PROTECTING PLANT-DERIVED DRUGS: PATENTS AND BEYOND

I. INTRODUCTION

The importance of plants and plant extracts for the treatment of illness has long been recognized. The Chinese have used herbal treatments for a variety of health related problems for thousands of years. Indigenous populations in many developing nations rely on traditional medicine, which employs many plant extracts, to "bridge the gap between the availability of and the demand for modern medicines."[1] In the United States, herbs and herbal products are a big business.[2] However, pharmaceutical companies seeking to develop modern drugs from plants or plant extracts are faced with a variety of scientific and legal problems. These problems have prevented pharmaceutical companies from conducting the large-scale research and development necessary to produce potentially large numbers of medically valuable plant-derived drugs.

This Note addresses the legal difficulties confronting pharmaceutical companies that attempt to obtain exclusive marketing rights, by way of patent protection, for newly developed plant-derived drugs. These rights are a necessary part of the drug development process. Pharmaceutical companies cannot recover large research and development investments without exclusive rights. As a result, companies are unwilling to make the initial investments required to develop potentially useful drugs.[3]

Part II of this Note discusses the economic significance that plant-derived drugs currently have on the market and the significance that the world's tropical rain forests have on the development of plant-derived drugs. Since the forests are home to a large portion of the plants from which these drugs come, the preservation of these rain forests is crucial to the development of the plant-derived drug industry. Part III presents a background of the plant-derived drug industry over the past few decades. This Part analyzes the patent system as it applies to plant-derived drugs and concludes that the patent system is not broad enough

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[1] O. Akerele, *Medicinal Plants and Primary Health Care: An Agenda for Action*, 59 FITOTERAPIA 355, 357 (1988).

[2] Varro E. Tyler, *Herbal Medicine in America*, 1987 PLANTA MEDICA 1.

[3] These investments do not come only in the form of research and development expenses. A pharmaceutical company will typically spend $200 million dollars to generate new drug approval from the Food and Drug Administration.

to provide protection for most plant-derived drugs. Part IV presents non-patent alternatives for the protection of plant-derived drugs. Foremost among these alternatives is the passage of new legislation that would provide patent-like protection, via exclusive marketing rights for limited periods of time, to provide pharmaceutical companies with incentives to invest money toward the research and development of new plant-derived drugs.

II. BACKGROUND

A. *Prescription Drugs Derived From Plants*

One fourth of all currently dispensed prescriptions in the United States contain at least one drug that is extracted from higher plants.[4] The American public pays billions of dollars annually for these prescriptions.[5] Presently, 121 prescription drugs are extracted from higher plants.[6] "[These] drugs are obtained from only . . . [ninety-five] of the known 250,000 species of plants . . . ."[7] Furthermore, thirty-five of the ninety-five species are found in and around tropical rain forests, and eighteen major drugs used in the United States are derived from these rain forest plants.[8]

B. *The Significance of the Rain forests*

The world's tropical rain forests,[9] which cover only about seven percent of the earth's surface,[10] contain at least half of its species.[11] Very little is known about most of these species, and

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[4] Norman R. Farnsworth, Ph.D., *The Value of Plants From Tropical Rainforests as Potential Drugs*, Speech at Conference for Conservation of Tropical Rainforests 3 (undated) (transcript available through the Program for Collaborative in the Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago).

[5] Peter Principe, *The Economic Significance of Plants and Their Constituents as Drugs*, 3 ECONOMIC AND MEDICINAL PLANT RESEARCH 1, 7-8 (1989).

[6] *Id.* at 1.

[7] *Id.*

[8] *Id.* at 1-2. For example, vincristine, a drug used to treat childhood leukemia, and vinblastine, a drug used to treat Hodgkin's disease, are both derived from the Rosy Periwinkle [*Vinca rosea*], a small red flower that grows in the tropical rain forests of Madagascar. Farnsworth, *supra* note 4, at 7. Oral contraceptives are made from the steroid Diosgenin, which is derived from the Mexican Yam [*Dioscorea mexicana*] and other wild tropical yam plants. NORMAN MYERS, THE PRIMARY SOURCE: TROPICAL FORESTS AND OUR FUTURE 217 (1984).

[9] Tropical rain forests and moist forests are forests in frost-free areas that have a mean annual temperature of at least 75 degrees Fahrenheit. These areas typically receive "2,000 mm. or more of rainfall per year and not less than 100 mm. of rainfall in any month for two out of three years. . . . [These evergreen forests are generally found] at altitudes below 1,300 meters." MYERS, *supra* note 8, at 40.

[10] Farnsworth, *supra* note 4, at 1.

[11] MYERS, *supra* note 8, at 46. Like terrestrial ecosystems, marine ecosystems, particularly coral reefs, have only been explored in a limited way as a drug source. Scientists

they, along with their rain forest habitat, are disappearing at a rate unparalleled in human history.[12] "Rain forest plants have been likened to 'complex chemical storehouses' containing thousands of natural chemical compounds with unrealized potential for modern medicine."[13] Fewer than one percent of tropical forest species have been examined for possible pharmacological use, despite the belief that at least 1400 tropical forest plant species have cancer-fighting potential.[14]

According to one study, in a random group of 10,000 plants, between one and ten plants would yield a marketable drug with a commercial value of $600 million (in 1980 dollars) in the countries that are members of the Organization for Economic Cooperation and Development.[15] If the present rate of plant extinction continues,[16] about twenty-five marketable prescription drugs will be lost in the next ten years, with an estimated economic loss of $15 billion in the year 2000 and an additional $15 billion lost in benefits to the pharmaceutical industry in each subsequent year.[17]

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discovered that marine organisms produce secondary metabolites that are quite different than those produced by terrestrial plants, animals and microbes. These structurally unusual metabolites also exhibit biological activity, including anti-tumor activity. *See generally Vast Potential Seen: Marine Research Yields Unique Drugs*, PHARMACY PRACTICE NEWS, Oct. 1988, at 1; Lucy Bunkey-Williams & Ernest H. Williams, Jr., *Global Assault on Coral Reefs*, NATURAL HISTORY, Apr. 1990, at 47.

