰ *See* Ley N° 27811 [Law No. 27811], *supra* note 75 at art. 26.

peoples receive for the use of their collective knowledge; such compensation shall include an initial monetary or other equivalent payment for its sustainable development, and a percentage ... of the gross sales resulting from the marketing of the goods developed ...;

(d) The provision of sufficient information on the purposes, risks and implications of the said activity ... ;

(e) The obligation on the licensee to inform the licensor periodically ... of progress in the research on and industrialization and marketing of the goods developed ...;

(f) The obligation on the licensee to contribute to the improvement of the ability of the indigenous peoples to make use of the collective knowledge ...⁹¹

[36] A “toolkit” to assist in compliance with this licensing process is available from WIPO.⁹² The required elements of a TMK license contract are designed to protect the interests and rights of the indigenous owners, and should be considered in the preparation of any drug co-development research agreements between Peruvian researchers and their U.S. or other foreign collaborators.⁹³

B. U.S.-Peru Trade Promotion Agreement (TPA)

⁹¹ *Id.* at art. 27.

⁹² See WORLD INTELLECTUAL PROP. ORG. (WIPO), *Traditional Knowledge Documentation Toolkit* (2012), http://www.wipo.int/export/sites/www/tk/en/resources/pdf/tk_toolkit_draft.pdf, archived at <https://perma.cc/85DN-5V4S> (last visited Nov. 11, 2013).

⁹³ See *id.* at 22.

[37] Beyond the scope of TRIPS (Trade Related Aspect of Intellectual Property) standards, the U.S.–with WTO (World Trade Organization) enforcement (as described in Section III(D))⁹⁴–has also pursued bi-lateral trade agreements with individual countries, typically seeking higher IPR standards.⁹⁵ Such bi-lateral agreements often lead to less protection for TK, so are often conceded to by developing countries only because of the other benefits they receive. While the end result may provide broader benefits to the government that signs, such bi-lateral agreements – and the associated concessions that are made – can anger indigenous groups and their representatives. This appears to have been the case in Peru as well.

[38] The U.S. and Peru signed the Trade Promotion Agreement (TPA) in 2006.⁹⁶ Within the TPA is a benefit to the so-called Andean Community countries (Bolivia, Peru, Ecuador, Columbia)⁹⁷, via the Andean Trade Protection Act (ATPA). This benefit to the Andean Community countries required that IPRs be protected adequately under WTO, as specified by TRIPS standards. Peru signed various amendments on Dec. 21st, 2008, to permit compliance with the TPA with the U.S. These changes generally strengthened IP, and weakened protections of TK, TMK and biodiversity,

⁹⁴ See *infra* Section III(D).

⁹⁵ See *Free Trade Agreements*, OFF. OF THE U.S. TRADE REPRESENTATIVE, <http://www.ustr.gov/trade-agreements/free-trade-agreements>, archived at <https://perma.cc/BQ9K-8X67> (last visited Sept. 9, 2016).

⁹⁶ See *Final Text United States – Peru Trade Promotion Agreement*, OFF. OF THE U.S. TRADE REPRESENTATIVE, (Apr. 12, 2006), <http://www.ustr.gov/trade-agreements/free-trade-agreements/peru-tpa/final-text>, archived at <https://perma.cc/GH7G-VSNX>.

⁹⁷ See COMUNIDAD ANDINA, <http://www.comunidadandina.org/Seccion.aspx?id=189&tipo=QU&title=somos-comunidad-andina>, archived at <https://perma.cc/B2U5-PASZ> (last visited Sept. 9, 2016) (describing the countries benefitting).

against patenting and bioprospecting.⁹⁸ At about this same time (Dec. 31st, 2008), likely in reaction to signing of the TPA, the local government in Cusco released an executive order to “protect traditional knowledge, practices and innovations of local communities.”⁹⁹ This protection included a requirement to use “informed consent, compulsory benefit sharing and the right of communities to say no to bioprospecting.”¹⁰⁰ Furthermore, any bioprospecting requires a permit, and the government will monitor such activities to protect the interests of local communities.¹⁰¹ These protections of TK and TMK are in keeping with the Article 5 priorities outlined in Peru’s *sui generis* protection (described above, in section III(A)(b)), and are consistent with the Constitutional IPR protections provided in Bolivia (described in section III(A)(a)).¹⁰²

[39] Importantly, the TPA with the U.S. included an “Understanding Regarding Biodiversity and Traditional Knowledge,” in an effort to provide some protection of TK and TMK.¹⁰³ The Understanding stated:

The Parties recognize the importance of traditional knowledge ... to cultural, economic, and social development. The Parties recognize the importance of the following: (1) obtaining informed consent from the

⁹⁸ See GRAIN, *The Struggle Against IPR in the Andes*, *supra* note 73 at 18.

⁹⁹ *Id.*

¹⁰⁰ *Id.* (emphasis added).

¹⁰¹ *Id.*

¹⁰² See *supra* Sections III(A)(a)-(b); see GRAIN, *The Struggle Against IPR in the Andes*, *supra* note 73, at 17.

¹⁰³ U.S.-Peru Trade Promotion Agreement: Potential Economy-wide and Selected Sectoral Effects. Inv. No. TA-2104-20, USITC Pub. 3855 at 6-12 (June 1, 2006).

appropriate authority prior to accessing genetic resources under the control of such authority; (2) equitably sharing the benefits arising from the use of traditional knowledge and genetic resources; and (3) promoting quality patent examination to ensure the conditions of patentability are satisfied ...

Each Party shall endeavor to seek ways to share information that may have a bearing on the patentability of inventions based on traditional knowledge or genetic resources by providing:

(a) publicly accessible databases that contain relevant information; and

(b) an opportunity to cite, in writing, to the appropriate examining authority prior art that may have a bearing on patentability.¹⁰⁴

[40] While the Understanding does not oblige each country or its nationals to undertake specific actions in relationship to TMK, the Understanding's basic recognition of TMK sets an important precedent. Previously, the U.S. had felt that TK and TMK protections should be secured through the WIPO; but, the Andean Community countries – operating as a regional group with enhanced political bargaining power – were successful in getting this Understanding added to the TPA.¹⁰⁵ This Understanding can hopefully serve as a starting point and model for how

¹⁰⁴ Understanding Regarding Biodiversity and Traditional Knowledge, U.S.-Peru, (April 12, 2006), http://www.ustr.gov/sites/default/files/uploads/agreements/fta/peru/asset_upload_file719_9535.pdf, archived at <https://perma.cc/66P2-X795>.

¹⁰⁵ *Id.*

the IPRs of indigenous peoples can and should be protected in trade agreements, as well as in other contexts. Noteworthy is its emphasis on informed consent, sharing of benefits, assistance in obtaining patents, and use of TK databases.¹⁰⁶ These are also key elements in regional regulations for the Andean Community, described in the next section.

C. Regional Protections: The Andean Community Intellectual Property Regime

[41] The Andean Community is an agreement that was signed in 1969, and currently includes Peru, Bolivia, Ecuador and Columbia (Venezuela withdrew in 2006 when Peru signed the Free Trade Agreement (FTA) with the U.S.).¹⁰⁷ The Andean Community has generated a number of supranational institutions, including the “Commission of national executives, a General Secretariat of regional administrators, and a Tribunal of Justice (the ATJ or the Andean Tribunal).”¹⁰⁸

[42] This Andean Community has had its most significant successes in the realm of protecting intellectual property (96% of rulings relate to IP), developing supranational laws called “Decisions” to regulate patents, trademarks and copyrights.¹⁰⁹ Andean IP Decisions are adopted at the

¹⁰⁶ *See id.*

¹⁰⁷ *See* GRAIN, *The Struggle Against IPR in the Andes*, *supra* note 73 at 17,19.

¹⁰⁸ Laurence R. Helfer & Karen J. Alter, *The Influence of the Andean Intellectual Property Regime on Access to Medicines in Latin America*, in *BALANCING WEALTH AND HEALTH: GLOBAL ADMINISTRATIVE LAW AND THE BATTLE OVER INTELLECTUAL PROPERTY AND ACCESS TO MEDICINES IN LATIN AMERICA 1* (Rochelle Dreyfuss & César Rodríguez-Garavito, eds., 2013).

¹⁰⁹ *See id.* at 2.

national level by member states. Then they are interpreted in national courts, administrative agencies in member states, or by the ATJ.¹¹⁰

[43] The Andean governments have used the political clout afforded to them, via participation in the Andean Community, to facilitate incorporation of normally optional TRIPS “flexibilities” as obligatory features of Andean law.¹¹¹ To this end, “member states made a collective decision to capitalize on TRIPS’ flexibilities as a way to promote public health,” and to resist pressure from stronger international forces, like pharmaceutical companies from the United States.¹¹² In effect, membership in the Andean Community gives strength to individual countries, by virtue of their banding together, to enforce what are sometimes optional and yet advantageous TRIPS features. This enhanced bargaining power plays a central role in securing TK and TMK protections for indigenous peoples, as in the U.S.-Peru TPA agreement discussed above.

[44] As a complement to regional treaties, local laws can provide additional protections – as Cusco had pursued in parallel with Peru’s signing of the U.S.-Peru TPA.¹¹³ As discussed above, the signing of this international agreement (the TPA) by Peru was closely linked to complementary and compensatory initiatives at the local (Cusco) and regional (Andean Community) levels, which ultimately led to stronger TK and TMK protections. Accordingly, any drug co-development initiative with Peru must recognize the complementary TMK protections that have been created at the local, national, regional, and international levels.

¹¹⁰ *See id.* at 1.

¹¹¹ *See id.* at 4.

¹¹² *Id.*

¹¹³ *See* GRAIN, *The Struggle Against IPR in the Andes*, *supra* note 73 at 17,18.

D. International Treaties: Role of UN, TRIPS, WTO and WIPO

[45] International protections for indigenous IPRs go beyond bi-lateral agreements like the TPA. Although they are not a focus of this paper, since regional and bi-lateral agreements are usually compliant with and more specific than the international treaties. Nonetheless, a brief overview of key international treaties and agreements will be presented. One such agreement is the United Nations (UN) Convention on Biological Diversity.¹¹⁴ This agreement protects TK, which is related to biological diversity, and encourages sharing of the benefits of that knowledge. Article 8(j) of the Convention provides that each Party shall:

[s]ubject to its national legislation, respect, preserve and maintain knowledge, innovations and practices of indigenous and local communities embodying traditional lifestyles relevant for the conservation and sustainable use of biological diversity and promote their wider application with the approval and involvement of the holders of such knowledge, innovations and practices and encourage the equitable sharing of the benefits arising from the utilization of such knowledge, innovations and practices.¹¹⁵

[46] The emphasis on preservation of TK is noteworthy, promoting the wider application of the TK and the sharing of benefits obtained through the use of the TK. More broadly, the Convention on Biological Diversity focuses on protecting biological diversity in the context of other goals such as the need for medicines.¹¹⁶ The treaty has importance for

¹¹⁴ See Convention on Biological Diversity, June 5, 1992, 1760 U.N.T.S. 79, 31 I.L.M. 818 (1992), <http://www.cbd.int/doc/legal/cbd-en.pdf>, archived at <https://perma.cc/4BVB-MTFW>.

¹¹⁵ *Id.* at 6.

bioprospecting, as well as collaborative research between countries involving natural products and TMK.

[47] The Trade Related Aspects of IP (TRIPS) agreement is an international treaty that seeks to harmonize IP laws between member countries while still honoring and respecting national laws and sovereignty.¹¹⁷ TRIPS is the most extensive multinational agreement on IP and covers patents, trademarks, copyrights, and trade secrets.¹¹⁸ But TRIPS has not provided significant protections for TMK (beyond certain “flexibilities”), since the interests of developing nations must often yield to those of more powerful developed countries (and opt-out of the “flexibilities”).¹¹⁹ The World Trade Organization (WTO) requires TRIPS ratification for membership. So it is not uncommon for developing countries to make undesired concessions regarding IP rights (defined in TRIPS), in order to secure the trade benefits they desire.¹²⁰ Counteracting this pressure is the strength that regional alliances, like the Andean Community, provide so that TMK protections can be obtained (e.g. making TRIPS “flexibilities” mandatory in member countries).¹²¹

¹¹⁶ *See id.* at 24.

¹¹⁷ *See generally*, Agreement on Trade-Related Aspects of Intellectual Property Rights, Annex 1C, Apr. 15, 1994, LEGAL INSTRUMENTS-RESULTS OF THE URUGUAY ROUND, 1869 U.N.T.S. 299, 33 I.L.M. 81 (1994) (supporting need for multilateral framework between member countries).