12 Rain forests are disappearing at an estimated rate of between 35.2 and 42 million acres per year. William R. Long, *Rain Forests Boycott Questioned*, L.A. TIMES, Sept. 17, 1991, at 1; Juliette Rouillon, *Forestry Experts Fail to Agree on Charter to Protect Trees*, REUTERS LIBRARY REPORT, Sept. 26, 1991.

13 *Biotechnology and Medicinal Plants*, RAFI COMMUNIQUE (Rural Advancement Fund International, Pittsboro, N.C.), Mar. 1989, at 2.

14 *Id.*

15 Principe, *supra* note 5, at 10. There are twenty-four OECD member countries including Australia, Canada, the United Kingdom and the U.S. *Id.* at 2.

16 It is estimated that 20-25% of the world's plant species may be lost by the year 2000. *id.* at 1.

17 *Id.* at 10. Norman Farnsworth, Professor of Pharmacology at the University of Illinois at Chicago, points out that beyond the economic value of plant-derived drugs, there is also tremendous value in alleviating human suffering.

> [H]ow many lives have been saved since the discovery of quinine and the anticancer alkaloids vinblastine and vincristine? How many people with glaucoma have had their eyesight conserved since the discovery of pilocarpine? How many major surgical procedures have been successful because of the discovery of tubocurarine? How many mental patients have been helped since the discovery of reserpine? The numbers required to answer these questions are inestimable, but surely count in the tens of millions.

Farnsworth, *supra* note 4, at 4.

Quinine, derived from the bark of the Cinchona tree, is used to treat malaria. Quinidine, an isomer of quinine, is used to control heart dysrhythmia. Pilocarpine is derived from the *Pilocarpus* plant, a tropical member of the citrus family, and is used to combat glaucoma. Tubocurarine is derived from the plant *Chondodendron tomentosum* of the family Menispermaceae. It is a neuromuscular blocking agent used during surgery to avoid muscle spasms. There are also several semi-synthetic drugs that have been derived from

The potential for developing new drugs from plants found in rain forests is great, as is the potential market value of these drugs. However, because the rain forests are being destroyed rapidly, their potential as a source of new drugs and revenue is diminishing drastically. These storehouses of complex chemicals should not be ignored as potential sources of new drugs. It is thus imperative for Congress to create a drug protection system that would give ample financial incentive to pharmaceutical companies to develop and market new drugs.[18] Without such a drug protection system, valuable plant-derived drugs may be permanently lost, particularly given the current rapid rate of plant extinction.

III. Patenting Plant-Derived Drugs

From the 1950s to the mid-1960s, plant research played a significant role in pharmaceutical discovery. However, a number of problems developed that discouraged pharmaceutical companies from pursuing plant research. These problems included the inability to identify plants in a reproducible or accurate way, the seasonal or geographic variations in the chemical compositions of plants and a lack of sophisticated testing techniques.[19]

In addition to these scientific problems, the legal problem of non-patentability[20] of a true "product of nature" largely contrib-

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the original drug. Reserpine is derived from the roots of the *Rauvolfia serpentina* plant and used in the treatment of schizophrenia and hypertension. *Id.* at 6-10.

Plants may hold valuable secrets that could, in the future, lead to cures for various types of cancer, AIDS or other diseases. In fact, evidence from studies of the eating habits of several wild primate species illustrates that certain secondary plant compounds they eat may act as control agents for a variety of different pathogens, including the STLV-III virus, a simian virus that is closely related to the AIDS agent in humans. It may be worth screening some of the plants eaten by African primates in the hope of finding some compounds that exhibit suitable anti-viral activity. Compounds isolated in this way are likely to be cheaper to manufacture than laboratory-synthesized drugs and may have already been screened (by the primates) for unpleasant side effects. E.R. Carper & A.P. Dobson, *What Else can Green Monkeys tell us about AIDS?* 2 Tree 374 (1987).

[18] A properly constructed protection system would not only encourage pharmaceutical development, but would also encourage a sustainable use of rain forest resources. For a discussion of possible protection systems for plant-derived drugs, see *infra* notes 123-34 and accompanying text.

[19] Interview with James McChesney, Univ. of Miss., p.1. "[C]apabilities of synthetic organic chemistry were increasing [simultaneously with these difficulties. Thus, many] new chemical compounds could be prepared [in the laboratory in a] relatively eas[y] and straightforward [manner], sufficient for evaluation by the compan[ies]." They no longer felt the need to look for new chemical compounds elsewhere. *Id.* Furthermore, the microbiological and fermentation aspects of the industry were rapidly growing. The discovery of antibiotics and many other important pharmaceutical products resulted from the evaluation of many microorganisms through fermentation procedures. *Id.*

[20] For a full discussion of the patentability of a product of nature, see *supra* notes 18-19 and accompanying text; *infra* notes 21-75 and accompanying text.

uted, and continues to contribute, to the pharmaceutical companies' reluctance to research and develop plant-derived drugs.[21] Because "[d]rugs are central to the American economy, . . . it is

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[21] Academics and industrialists have a general sense that over the past few years there has been a renewed interest in natural drug research, but the precise extent of this interest is unclear and difficult to determine. Generally, large pharmaceutical companies have developed small departments for plant research. Several smaller start-up companies work exclusively with plant-derived drugs. These companies, precisely because they are new, have no prior vested interest in other research projects and are thus able to devote incoming capital to plant research projects. *See generally* Interview with Raffauf; Interview with Brad Carte, Dep't of Biomolecular Discovery (Smith-Kline); Interview with James McChesney, Univ. of Miss.; Telephone interview with Janice Thompson (Affymax, Natural Prods. Sciences, Utah) [hereinafter Thompson Interview] (Christina Findeisen did the preceding series of interviews, informally entitled *Interviews Concerning Current Interest in Tropical Plant Research* [hereinafter *Research Interviews*]; the transcripts are on file with the author. The biographical and historical information about the interviewees is unavailable).