¹¹⁸ *See Overview: The TRIPS Agreement*, WORLD TRADE ORG., https://www.wto.org/english/tratop_e/trips_e/intel2_e.htm, archived at <https://perma.cc/9ZST-3HXV> (last visited Sept. 9, 2016).

¹¹⁹ *See* J.H. Reichman, *The TRIPS Agreement Comes of Age: Conflict or Cooperation with the Developing Countries?*, 32 CASE W. RES. J. INT’L. L. 441, 452 (2000).

¹²⁰ *See id.*

¹²¹ *See* WORLD INTELLECTUAL PROP. ORG. (WIPO), *Advice on Flexibilities under the*

[48] Both Peru and the United States are members of TRIPS. Membership in TRIPS requires compliance with earlier IP treaties and conventions, including WIPO, the Paris Convention for the Protection of Industrial Property (Paris Convention),¹²² and the Berne Convention for the Protection of Literary and Artistic Works (Berne Convention).¹²³ While TRIPS provides the underlying IP principals, enforcement typically occurs within member states and disputes are handled by the World Trade Organization (WTO).¹²⁴ Since any IPR agreement or treaty developed by or between Peru and the U.S. must be compliant with TRIPS, the agreements and treaties with greatest impact on drug co-development between researchers in Peru and the U.S. are the bi-lateral, regional and national agreements discussed in sections III A-C.

E. Changes in U.S. Patent Law: the America Invents Act (AIA)

[49] What effect do the America Invents Act (AIA) changes to U.S. patent law have on protections of indigenous IPR?¹²⁵ Under the old 35

TRIPS Agreement, http://www.wipo.int/ip-development/en/legislative_assistance/advice_trips.html, *archived at* <https://perma.cc/DE85-UJEE> (last visited Aug. 30, 2016).

¹²² See Paris Convention for the Protection of Industrial Property, Mar. 20, 1883, as last revised July 14, 1967, 21 U.S.T. 1583, 828 U.N.T.S. 311 (applying international treaty to industrial intellectual property).

¹²³ See Berne Convention for the Protection of Literary and Artistic Works, Sept. 9, 1886, as last revised July 24, 1971, 25 U.S.T. 1341, 828 U.N.T.S. 221 (international agreement governing copyright law).

¹²⁴ See *e.g.*, *Overview: the TRIPS Agreement*, *supra* note 118.

¹²⁵ See *generally* Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (modernizing the United States Patent Law system).

U.S.C. §102, if TMK was “in use” for hundreds of years by shamans in Peru but never recorded in a printed publication, then there would be no prior art bar to patenting in the U.S. This would seem to enable biopiracy of TMK in an undesirable way. Prior to March 16th, 2013 (when the AIA went into effect), U.S. patent law did not recognize TK and TMK as prior art if it was only “in use” in a *foreign country*.¹²⁶ Indeed, the Patent Act of 1952 would have permitted patenting of an invention based on long-held TMK (as long as it was undocumented) based on the previous version of 35 U.S.C. §102 (key elements underlined):

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States.¹²⁷

[50] According to the plain language of the statute, while an invention may have been used in the country of origin (*e.g.* Peru), 35 U.S.C. §102 will only prevent patenting of inventions that were in use in the U.S. or described in a printed publication anywhere.¹²⁸ Thus, when the University of Mississippi Medical Center tried to patent turmeric for healing wounds,

¹²⁶ See 35 U.S.C. § 102(a), (b) (2006) (emphasis added).

¹²⁷ *Id.* (emphasis added).

¹²⁸ See *id.* (emphasis added).

they were not prevented from patenting simply because turmeric was widely used for that purpose in India.¹²⁹ Rather, what led to the patent being revoked was the appearance of this use of turmeric in printed publications.¹³⁰ Likewise, even though ayahuasca had been used for centuries by Amazonian shamans (*i.e.* been “in use”), this did not produce a 35 U.S.C. §102 prior art rejection (see section II). Rather, the rejection of the Miller patent on ayahuasca was based on the presence of herbarium sheets that described the ayahuasca plant.¹³¹ Indeed, this is a significant reason why countries like Peru are documenting the plants associated with their TMK in registries and using herbarium sheets. One of the objectives of Peru’s *sui generis* protections (section III(A)(b)) is to ensuring that foreign bioprospectors are barred from patenting due to the existence of this prior art.¹³² But the situation has changed under AIA, where the new language of 35 U.S.C. §102 is:

(a) A person shall be entitled to a patent unless:

(1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention;¹³³

[51] Notably, now 35 U.S.C. §102 considers “public use ... or

¹²⁹ See *supra* note 59.

¹³⁰ See *supra* note 60.

¹³¹ See Leanne M. Fecteau, *The Ayahuasca Patent Revocation: Raising Questions About Current U.S. Patent Policy*, 21 B.C. THIRD WORLD L. J. 69, 86 (2001).

¹³² See *id.* at 73-74.

¹³³ 35 U.S.C. §102(a)(1).

otherwise available” anywhere (in foreign countries and in the U.S.) as creating a prior art bar to patenting.¹³⁴ Thus, under the AIA, the need for countries to maintain registries and herbarium sheets of plants used in TMK is lessened, as long as they have other means to establish that the plant and/or TMK had been “in use ... or otherwise available.”¹³⁵ This is a significant step forward in the prevention of biopiracy, and the protection of TK and TMK.

IV. MODEL FOR U.S.-PERU COLLABORATIVE DRUG DEVELOPMENT

A. Building on Current IPR Protections for TMK in Peru

a. Key Elements of TMK Protections to Include in Research Agreements Involving Indigenous Communities

[52] Constitutional protections of TMK in Peru are limited to “conservation of biological diversity,” which includes plant-based medicines.¹³⁶ Bolivia, a member of the Andean Community along with Peru, has constitutional protections (see section III(A)(a)) that go further to explicitly ensure “promotion of traditional medicine” by mandating a “registry of natural medicines and of their curative properties ... as well as the protection of their knowledge as intellectual ... property ... of nations

¹³⁴ *Id.*

¹³⁵ *Id.*

¹³⁶ See Ley N° 27811 [Law No. 27811], *supra* note 75 at art. 2(e) (explaining the protections created by the Peruvian government for collective knowledge of indigenous peoples in regard to biological resources).

and indigenous peoples.”¹³⁷ This theme of protecting TMK in registries and protecting it as the IP of indigenous peoples, is also manifested in Peru’s *sui generis* protections (see section III(A(b))).

[53] Peruvian *sui generis* protections emphasize creation of databases of TMK, both public (as a defense against foreign patents) and private (as a source of licensable trade secrets). Other elements of the *sui generis* protections include: (a) promotion of respect, preservation, and wider application of TMK, (b) promotion of the use of TMK to benefit the “indigenous peoples and mankind in general,” (c) freedom to license TMK (with state oversight; to be registered using the WIPO “toolkit”), (d) release of TMK only with informed consent of the indigenous owners, based on full disclosure of risks and benefits, (e) equitable sharing of benefits derived from the use of TMK (including >10% for the Fund for Development of Indigenous People), and (f) a desire to prevent patenting of indigenous peoples’ TMK by others.¹³⁸ These elements and priorities should be addressed in any collaborative research agreement between research scientists in Peru and foreign collaborators seeking to co-develop drugs derived from TMK. Significantly, all of these elements fall under the broader umbrella of the U.S.-Peru TPA (e.g. informed consent; equitable sharing of benefits). So, there is a strong foundation for

¹³⁷ PLURINATIONAL STATE OF BOLIVIA [CONSTITUTION] 2009, Ch. V, art. 43 (Bol.), https://www.constituteproject.org/constitution/Bolivia_2009.pdf, archived at <https://perma.cc/A9YV-8AP5>.

¹³⁸ See WORLD INTELLECTUAL PROP. ORG. (WIPO), *Comparative Summary of Existing National SUI GENERIS Measures and Laws for the Protection of Traditional Knowledge*, Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore, Fifth Session, WIPO Doc. WIPO/GRTKF/IC/5/INF/4 http://www.wipo.int/meetings/en/doc_details.jsp?doc_id=17394, archived at <https://perma.cc/D7HC-DJY8> (June 20, 2003).

including them in collaborative agreements between U.S. and Peruvian researchers.¹³⁹

b. Defensive Strategy to Protect TMK - Creation of Public Databases of TMK as Prior Art

[54] One of the key elements in the Bolivian Constitutional protections and the Peruvian *sui generis* protections is the creation of public databases of TMK. The stated purpose of these databases is, in part, to create prior art that prevents others from patenting – without permission – the TMK that belongs to indigenous peoples.¹⁴⁰ The need for and value of such databases is illustrated within the ayahuasca patent dispute described in section II. While post AIA changes in U.S. patent law lessened the need for such databases, they still provide a clear demonstration of what TMK was “in use or otherwise available.” This serves the stated goal of providing a strong defense against uninvited and undesired foreign patents, like the Miller “Da Vine” patent. Such patents could exploit the TMK of indigenous peoples, without equitable sharing of the benefits derived from that TMK and without informed consent.

[55] It is important to point out that this defensive use of databases as prior art can have undesired consequences if the indigenous peoples ever want to patent their own TMK. A key element of the indigenous peoples’ TMK protections (sections III(A)(b) and IV(A)(a)) was a desire to benefit “indigenous peoples and mankind in general” and to permit – with informed consent – licensing of TMK-based discoveries in a co-development initiative.¹⁴¹ But, pharmaceutical companies will not develop

¹³⁹ See *Peru Trade Promotion Agreement*, OFFICE OF THE U.S. TRADE REPRESENTATIVE <https://ustr.gov/trade-agreements/free-trade-agreements/peru-tpa>, archived at <https://perma.cc/AW2U-RUYC> (last visited Sep. 9, 2016).

¹⁴⁰ See Ley N° 27811 [Law No. 27811], *supra* note 75 at art 42.

¹⁴¹ See *supra* note 138.

a drug if they cannot obtain composition of matter patent protection. Therefore, the inability to patent TMK-derived medicines – or active substances derived from them – prevents any co-development of drugs.

[56] The most likely patentable subject matter in a drug co-development collaboration, since the plant cannot be patented (*i.e.* as TMK, it has already been “in use”), are the extracted chemical substances – or combinations thereof. For example, the ayahuasca plant could not have been patented under AIA, even if there were no “printed documents” describing it, since it was already “in use” by shamans. But, the active ingredients shown in **Fig. 2**, mixing in the ratios needed to obtain clinical effect, might have been patentable as composition of matter (ignoring for now any potential § 101 issues because they are “products of nature”).¹⁴² In this regard, the registry suggested in the Bolivian Constitution seems to anticipate the patenting of active substances (like those in **Fig. 2**) since it suggests adding “active substances” to the registry.¹⁴³ This would enlarge the prior art shield beyond plants, to include the active components contained in the plants.

[57] While the inclusion of active chemical substances in national registries might prevent undesirable patenting by foreign bioprospectors, it would also prevent desired patenting by Amazonian researchers seeking to develop or co-develop drugs derived from TMK. This is unfortunate, since there may be situations where an Amazonian research scientist may want to co-develop a drug derived from TMK, but now will not be able to do so. The irony of pharmaceutical development is that no matter how noble one’s intentions are (*e.g.* to “benefit mankind”), a strong patent position is needed so that a company financing the drug development can at least

¹⁴² See *supra* Figure 2.

¹⁴³ See *id.*

recoup its significant investment, often estimated to be in excess of \$1 billion.¹⁴⁴ How can the stated goal of using TMK to benefit mankind be achieved, if there is no way to finance the clinical trials that are required as part of drug co-development? This should be considered when Andean countries decide to pursue registries as a source of prior art; and, it is a reason to consider keeping chemical structures of active substances in private rather than public registries.

c. Trade Secrets – Private Databases of Licensable TMK

[58] The above dilemma is largely solved by using private rather than public databases of TMK, so that the ability to patent is not lost. For this reason, and in light of the recent passage of AIA, the private database should be considered the preferred strategy for protecting the IPR of indigenous peoples. It is preferred because it leaves open the option to license their TMK-based IP if and when it is desired, as part of a license agreement. Such an agreement would of course only be executed with informed consent and the promise of equitable sharing of benefits. Although, given that TMK is typically already “in use,” it is questionable whether – under AIA – it will ever be possible to patent TMK-based treatments again. But, combinations of active chemical substances, like those in **Fig. 2**, may still be patentable; so, that type of information should be kept private, if indigenous peoples may ever want to patent and/or license this valuable TMK-derived knowledge.¹⁴⁵ It is these active chemical substances, and strategic combinations thereof, that may be the only patentable subject matter based on TMK. It is this IP that is most likely to be the topic of drug co-development projects. And, it is in

¹⁴⁴ *Drug Developers Are Aggressively Changing the Way They Do R&D*, TUFTS CENTER FOR THE STUDY OF DRUG DEV. (Jan. 5, 2011), http://csdd.tufts.edu/news/complete_story/pr_outlook_2011, archived at <https://perma.cc/55GK-T5BA>.