There are several reasons for this resurgence of activity. Scientists have become more knowledgeable about how to collect and identify plants. Bioassay technology has become more sophisticated. Bioassays can now be done on cells, rather than on live animals, by robots working day and night. The robots are so efficient in doing chemical syntheses that companies are beginning to look for other sources for bioassays. Natural sources seem to be the next logical step. *See Research Interviews*, *supra*. Plants in particular can be tested more efficiently both for subtle effects and for a greater variety of effects. *Id.* Additionally, the likelihood of finding a successful plant-derived drug can be increased somewhat by using one of two approaches, either of which will limit what was previously a random sampling process through either of two approaches. The first is an ethnobotanical approach to the screening process. *Id.* Indigenous populations, living in the same regions for thousands of years, can lead researchers to plants that have been used locally over a period of time with some proven success. The second approach may be described as a "chemically similar" approach. For example, we know that many of the useful drugs that have come from plants are alkaloids. In the second approach, then, only plants containing alkaloids would be examined. *Id.*

Despite all of this encouraging activity, new trends in the pharmaceutical industry continue to evolve that may delay a fuller commitment by the larger pharmaceutical companies to plant research. Rational drug design, for example, is seen by some members of the industry as the wave of the future: Thompson Interview, *supra*. Rational drug design is a method of drug development in which "scientists use powerful computer models to analyze the target cells and design a drug molecule that can latch on in the needed way." Rami Grunbaum, *Biotech Veterans Seek Secrets of 'Jungle Medicine,'* PUGET SOUND BUS. J., Sept. 30, 1991, § 1, p. 3, *available in* LEXIS, Nexis Library, UMI/Data Courier File. An additional problem that may delay a full-fledged investment in plant-derived drug development is sourcing. Pharmaceutical companies have attempted to synthetically produce valuable natural compounds, but for the most part have been unsuccessful. Of all plant-derived drugs, only ten are currently synthesized, and two are chemically modified. Pharmaceutical companies still rely heavily on the plants themselves as sources for these drugs. Farnsworth, *supra* note 4, at 1. Heavy harvesting in a particular area may deplete the resources to the extent that they are no longer renewable. In addition to the reduced profitability that unsustainable harvesting of resources may cause, the conservation of ecosystems from which we derive these plants is a critical concern. For example, in Madagascar all of the native rosy periwinkle habitat is gone. In several developing nations, natural resources are being destroyed and sold off both by commercial interests and by the local people. Jay Hair, President of the National Wildlife Federation, said that "[w]e are losing entire genetic stocks of wild living resources at a time when we're learning about the potential medical marvels of some of these plants." Cindy Harger, *International Trade Wipes Out Life-Saving Plants*, CONSERVATION, July 13, 1990, at 12.

Both the rain forests and the coral reefs are considered "key players in the greenhouse scenario" and play extremely significant roles in reducing greenhouse gases by

perfectly logical from a business point of view to seek a cure for cancer [and other diseases] in the form of a patentable and marketable drug."[22] Without the economic incentive and the market exclusivity, which ordinarily result from a patent, pharmaceutical companies will not invest in the research and development needed to bring plant-derived drugs to market.

A. *Utility Patents*

There are no separate or unique rules for examining an invention such as a plant-derived drug that has its source in nature.[23] An invention or discovery will receive a patent, under the Patent Act,[24] if it is either a "manufacture," "process," or "composition of matter"[25] that meets the statutory requirements of

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removing large volumes of Carbon dioxide from the atmosphere. Williams & Williams, *supra* note 11, at 54.

Incentive must be provided to pharmaceutical companies and to developing countries to preserve the biodiversity that is invaluable to the discovery of new drugs and the future health and welfare of the planet.

22 RALPH W. MOSS, THE CANCER INDUSTRY: THE CLASSIC EXPOSÉ ON THE CANCER ESTABLISHMENT 83 (First Paragon House paperback ed., 1991).

23 Not all plant-derived drugs are patentable under current law. Although courts and the U.S. Patent and Trademark Office have traditionally used the term "work of nature" to label subject matter unpatentable, *see* Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948), they have also held that certain chemicals, *see* In re Williams, 80 U.S.P.Q. (BNA) 150 (1948), biochemicals, *see* Merck & Co. v. Olin Mathieson Chem., 116 U.S.P.Q. (BNA) 484 (4th Cir. 1958), and organisms, *see* Diamond v. Chakrabarty, 447 U.S. 303 (1980); U.S. pat. 4,736,866 (1988) (patent granted for transgenic mouse with propensity to develop cancerous tumors), all of "natural origin," are patentable. The *Manual of Patent Examining Procedure*, which represents the Patent Office interpretation of the Patent Act language, "instructs Examiners [that] . . . a thing occurring in nature, which is substantially unaltered, is not a 'manufacture' " and is therefore not patentable subject matter. M. Jacob, *Patentability of Natural Products*, 52 J. PAT. [& TRADEMARK] OFF. SOC'Y 473 (1970) (citing the *Manual of Patent Examining Procedure* § 706.03(a)). But as Justice Frankfurter pointed out more than forty years ago:

> It only confuses the issue, however, to introduce such terms as "the work of nature" and the "laws of nature." For these are vague and malleable terms infected with too much ambiguity and equivocation. Everything that happens may be deemed "the work of nature," and any patentable composite exemplifies in its properties "the laws of nature." Arguments drawn from such terms for ascertaining patentability could fairly be employed to challenge almost every patent.

Funk Bros., 333 U.S. at 134-35 (Frankfurter, J., concurring). Thus, the terms "product of nature" and "product derived from nature" are not definitions but are instead legal conclusions used as labels once the patentability of a particular invention has been determined. Patent application examiners should use great care to insure that they do not reject patent applications based on inappropriate legal conclusions rather than on definitions. A product that has its source in nature may still, if it meets the statutory requirements, receive patent protection.

24 35 U.S.C. §§ 101-104 (1988).

25 *Id.* § 101; Brenner v. Manson, 383 U.S. 519, 528-31 (1966). Inventions that are machines are also included in section 101 and can thus receive patent protection. However, because plant-derived drugs are never machines, the option of achieving "machine" status as a threshold requirement to obtaining patent protection is not discussed in this Note.

"utility,"[26] "novelty"[27] and "non-obviousness."[28] Patent protection lasts for seventeen years and is not renewable.[29]

1. Threshold Statutory Requirements

a. Manufacture or Composition of Matter

Articles are "manufactured" if they are produced " 'for use from raw or prepared materials by giving . . . these materials new forms, qualities, properties, or combinations, whether by hand-labor or by machinery.' "[30] " '[C]omposition[s] of matter' . . . [include] all compositions of two or more substances and . . . all composite articles, whether they be [the] results of chemical union, or of mechanical mixture, or whether they be gases, fluids, powders or solids."[31]

A compound or composition of materials that is simply discovered from nature is not patentable.[32] For an invention to qualify as a manufacture it must be substantially altered from its natural state.[33] A patent does not issue for a substance, such as a product of nature, which the public might already be able to use.[34] Thus, to be patentable, plant-derived drugs must be substantially altered from their plant sources.

It is possible to obtain patent protection for a chemical compound that exists in nature, but only if it exists in nature in combination with other compounds.[35] In *Farbenfabriken Co. v. Kuehmsted*,[36] the claimed compound, acetylsalicylic acid, now commonly known as aspirin, had previously existed only in a crude form. In its original state, as part of another compound, acetylsalicylic acid had no medicinal use. However, as a pure compound, aspirin, it has many medicinal uses. This alteration was substantial enough to allow the product to achieve the

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26 35 U.S.C. § 101.

27 *Id.* §§ 101-102.

28 *Id.* § 103.

29 *Id.* § 154; Brulotte v. Thys, 379 U.S. 29, 31 (1964) (holding patent "rights become public property once the 17-year [term] expires").

30 American Fruit Growers v. Brogdex Co., 283 U.S. 1, 11 (1931) (quoting CENTURY DICTIONARY).

31 Shell Dev. Co. v. Watson, 149 F. Supp. 279, 280 (D.C. 1957).

32 *See* Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127 (1948).

33 Jacob, *supra* note 23, at 473 (citing the *Manual of Patent Examining Procedure* § 706.03(a)).

34 John M. Czarnetzky, *Altering Nature's Blueprints For Profit: Patenting Multicellular Animals*, 74 VA. L. REV. 1327, 1335 (1988); *see also Funk Bros.*, 333 U.S. at 130 (Patents may not issue for naturally occurring items.).

35 Karl Bozicevic, *Distinguishing 'Products of Nature' From Products Derived From Nature*, 69 J. PAT. [& TRADEMARK] OFF. SOC'Y 415, 420 (1987).

36 171 F. 887 (C.C. N.D. Ill. 1909), *aff'd*, 179 F. 701 (7th Cir. 1910).

threshold patentability status of manufacture.[37] In *In re Williams*,[38] the Court of Customs and Patent Appeals found that the existence of a compound as an ingredient of another substance does not render a claim to the pure compound unpatentable for lack of novelty.[39] While the *Williams* decision is based on a novelty claim, the "conceptual holding and its reasoning"[40] help to illustrate that compounds that do not exist alone in nature but do exist in combination with other compounds may be patentable.[41]

In *Merck & Co. v. Olin Mathieson Chemical*,[42] "[t]he 'claimed vitamin B_{12},' [a fermentation product,] was distinguished from 'natural vitamin B_{12},' [a liver extract,] by its means of production and level of activity."[43] Until the invention of the new vitamin B_{12}, no one had succeeded in isolating and identifying the active substance in cattle liver that was capable of alleviating pernicious anemia. The new product could be produced more economically and administered in controlled dosages, making its use safer, more predictable and more efficient than the use of liver extract.

By manipulating claim language in a patent application to highlight the "manufactured" aspects of the invention, patent protection on a product originally discovered in nature may be obtained.

> [T]he discovery of a product in nature, although not an invention, may well lead to an invention by the use of proper claim language [in the patent application]. Claim limitations can be used to describe a physical separation of the discovered compound from its natural surroundings (as in *Williams*) or to describe its means of production and activity (as in *Merck*).[44]

In *Williams* and *Merck*, it was not the discovery of previously known compounds, by itself, that provided for patentability. The discovery of those known compounds allowed the inventors to derive chemicals distinct from their natural sources.

In *In re Bergstrom and Sjovall*,[45] the inventors isolated certain compounds from animal gland secretions. These secretions were

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37 *Id.* at 890.

38 80 U.S.P.Q. (BNA) 150 (C.C.P.A. 1948).

39 *Id.* at 151 (but also holding that such existence may "render the claim unpatentable for lack of invention").

40 Bozicevic, *supra* note 35, at 420.

41 *Id.*

42 116 U.S.P.Q. (BNA) 484 (4th Cir. 1958).

43 Bozicevic, *supra* note 35, at 421 (discussing *Merck & Co.*, 116 U.S.P.Q. (BNA) 484).

44 *Id.*

45 166 U.S.P.Q. (BNA) 256 (C.C.P.A. 1970).

known to have a pharmacodynamic effect.[46] The isolated compounds could be used without negative side effects. These compounds were claimed to be "sufficiently pure to give a substantially ideal curve on partition chromatography."[47] This claim language successfully overcame the "product of nature" threshold because it differentiated the new drug from the product found in nature. "*Bergstrom* is like *Williams* in that the claimed compound is described as being physically separated . . . from its natural surroundings and like *Merck* in that the claimed compound had a different functional characteristic than the complete composition existing in nature."[48]

One of the clearest ways to meet the threshold requirement of "manufacture" or "composition of matter" is to induce a product of nature to possess a new characteristic. This method is illustrated by *Diamond v. Chakrabarty*,[49] in which "four different plasmids,[50] capable of degrading four different oil components, could be transferred to and maintained stably in a single . . . bacterum, which itself has no capacity for degrading oil"[51] by means of genetic engineering.[52] This type of bacteria was not found to be a product of nature because its capability to break down four different oil components did not occur naturally in a single organism.[53] Similarly, in *Ex parte Hibberd*,[54] a new corn plant with a very high tryptophan[55] content was produced by cross breeding. The court found that "the work of the plant breeder 'in aid of nature' was [a] patentable invention."[56] Thus, a "product of nature" may be patentable if it is induced by man to have a new characteristic.

b. Process

If a company cannot obtain patent protection for a drug it has developed, either because it cannot achieve the status of manufacture or composition of matter, or because it does not

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46 *Id.* at 257. *Pharmacodynamics* is a branch of pharmacology that deals with reactions between drugs and living structures. WEBSTER'S NEW INTERNATIONAL DICTIONARY 1694 (3d ed. 1971).