¹⁴⁵ See *supra* Figure 2.

enabling these drug co-development projects, eventually involving a pharmaceutical company that demands composition of matter patent protection, that the lofty goal of benefiting mankind with TMK can be best achieved.

d. Strategies to Obtain Composition of Matter Patent Protection for TMK-derived Drugs

[59] Given the stated desire to benefit the world with TMK, and to – in some cases – license TMK, there may be times when indigenous peoples, in collaboration with academic researchers in Peru and abroad, would want to patent TMK-related inventions, including active substances.¹⁴⁶ Is it possible that the active chemical substances extracted from these plants – the “drugs” – may be patented as composition of matter (e.g. see **Fig. 2**)? Naturally occurring chemicals (aka “natural products”) are not patentable subject matter under 35 U.S.C § 101 if those chemicals are considered “products of nature.”¹⁴⁷ Thus, the answer to this question is, or was, thought to be no. In general natural products are not thought to be patentable, unless there is some unique manmade combination of natural products that is useful in an unanticipated way; and, that combination may be patentable as composition of matter.¹⁴⁸

[60] But, the definition of a “product of nature” may be changing in a

¹⁴⁶ This is an example situation.

¹⁴⁷ See *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2116 (2013).

¹⁴⁸ See e.g., U.S. Patent No. 7,915,265 B2 (filed Feb. 15, 2006); see also U.S. Patent No. 8,067,433 B2 (filed Nov. 8, 2006); Alice Yuen-Ting Wong & Albert Wai-Kit Chan, *Myriad and Its Implications for Patent Protection of Isolated Natural Products in the United States*, CHINESE MEDICINE, <http://cmjournal.biomedcentral.com/articles/10.1186/1749-8546-9-17>, archived at <https://perma.cc/K3VL-4SGX> (last visited Sep. 7, 2016).

way that could open the door to patenting natural products. While an early case decided by Justice Learned Hand allowed patenting of adrenalin¹⁴⁹, a purified natural product with clinical value, there has not been subsequent case law to support patenting of natural products simply because they have been purified.¹⁵⁰ This may change, as the U.S. Supreme Court recently clarified what molecules fall under the “product of nature” exclusion, in *Ass’n for Molecular Biology v. Myriad*.¹⁵¹ In this case, Myriad identified mutated genes (BRCA1 and BRCA2) associated with breast cancer, and sought to patent this for use as a breast cancer diagnostic.¹⁵² The issue is whether purified naturally occurring deoxyribonucleic acid (DNA) segments are patentable subject matter, or whether they are excluded as a product of nature under 35 U.S.C. § 101. Justice Thomas, speaking for the majority, held that purified DNA was naturally occurring, and therefore could not become “patent eligible under § 101 simply because they have been isolated.”¹⁵³ In contrast, complementary DNA (cDNA) that was synthesized in the laboratory based on that same DNA sequence was not considered naturally occurring, so was not excluded as patentable subject matter; and, therefore, was not considered a product of nature.¹⁵⁴ This is because cDNA is prepared synthetically in the laboratory, and because it differs from naturally occurring genomic DNA (gDNA) in that it has noncoding DNA segments (called “introns”) removed, making it distinct

¹⁴⁹ *See Parke-Davis & Co. v. H. K. Mulford & Co.*, 189 F. 95., 114 (S.D.N.Y. 1911); *see also* Michael D. Davis, *The Patenting of Products of Nature*, 21 RUTGERS COMPUTER & TECH. L. J. 293, 326 (1995).

¹⁵⁰ *See id.* at 324.

¹⁵¹ *See supra* note 147 at 2111.

¹⁵² *See id.* at 2113.

¹⁵³ *Id.* at 2120.

¹⁵⁴ *See id.*

from gDNA.¹⁵⁵

[61] *Myriad* teaches that naturally occurring molecules like gDNA (and by analogy, the ayahuasca active substances in **Fig. 2**) cannot be patented, because they are simply purified products of nature. But, if the chemical substance that is a product of nature is synthesized in a laboratory, and modified in a routine manner that makes it distinct from its naturally occurring form, then the molecule is no longer excluded as patentable subject matter.¹⁵⁶ By analogy, one would only need to synthesize and make routine modifications to the molecules shown in **Fig. 2**, to be able avoid the product of nature exclusion. This is a significant change in IP law surrounding natural products, and may increase the interest of pharmaceutical companies in the pursuit of such molecules as drugs.

[62] It remains to be seen whether the post-*Myriad* broadened definition of “product of nature” will extend to natural products, like the active chemical substances from ayahuasca (**Fig. 2**); and, if it does, what will be the nature of the routine modifications (if any) that are needed. It is possible that copies of plant-derived molecules, which are synthesized in the laboratory by chemists, will be considered patentable as composition of matter under 35 U.S.C. § 101, just as the manmade cDNA copy of gDNA was found to be patentable in *Myriad*. It might be argued that the cDNA molecule is more than simply a manmade copy of the naturally occurring gDNA molecule, because it has been modified by removal of introns.¹⁵⁷ But, intron removal is a trivial and routine change that is

¹⁵⁵ *Id.* at 2119.

¹⁵⁶ *See supra* note 147 at 2111.