47 *In re* Bergstrom and Sjovall, 166 U.S.P.Q. at 257.

48 Bozicevic, *supra* note 35, at 421-22.

49 447 U.S. 303 (1980).

50 "Plasmids are hereditary units physically separate from the chromosomes of the cell." *Chakrabarty*, 447 U.S. at 305 n.1.

51 *Id.*

52 It was thought that this new organism would be helpful in breaking down oil spills. *Id.* at 305 n.2.

53 *Id.* at 306 n.3.

54 227 U.S.P.Q. (BNA) 443 (Bd. App. & Int. 1985).

55 Tryptophan is an amino acid (*i.e.*, a protein building block) that neither the human nor animal body is capable of synthesizing in sufficient amounts. As a consequence it is "essential" that it be absorbed through the diet.

56 *Hibberd*, 227 U.S.P.Q. at 445.

meet the remaining statutory requirements, it may still be possible to obtain a process patent.[57] In determining patentability, the process or method of creating the new drug, rather than the drug itself, is viewed as the invention; thus, it is the process rather than the drug that receives patent protection. For example, when Reserpine, an antihypertensive drug, was developed from the *Rauvolfia sepentina* plant, it was not patentable, although the preparation process for the drug was patentable.[58]

2. Statutory Requirements

Once it has been determined that a plant-derived drug is a manufacture or composition of matter it must be determined whether it meets the statutory requirements of utility, novelty and non-obviousness. Similarly, if a drug is produced by way of a process that the developer wishes to patent, the process must meet the same statutory requirements.

a. Utility

"Of the three requirements for patentability, the utility requirement is the easiest to meet. A statement of the purpose to which the invention will be put will usually suffice."[59] The invention, however, must have some utility apart from research.[60] In the case of a process claim, the process must be "reduced to [the] production of a product shown to be useful."[61] By their nature, drugs are useful and almost always intended for practical purposes. Therefore, the utility requirement for drugs is usually met. The process used to produce a drug, a useful product, would also meet the statutory requirement of utility.

b. Novelty

For an invention to be novel, it must be "different from prior inventions and represent[] an advance over prior knowledge. If every element of the invention can be found in a single prior device or printed publication, novelty is lacking and the invention is

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57 35 U.S.C. § 101 (1988).

58 U.S. Patent No. 2,833,771 (1958).

59 Gary M. Ropski & Michael J. Kline, *A Primer on Intellectual Property Rights: The Basics of Patents, Trademarks, Copyrights, Trade Secrets and Related Rights*, 50 ALB. L. REV. 405, 409 (1986).

60 *See* Brenner v. Manson, 383 U.S. 519, 534-35 (1966); Edward C. Walterscheid, *Insufficient Disclosure Rejections* (Part II), 62 J. PAT. [& TRADEMARK] OFF. SOC'Y 229 (1980) (discussion of cases in which patents were not obtained because of lack of utility).

61 *Brenner*, 383 U.S. at 534.

unpatentable."[62]

If a plant has traditionally been used in its raw state for a specific medicinal purpose by an indigenous population, a drug developed from that plant to be used for the same medicinal purpose will not be considered "novel" or "non-obvious." One of the most effective ways of pursuing a successful plant screening program is to examine the plants that indigenous populations have been using for many years.[63] While this method of plant screening increases the likelihood of finding a plant with useful bioactive properties that could be used to develop a new drug, it also decreases the likelihood that the drug, once developed, could be patented. Therefore, although plant screening is vital to the discovery of useful plant-derived drugs, the current patent protection system discourages it.

If a plant has been used for different medicinal purposes than that for which the plant-derived drug will be used, the result may be different. For example, the Rosy Periwinkle originally was used in its "natural" form in Madagascar to treat diabetes. Its derivative drugs, vincristine and vinblastine, are used to treat Hodgkin's disease and childhood leukemia. These drugs were patented. Now, however, after many years, research is being conducted to develop a diabetes drug from the Rosy Periwinkle. This new drug, if it is ever developed and marketed, may not be patentable because the use of this particular plant to treat this particular disease is neither novel nor non-obvious.[64]

c. Non-obviousness

An invention is non-obvious if the differences between the invention and the prior art are such that at the time the invention was made, the invention as a whole would not have been obvious to one of ordinary skill in the art.[65] In *Graham v. John Deere Co.*,[66] the Supreme Court ruled that obviousness is based on three factual determinations. First, "the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved."[67]

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62 Ropski & Kline, *supra* note 59, at 409 (footnote omitted).

63 For a discussion of the ethnobotanical approach to plant screening, see *supra* notes 17 and 21 and *infra* note 75 and accompanying text.

64 *See supra* notes 62-63 and accompanying text and *infra* notes 65-75 and accompanying text.

65 35 U.S.C. § 103 (1988).

66 383 U.S. 1 (1966).

67 *Id.* at 17.

There are also several secondary considerations the courts may take into account when determining obviousness. These include: "commercial success, long felt but unresolved needs and failure of others to solve the problem."[68] Once the factual determinations are made, and the secondary considerations are taken into account, a court can "make the legal determination of whether the invention would have been obvious, at the time the invention was made, to a person having ordinary skill in the art."[69]

To determine the obviousness of a claimed drug, it must first be compared with the product as it exists in nature. This comparison should employ the criteria set forth in *Graham*.[70] The criteria can be applied to products derived from nature by determining the chemical, physical and functional characteristics of the naturally occurring product. This would include a determination of its structural formula, its purity and its degree of activity.[71] Then the differences between the claimed invention and the naturally occurring material must be ascertained.[72] This can be done by determining the chemical, physical and functional characteristics of the claimed invention and comparing them to the characteristics of the naturally occurring material. Finally, the level of ordinary skill in the art must be determined by examining how one of ordinary skill in the art would use the existing knowledge and techniques to extract the claimed drug from its natural state.[73] "Obvious" may not mean "obvious to try," because all inventions are in some sense the result of an obvious course of inquiry to a skilled researcher in the field. The invention as a whole must be the subject of the patent, and therefore the entire invention must be considered in the obviousness inquiry.[74]

Plant-derived drugs, however, may not vary significantly enough from their natural sources to meet the *Graham* requirements. Furthermore, the success of plant screening programs will depend on certain "hints" gleaned by researchers either from

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68 Ropski & Kline, *supra* note 59, at 410. *See also* Connell v. Sears, Roebuck & Co., 722 F.2d 1542 (Fed. Cir. 1983) (The four factual inquiries in *Graham* must be answered before a conclusion of obviousness can be made.).

69 Ropski & Kline, *supra* note 59, at 410.

70 For a discussion of the *Graham* criteria for non-obviousness, see *supra* notes 66-68 and accompanying text.

71 Bozicevic, *supra* note 35, at 423-24.

72 *Id.*

73 *Id.* at 424.

74 *See In re* Antonie, 559 F.2d 618, 619 (C.C.P.A. 1977); *In re* Tomlinson, 363 F.2d 928, 931 (C.C.P.A. 1966).

science or from indigenous populations.[75] Screening programs are discouraged by the patent system because what tends to make them successful—prior use of a particular plant for medicinal purposes or prior use of a chemical similar to that found in a particular plant—also tends to make the end product of these programs, the plant-derived drugs, unpatentable. These drugs seem obvious or lacking in novelty.

IV. When a Patent Does Not Issue

In cases where neither a utility patent nor a process patent can issue, no patent protection is afforded at all. Pharmaceutical companies and other researchers have no way of determining in advance what the results of their research will be, that is, what type of drug will be extracted from which plants and by which means. They have no assurance that a patent will issue upon the discovery of a "new" drug; and, therefore, there is little incentive for the companies to make the initial research investments.

A. *Trade Secrets*

One possible alternative to federal patent protection is the common law doctrine of trade secrets. "A trade secret [is any] . . . formula, [such as a chemical compound,] pattern, device or compilation of information which is used in one's business, and which gives . . . an opportunity to obtain an advantage over competitors who do not know or use it."[76] A trade secret may—but need not—consist of subject matter that is patentable.[77] Trade secret protection "is not based on a policy of rewarding or otherwise encouraging the development of secret processes or devices."[78] Rather, protection is offered to deter breaches of confidentiality and the use of "reprehensible means of learning another's secret."[79] Under one view, the discovery of a trade secret absent "improper means" or breach of a confidential relationship, such as between an employer and an employee or as between joint venturers, is not a misappropriation of a trade secret.[80] Thus, a pharmaceutical company would not have a remedy if, for example, a competitor used reverse engineering to

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75 For a discussion of the ethnobotanical and "chemically similar" approaches to screening programs, see *supra* notes 17 and 21.

76 Restatement (First) of Torts § 757 cmt. b at 5 (1939).

77 *Id.* at cmt. a.

78 *Id.* at 7.

79 *Id.*

80 *See id.* § 757.

discover the formula of a new drug, or came upon the formula by way of independent research. Under another more radical view, no trade secret exists in the first place if the information could have been ascertained by permissible means.[81] This view reflects the definition of trade secret provided by the Uniform Trade Secrets Act:

> 'Trade secret' means information, including a formula . . . that: (i) derives independent economic value, actual or potential, from not being generally known to, and not being readily ascertainable by proper means by, other persons who can obtain economic value from its disclosure or use, and (ii) is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.[82]

Under either definition, the "discovery" of the formula of a drug by means of reverse engineering[83] or independent research would not be a violation of trade secret protection. Furthermore, the Uniform Trade Secrets Act has not been adopted by all of the states.[84] This lack of uniform national regulation further deters national or multinational pharmaceutical corporations from investing more confidently in plant-derived drug research because their secrets will only enjoy protection in limited geographic areas.

B. *The Case for a Plant-Derived Drug Act*

1. Historical Precedent

The Plant Patent Act was enacted in 1930 to remove the existing distinction drawn between plant developers and industrial inventors in the Utility Patent Act[85] and to avoid doctrinal problems with the "products of nature" limitation on obtaining a utility patent.[86] Until the passage of the Plant Patent Act, plants were not patentable.[87] Under the Act, all the statutory require-

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81 *See* Van Prods. v. General Welding & Fabricating, 213 A.2d 769 (1965).

82 Uniform Trade Secrets Act § 1 (1985).

83 "Reverse engineering is the first step a company takes in creating a compatible product that targets a competitive product. It's taking it apart, figuring out how the product works." Stephen H. Lacount, *A Harder Line on Software: Owners, Courts Getting with the Copyright Program*, L.A. TIMES, Jan. 7, 1991, at 6.

84 Thirty-five states and the District of Columbia have adopted the Uniform Trade Secrets Act. *Customer is Held Not to be Confidential Trade Secret*, N.Y.L.J., Oct. 15, 1991, at 25.

85 S. REP. No. 315, 71st Cong., 2d Sess. 1(1930); H.R. REP. No. 1129, 71st Cong., 2d Sess. 1 (1930).

86 *See In re* Bergy, 596 F.2d 952, 980-84 (C.C.P.A. 1979), *vacated sub nom.* Diamond v. Chakrabarty, 444 U.S. 1028 (1980).

87 Eileen M. Baker, *Patents, Plants and Biotechnology*, 14 W. ST. U. L. REV. 529 (1987); *see* Nancy J. Linck, *Patentable Subject Matter Under Section 101—Are Plants Included?*, 67 J. PAT. [& TRADEMARK] OFF. SOC'Y 489, 498 (1985).

ments that apply to patents for inventions also apply to plant patents.[88] Plant patent protection, however, is more limited than utility patent protection because it protects only asexually reproducing plants[89] of one variety[90] and only the plant itself, not its products or parts.[91] The vast majority of plants, those which sexually reproduce by seed, are left unprotected by the Plant Patent Act.