¹⁵⁷ *See* Jason Rantanen, *Myriad: Isolated DNA out, cDNA in*, PATENTLYO (June 13, 2013), <http://patentlyo.com/patent/2013/06/myriad-isolated-dna-out-cdna-in.html>, archived at <https://perma.cc/3AZD-BQLW> (discussing the outcome of *Ass’n for Molecular Pathology v. Myriad*, 133 S. Ct. 2107, 2118 (2013)).

inspired by what nature does anyhow (introns are removed in making mRNA).¹⁵⁸ It cannot be considered a novel or inventive modification to the naturally occurring gDNA molecule; although, admittedly, novelty and inventiveness do not have direct bearing on this § 101 question. *Myriad* seems to indicate that one can patent a synthetic copy of a naturally occurring molecule, if a routine modification is made.¹⁵⁹ The key point is that the molecule does not occur in nature.¹⁶⁰ Applying this new test to other natural products, like the active substances in **Fig. 2**, there are a number of foreseeable routine chemical changes that would make the molecule chemically distinct. A non-exclusive list of possibilities is provided here:

- a) Synthesize chemical variants that have isotopic substitutions, such as replacing hydrogen atoms with deuterium atoms. This is a commonly used chemical substitution in drug design.¹⁶¹
- b) Convert the basic amine to HCl or other salts. This is also a routine change to the naturally occurring molecules, and often has utility for increasing drug bioavailability.¹⁶²

¹⁵⁸ See Z. Peter Sawicki et al., *Patenting Biologicals: Myriad Issues and Options in the Wake of Myriad*, BENCH & BAR (Sept. 9, 2013), <http://mnbenchbar.com/2013/09/patenting-biologicals/>, archived at <https://perma.cc/GR3J-8PBT>.

¹⁵⁹ See *supra* note 147 at 2112, 2117 (indicating that a small modification to naturally occurring DNA would likely qualify as a patentable product).

¹⁶⁰ *Id.* at 2116.

¹⁶¹ See, e.g., Kristin C. Buteau, *Deuterated Drugs: Unexpectedly Nonobvious?*, 10 J. HIGH TECH. L. 22, 26–27 (2009); Amanda Yarnel, *Heavy-Hydrogen Drugs Turn Heads, Again: Firms Seek to Improve Drug Candidates by Selective Deuterium Substitution*, CHEM. & ENG'G NEWS (June 22, 2009), <http://cen.acs.org/articles/87/i25/Heavy-Hydrogen-Drugs-Turn-Heads.html>, archived at <https://perma.cc/NSX4-7CRN>.

- c) Make a simple chemical modification, such as acetylation of amines or alcohols (*e.g.* with acetic anhydride).¹⁶³ This type of modification is what led to drugs like aspirin (acetylated salicylic acid, from willow tree bark) and heroin (acetylated morphine, from opium).¹⁶⁴

[63] All of the above chemical modifications are routinely used in drug development, so do not represent novel techniques or changes. But, they are analogous to and at least as novel as the changes made and techniques used in going from gDNA or mRNA to cDNA.¹⁶⁵ The latter techniques are performed so routinely that scientists can purchase kits to perform the production of cDNA from mRNA.¹⁶⁶ Thus, it seems that Myriad has

¹⁶² See, *e.g.*, Patrick Makary, *Principles of Salt Formation*, 2 U.K. J. PHARMACEUTICAL & BIOSCIENCES 4, 1, 3 (2014), http://www.ukjpb.com/pdf/UKJPB_SuperAdmin_49_49_1411846931.pdf, archived at <https://perma.cc/9CXQ-BHVY>.

¹⁶³ See C.R.A. Wright, *On the Action of Organic Acids and their Anhydrides on the Natural Alkaloids*, 27 J. CHEM. SOC'Y. 1031, 1032 (1874), <http://pubs.rsc.org/en/content/articlepdf/1874/js/js8742701031>, archived at <https://perma.cc/ECR9-V8UC>.

¹⁶⁴ See *id.*; see also U.N. OFFICE ON DRUGS & CRIME, *History of Heroin*, 5 BULL. ON NARCOTICS 3, 3 (1953), https://www.unodc.org/unodc/en/data-and-analysis/bulletin/bulletin_1953-01-01_2_page004.html, archived at <https://perma.cc/S5SP-3FSE>; BAYER, *Felix Hoffmann*, <http://www.bayer.com/en/Felix-Hoffmann.aspx>, archived at <https://perma.cc/HF2J-8JL4> (last visited Sep. 8, 2016).

¹⁶⁵ See *cDNA Production*, DAVIDSON COLL. DEPT. OF BIOLOGY, <http://www.bio.davidson.edu/genomics/method/cDNAproduction.html>, archived at <https://perma.cc/4PZE-F428> (last visited Sep. 8, 2016).

¹⁶⁶ See *e.g.*, THERMO FISHER SCIENTIFIC, <http://www.thermofisher.com/us/en/home/life-science/pcr/reverse-transcription/cdna-synthesis-kits.html>, archived at <https://perma.cc/FKX6-FYBQ> (last visited Sep. 8, 2016).

opened the door to patenting natural products, after small and even routine chemical structure changes are made.

[64] If natural products (after routine chemical alteration) can be patented as composition of matter, this would increase the pharmaceutical industry's interest in pursuing natural products as drugs. This would open the door to more patenting of drugs derived from TMK in co-development initiatives. This could lead to significant revenue generation (to be shared equitably with indigenous peoples) and to medical benefits for the rest of the world.

[65] Even if individual plant-derived molecules (after modification) cannot be patented as easily as just described, combinations like those shown in **Fig. 2** could be patentable.¹⁶⁷ Indeed, combinations of active substances are central to how many traditional medicines, like ayahuasca, work (see section II). This is a distinguishing feature of traditional medicines relative to western medicine.¹⁶⁸ Only the shaman, based on TMK, knows which combinations of plants will produce the desired therapeutic effect. Then, the chemist can build on this TMK to identify which combinations of purified active chemical substances extracted from those plants are needed to reproduce these clinical effects. This combination, discoverable only through a collaborative co-development effort between indigenous peoples and scientific researchers, could then be patented.¹⁶⁹

[66] In summary, indigenous peoples should consider the value of

¹⁶⁷ See *supra* Figure 2.

¹⁶⁸ E. Chan, M. Tan, J. Xin, S. Sudarsanam & D.E. Johnson, *Interactions Between Traditional Chinese Medicines and Western Therapeutics*, 13 CURRENT OPINION DRUG DISCOVERY & DEVEL. 50, 52 (2010); see *supra* Section II.