Forty years after the Plant Patent Act was passed, Congress enacted the Plant Variety Protection Act[92] "[t]o encourage the development of novel varieties of sexually reproduced plants and to make them available to the public."[93] The Plant Variety Protection Act is not part of the patent system but is instead an example of a registration system.[94] Under this registration system, a Certificate of Plant Variety Protection is issued to the "breeder of any novel variety of sexually reproduced plant."[95] Although novelty is required to obtain a Certificate of Protection, non-obviousness is not.[96] During the term of the Certificate, which lasts eighteen years from the Certificate's date of issue,[97] the breeder has the right to "exclude others from selling the variety, or offering it for sale, or reproducing it, or importing it, or exporting it, or using it in producing (as distinguished from developing) a hybrid or different variety therefrom."[98] Neither the Plant Patent Act[99] nor the Plant Variety Protection Act[100] protect plant-derived drugs, since these acts are intended to protect inventions that are themselves plants and not inventions that are plant derivatives. Nonetheless, both acts offer some insight into the development of an act that would provide patent-like protection for plant-derived drugs.

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88 35 U.S.C. § 161 (1988).

89 Asexually reproducing plants are plants that reproduce in ways other than by seed, with the exception of tuber propagated plants and plants found in an uncultivated state, both of which cannot receive patent protection. *Id.*

90 One variety and not the entire genus or family is protected. *Id.* § 162.

91 *Id.*

92 7 U.S.C. §§ 2321-2582 (1988).

93 *See* Plant Variety Protection Act, Pub. L. No. 91-577, 84 Stat. 1542, preamble (1970).

94 *See* Sidney B. Williams, Jr., *Protection of Plant Varieties and Parts as Intellectual Property*, SCIENCE, July 6, 1984, at 18-19.

95 7 U.S.C. §§ 2402, 2481 (1988).

96 *See* Baker, *supra* note 87, at 530.

97 7 U.S.C. § 2483(b) (1988).

98 *Id.* § 2483(a).

99 35 U.S.C. §§ 161-164 (1988).

100 7 U.S.C. §§ 2321-2582 (1988).

The Orphan Drug Act,[101] passed in 1983 as an amendment to the Federal Food, Drug, and Cosmetic Act,[102] is another example of Congress's attempt to provide financial incentive for the development of a product that might not otherwise be developed. By passing the Act, Congress intended to stimulate the development of drugs to treat rare diseases and conditions.[103] Congress thought that the small market for these drugs, combined with the high price of developing them, was a disincentive for pharmaceutical companies to produce them. Therefore, to help stimulate development, the Act includes both tax incentives for certain aspects of testing procedures[104] and a seven year market exclusivity term.[105] The House Report on the Act states that "a substantial number of orphan drugs are not patentable. In order to provide some incentive for the development of these particular orphan drugs, the Committee's bill includes an exclusive marketing right for the sponsor of such a drug."[106]

The original language of the statute only provided "protection for unpatented drugs for rare diseases or conditions."[107] A 1985 amendment eliminated the unpatentability of the drug.[108] Protection under the Orphan Drug Act is subject to two exceptions. First, protection will cease if the holder of the license for the protected drug gives written approval allowing other licenses for the same orphan drug to issue.[109] Second, other licenses may be issued, thus ending exclusive protection, if "the holder of the . . . [original] license cannot assure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated."[110] These exceptions illustrate that Congress was not willing to grant

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101 Pub. L. 97-414, 96 Stat. 2049 (codified in part at 21 U.S.C. §§ 360aa-360ee)(1988).

102 21 U.S.C. §§ 301-393 (1988).

103 Section 1 of Public Law 97-414 provides, in part, that

> there is reason to believe that some promising orphan drugs will not be developed unless changes are made in the applicable Federal laws to reduce the costs of developing such drugs and to provide financial incentives to develop such drugs; and . . . it is in the public interest to provide such changes and incentives for the development of orphan drugs.

Pub. L. 97-414, § 1(b)(5)(b), 96 Stat. 2049 (codified as amended at 21 U.S.C. § 360aa note (1988)).

104 26 U.S.C. § 28 (1988).

105 21 U.S.C. § 360cc (1988).

106 H.R. REP. No. 840, 97th Cong., 2d Sess., pt. 1, at 11 (1982), *reprinted in* 1982 U.S.C.C.A.N. 3577, 3583.

107 Orphan Drug Act, Pub. L. No. 97-414, § 527, 96 Stat. 2049, 2050 (1983) (codified with some differences in language 21 U.S.C. § 360cc).

108 21 U.S.C. § 360cc (1988)).

109 *Id.* § 360cc(b)(2).

110 *Id.* § 360cc(b)(1).

blanket exclusivity to motivate drug developments, since the final end of the Act is not to develop the drugs, but to treat the conditions.

The Semiconductor Chip Protection Act[111] also provides inferable support for the protection of plant-derived drugs. The Act, passed in 1984, extends protection to "mask works."[112] The statute was enacted to protect the investment necessary to design integrated circuits in semiconductor designs. Chip engineering could cost a company thousands or millions of dollars, yet competitors were free, before the Act was passed, to photograph a chip and use that photograph to create an exact copy. Before Congress passed the Act, these chips were not patentable, because the design methods used to create them were known, and thus obvious to a skilled chip designer.[113] The chips were not copyrightable because the circuits' form was determined by functional needs and not design considerations.[114] The Act now protects mask works for ten years[115] and is limited to the actual reproduction of the mask work and the "import[ation] or distribut[ion] [of the] semiconductor chip product in which the mask work is embodied."[116] As in the case of trade secrets, reverse engineering is not considered an infringement.[117]

The purpose of patent law is to encourage "science and the useful arts."[118] In light of the number of people dying yearly from cancer,[119] AIDS[120] and other diseases, there would be few inventions more useful than effective drugs. Yet, there is a conflict between the goals of patent law and the methods for achiev-

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111 17 U.S.C. §§ 901-914 (1988).

112 A "mask work" is:

> a series of related images, however fixed or encoded — (A) having or representing the predetermined, three-dimensional pattern of metallic, insulating, or semiconductor material present or removed from the layers of a semiconductor chip product; and (B) in which series the relation of the images to one another is that each image has the pattern of the surface of one form of the semiconductor chip product.

Id. § 901(a)(2)(A),(B).