¹⁶⁹ *Id.* at 63.

composition of matter patent protection, if they hope to reap the full benefit of their TMK for themselves and the world. Recent developments in U.S. patent law suggest new strategies to obtain composition of matter protection to increase the value of indigenous peoples' TMK to a potential drug co-development partner from the pharmaceutical industry.

e. Proposed Structure for a Drug Co-Development Research Agreement

[67] In the interest of transparency and ensuring that the interests of all parties are considered, it is advisable that drug co-development projects between Peruvian and U.S. researchers execute a research agreement when working with indigenous peoples. Such an agreement should build upon the above legal protections for TMK (section IV(A)(a)), and be consistent with regional and international laws. A sample agreement is provided below:¹⁷⁰

(SAMPLE) TMK-BASED DRUG CO-DEVELOPMENT RESEARCH AGREEMENT

[68] This research and drug co-development agreement (“Agreement”) is made by and among the following collaborating parties (“Parties”): Indigenous Peoples Representative (“Party 1”), Peruvian Research Team Representative (“Party 2”), and U.S. Research Team Representative (“Party 3”).

DEFINITIONS

[69] “**TMK**” means traditional medical knowledge: “knowledge, know-how, skills and practices that are developed, sustained and passed on from

¹⁷⁰ This sample agreement was created for purposes of this article.

generation to generation within a community, often forming part of its cultural or spiritual identity.”¹⁷¹

[70] “**INDECOPI**” means National Institute for the Protection of Competition and Intellectual Property: an organization that manages the Local, National and Public Registers of Collective Knowledge of Indigenous Peoples.¹⁷²

[71] “**TPA**” means The U.S.-Peru Trade Promotion Agreement, the agreement between the U.S. and Peru that governs trade, but also includes the “Understanding Regarding Biodiversity and Traditional Knowledge.”¹⁷³

[72] “**Indigenous Peoples**” means “aboriginal peoples holding rights that existed prior to the formation of the Peruvian State, maintaining a culture of their own, occupying a specific territorial area and recognizing themselves as such. These include peoples in voluntary isolation or with which contact has not been made, and also rural and native communities.”¹⁷⁴

[73] “**Informed Consent**” means authorization given under this protection regime, by the representative organization of the indigenous peoples possessing collective knowledge and in accordance with provisions recognized by them, for the conduct of a particular activity that entails access to and use of the said collective knowledge, subject to the provision of sufficient information on the purposes, risks or implications

¹⁷¹ See *supra* note 16.

¹⁷² See Ley N° 27811 [Law No. 27811], *supra* note 75 at art. 20.

¹⁷³ See *supra* note 96.

¹⁷⁴ See Ley N° 27811 [Law No. 27811], *supra* note 75 at art. 2(a).

of the said activity, including any uses that might be made of the knowledge, and where applicable on its value.¹⁷⁵

[74] “**CDA**” means confidential disclosure agreement.

PROVISIONS

[75] **WHEREAS**, the Parties share a common interest in developing drugs derived from TMK;

[76] **WHEREAS**, the Parties share a desire to see TMK and associated intellectual property rights (IPRs) protected, yet also benefiting the world;

[77] **WHEREAS**, the Parties agree to equitably share financial and other benefits that could result from this collaboration;

[78] **WHEREAS**, the Parties agree to show mutual respect for each other’s governing laws, customs and values;

[79] **WHEREAS**, the Parties agree that TMK is owned by Indigenous Peoples, and any development and patenting of drugs derived from TMK will only occur with permission that is be granted by Party 1, after being fully informed of all relevant risks and benefits via Informed Consent;

[80] **WHEREAS**, Parties 1 and 2 agree to collaboratively pursue studies directed to identifying the active chemical component(s) derived from TMK-based plants, which are responsible for desirable medical effects;

[81] **WHEREAS**, the Parties agree to negotiate in good faith any license agreements for TMK and TMK-derived patents, including composition of matter patents on active chemical substances;

¹⁷⁵ *Id.* at art. 2(c).

[82] **NOW, IT IS THEREFORE RESOLVED**, in consideration of the forgoing, that the parties hereby agree to the following:

[83] **1. Purpose and Scope**

The Parties recognize that Amazonian TMK is a rich source of useful medical treatments that have been collectively developed over many years, and is owned by the Indigenous Peoples which Party 1 represents. Parties are mutually committed to the promotion of respect, preservation and wider application of TMK, as well as the use of TMK to benefit Indigenous Peoples, and mankind in general. Such benefits include the development and dissemination of new and better medical treatments. Benefits may also be financial, based on revenue generated from sales drugs and/or licensing of IP based on development of TMK-based medicines. Such development is only to be pursued according to the other sections of this agreement, which emphasis equitable sharing of benefits, and Informed Consent (Appendix A) from Party 1, before developing TMK-derived drugs.

The research and drug co-development team shall engage in activities that include biological demonstration of safety and efficacy of TMK-derived treatments, including plant extracts that are prepared by Party 1. Activities performed by Parties 2 and 3 may also include purification and chemical characterization of the active chemical components present in TMK-derived treatments. This may be followed by chemical synthesis of these active chemical components, and demonstration of their biological safety and efficacy, alone and in combinations. Parties 2 and 3 agree to keep Party1 informed of significant developments in these studies, and to seek the Informed Consent (Appendix A) of Party 1 before filing patent applications on composition of matter identified in these studies. Likewise, Parties 2 and 3 agree to enter these chemical structures into Peru's National Registries for TK. If a decision is made to patent the composition of matter, submission will only be made to the private registry (until the patent publishes). If Party 1 decides to keep the chemical structure information as a trade secret,

Parties 2 and 3 agree to honor this request, subject to §2 of this agreement.

[84] **2. Decision-making**

Party 1 agrees to develop governance procedures that ensure they are representing the broader interests of the Indigenous Peoples that own the TMK which is the topic of this research and drug co-development collaboration. Party 1 has the sole power to decide if chemical structures of active substances, derived from plant extracts, are to be: (a) kept as trade secrets, (b) the subject of a patent application, or (c) entered in the National Public Registry of Collective Knowledge of Indigenous Peoples. Party 1 agrees to not unreasonably withhold permission to patent; and, if both Parties 2 and 3 wish to file a patent application, but Party 1 refuses, Parties 2 and 3 may appeal the decision to an appellate body that has previously been chosen by the Indigenous People who Party 1 represents. Other project decisions, which do not directly relate to IPRs, will be made by majority vote of the three representatives.

[85] **3. Confidential Information**

Parties agree to sign a CDA (Appendix B) to protect all confidential information that is shared or developed in this collaboration. Such information may include TMK-related trade secrets of Party 1, including those that are kept in the National Private Register of Collective Knowledge of Indigenous Peoples. Parties agree to not publicly disclose chemical structures that are identified during this collaborative co-development initiative, without unanimous agreement by all three representatives. Likewise, Parties 2 and 3 agree to not publicly disclose trade secrets that have been revealed to them by Party 1, unless Party 1 grants permission to do so.

[86] **4. Intellectual Property (IP)**

Parties 2 and 3 agree that all TMK-related trade secrets that pre-date this agreement, including those that were previously entered into the National Private Registry of Collective Knowledge of Indigenous Peoples,

are property of Party 1. Such trade secrets will be revealed and/or licensed at the discretion of Party 1. Parties 2 and 3 will not patent any TMK-derived invention without first obtaining permission from Party 1, and this permission is to be granted only after Party 1 has signed the Informed Consent document in Appendix A that outlines all significant risks and benefits.

The IP that is most likely to result from this collaborative co-development initiative includes chemical structures of active substances that are purified from plant extracts of TMK-based therapies. These chemical structures will be protected via composition of matter patents or trade secrets or, at the discretion of Party 1, publicly released via the Public National Register of Collective Knowledge of Indigenous Peoples, in order to create prior art that prevents patenting by other parties (subject to § 3 of this agreement). Parties will work with INDECOPI to enter TMK-derived information into the National Registers of Collective Knowledge of Indigenous Peoples, including chemical structures.

[87] **5. Licensing of TMK and TMK-derived Intellectual Property**

Since Parties share an interest in benefiting the world based on TMK-derived therapies, and associated discoveries, and since drug development is extremely expensive, it may become necessary to license IP to an external partner. Such an external partner would typically be a pharmaceutical or biotechnology company that has the resources and experience needed to develop drugs that result from this collaboration. Such arrangements typically require that the composition of matter patent protecting the drug lead molecule be licensed to them; and, it is expected that the pharmaceutical partner and Parties would negotiate a revenue sharing arrangement that could include upfront financial payments, payments upon achievement of certain milestone events (*e.g.* completion of different phases of clinical trials), and royalties on net or gross profits from drug sales, once the drug is approved by appropriate regulatory agencies, such as the Food and Drug Administration in the U.S.

Parties agree to negotiate in good faith an agreement that equitably

shares benefits between all three groups, and will be defined in detail in the license agreement (Appendix C). Such an agreement might include an equal sharing of revenues between all three groups, although other arrangements could be negotiated. In negotiating terms, Parties agree to consider and honor existing legal structures, such as those associated with the TPA, the Andean Community, and the *sui generis* protections in Peru (esp. Law No. 27811).¹⁷⁶ Accordingly, Parties agree that the license agreement will be prepared, executed and properly recorded using the WIPO “toolkit”¹⁷⁷. Any license agreement will ensure equitable sharing of benefits derived from the use of TMK, including >10% of revenues provided to the Fund for Development of Indigenous People, before distribution to the three groups that comprise the Parties.¹⁷⁸ Such an agreement will only be executed after Party 1 has been made aware, via Informed Consent (Appendix A), of all the risks and benefits associated with pursuit of the license agreement (Appendix C). Any license agreement that is executed, even those which are categorized as “exclusive,” will provide an exception for the Indigenous People that Party 1 represents, to ensure that they will be able to continue to use their TMK as they had before the license agreement was executed.

[88] **Appendices:** (A) Informed consent form, (B) Confidential disclosure agreement (CDA), (C) Draft license agreement.

V. CONCLUSION

¹⁷⁶ *See id.*

¹⁷⁷ *See* WIPO Toolkit, *supra* note 92 .

¹⁷⁸ *See* Ley N° 27811 [Law No. 27811], *supra* note 75 at art. 8.

[89] The TMK underlying medical treatments used by indigenous peoples has great value to their communities and may also have great untapped value for the rest of the world. The goal of the collaborative drug development projects described herein, involving researchers in the U.S. and Peru, is to extend the benefits of TMK to the rest of the world, while respecting the IPR of the indigenous peoples from whom TMK-based discoveries may be derived. Of particular importance is ensuring equitable sharing of any future benefits of drug co-development successes with the indigenous peoples, and making sure all decisions are made based on informed consent that fully discloses all material risks and benefits.

[90] A model example of a TMK-based medicine is ayahuasca (**Fig. 1**).¹⁷⁹ For ayahuasca to work effectively, the shaman mixes two or more plants and prepares a tea – a type of plant extraction. Subsequent scientific research has established why it is necessary to mix these plants, based on chemical substances that have been extracted and identified from each (**Fig. 2**).¹⁸⁰ While the researchers who identified these active chemical substances did not pursue a *composition of matter* patent on them, such a strategy could have been taken. If it had, it should only have been pursued with the informed consent of the indigenous peoples who owned this TMK-based IP; and, there should be equitable sharing of future benefits. The example of the Miller patent on the ayahuasca plant (**Fig. 3**) illustrates an unsavory effort to bypass this process, which led to public outcry and the subsequent creation of laws and procedures to ensure protection of Peru's IPRs.¹⁸¹

[91] Future drug co-development initiatives should build on these lessons from ayahuasca, to ensure protection of IPR via compliance with

¹⁷⁹ See *supra* Figure 1.

¹⁸⁰ See *supra* Figure 2.

¹⁸¹ See *supra* Figure 3.

national, regional and international laws and treaties, including those embodied in Peru's *sui generis* protections (Law No. 27811), the Andean Community, and the U.S.-Peru TPA. With these constraints and guidelines, research collaborations between U.S. researchers, Peruvian researchers, and indigenous communities can proceed to co-develop TMK-derived drugs. To guide this process, a draft drug co-development agreement has been provided in this paper (section IV). Central to this agreement is a focus on identifying active chemical components from plant extracts and patenting them as *composition of matter*. This focus is a pragmatic requirement, since pharmaceutical companies who may license these patents for further co-development will only make a significant financial investment if they have the strong protection that *composition of matter* (not *method of use*) patents provide. This co-development process has the potential to extend the benefits of TMK to the rest of the world, which is a shared goal of all parties involved.