113 H.R. REP. No. 781, 98th Cong., 2d Sess. 3 (1984), *reprinted in* 1984 U.S.C.C.A.N. 5750, 5752.

114 *Id.* at 5752-53.

115 17 U.S.C. § 904(b).

116 *Id.* § 905.

117 *Id.* § 906.

118 U.S. CONST. art. I, § 8, cl. 8.

119 In the United States (excluding Puerto Rico), the estimated number of new cancer cases will reach 1,100,000 and the estimated number of deaths will reach 514,000. AMERICAN CANCER SOC'Y, CANCER FACTS & FIGURES-1991, at 1 (1991).

120 Between January 1981 and February 1991 there have been 167,803 reported new cases of AIDS and 106,351 reported deaths. Telephone Interview with Information Specialist #186, *HIV & AIDS Information Hotline* (Apr. 12, 1991).

ing these goals. It is patent protection and not the drug that creates the financial incentive to invest in drug development.[121] Rather than investing in the development of a drug that may not be patentable, a pharmaceutical company may opt for the more certain copycat patent. By working backward from a patented drug, a company may make beneficial changes significant enough for the new drug to be patentable. Companies may avoid high research and development this way. Innovative research projects, however, also are nipped in the bud.

Congress should pass a Plant-Derived Drug Protection Act. The passage of the Plant Patent Act, the Plant Variety Protection Act, the Orphan Drug Act and the Semiconductor Chip Protection Act indicate that Congress has the power to,[122] and is willing to, protect inventions that are not adequately protected by current patent law. Congress would not create a new policy by passing a Plant-Derived Drug Protection Act, but rather would address a policy it has considered in a variety of contexts. In passing the above Acts, Congress determined that it is in the public interest to encourage the development of plants, orphan drugs and semiconductor chips, although they are not patentable, by administering certain exclusive marketing rights for limited periods of time. The potential is great for discovering anti-cancer and anti-AIDS drugs, for example, in the bioactive compounds of plants. In light of these and other potential benefits to the public, Congress should provide patent-like protection for plant-derived drugs.

2. Proposal for a Plant-Derived Drug Protection Act

A Plant-Derived Drug Protection Act should provide exclusive marketing rights for a limited period of time. These rights should be recognized by way of a certificate, similar to the certificate available under the Plant Variety Protection Act.[123] To receive a certificate under the Plant Variety Protection Act, novelty is required, but non-obviousness is not. Thus, plant-derived drugs that fall under the Act would not be limited to those drugs that are both novel and non-obvious.

Furthermore, "novelty" in the proposed Act would have a meaning similar to "novelty" in the Plant Variety Protection Act

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121 *See* Moss, *supra* note 22, at 85-86.

122 The power of Congress to protect plant-derived drugs does not stem from the patent law, but from the Commerce Clause. U.S. CONST. art. I, § 8, cl. 3.

123 7 U.S.C. §§ 2481-2483.

and not to "novelty" in the patent statute.[124] The Plant Variety Protection Act's definition of "novel variety" has three parts. First, the variety must be distinct "in the sense that the variety clearly differs by one or more identifiable morphological, physiological or other characteristics . . . from all prior varieties of public knowledge."[125] Second, the variety must be uniform "in the sense that any variations are describable, predictable and commercially acceptable."[126] Third, the variety must be stable "in the sense that the variety, when sexually reproduced or reconstituted, will remain unchanged with regard to its essential and distinctive characteristics with a reasonable degree of reliability."[127] Applying a similar standard to plant-derived drugs, a drug would receive a certificate of protection if it were distinct from other existing drugs. Patent protection predicated on novelty would not be withheld because the plant from which the drug was derived was used for medicinal purposes prior to its commercialization. To be novel under the proposed Act, a drug would need to be uniformly and stably reproducible. Additionally, there should be an exception to plant-derived drug protection, as there is in the Orphan Drug Act, if a certificate holder is unable to insure a reasonable supply of the drug for which he holds the Certificate.

Finally, in exchange for protection under this registration system, pharmaceutical companies should be required to pay a percentage of the profits they earned during the period of marketing exclusivity to the plant's country of origin. Conceptually, the country of origin would be a partner in the marketing right. The country of origin should receive credit for the intellectual property aspects of the pharmaceutical company's development if that country played a part in that development. It should also receive compensation for allowing the harvesting of the source plants.

A recently published proposed treaty on deforestation makes several suggestions that may be useful in constructing a program for carrying out an intellectual property partnership.[128]

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124 For a discussion of patent novelty requirements, see *supra* notes 62-64 and accompanying text.

125 7 U.S.C. § 2401(a)(1) (1988).

126 *Id.* § 2401(a)(2).

127 *Id.* § 2401(a)(3).

128 NEW YORK STATE BAR ASSOCIATION, INTERNATIONAL COOPERATIVE LEARNING MODEL FOR RESOLVING WORLD ISSUES: PROPOSED TREATY ON DEFORESTATION (1990). High school students from Belgium, the Soviet Union and the United States collaborated under the auspices of the New York State Bar Association's Law Youth and Citizenship Program to develop this proposed international deforestation treaty. The treaty

Under the treaty a council would be established to maintain and enforce the treaty.[129] The council would be composed of representatives of the treaty's ratifying or acceding states.[130] Three departments, each divided into divisions, would be created and be responsible to the council.[131]

One of the proposed departments, finance, which would have an external operations division,[132] would be "responsible for raising funds and monitoring distribution to member states for reforestation activities as compensation for economic loss from limiting deforestation."[133] Under this system, plant research as well as plant harvesting would be monitored by this division. This division would determine who is researching and harvesting in member states and who, therefore, could demand payment from those who successfully develop drugs from plants harvested within the borders of member states. Funds could then be distributed to the precise country from which plants were harvested or could be pooled and distributed to the member countries most in need of funds for deforestation prevention. The proposed information department would have an education division responsible for "teach[ing] farmers and villagers methods of utilizing the forests without destroying them."[134] Farmers and villagers could be taught, under the auspices of this division, to harvest and grow plants that could then be employed by drug researchers. In this way, both fragile ecosystems and fragile populations could be sustained, while bringing useful drugs to market that might not otherwise have come to the attention, or the aid, of the developed world.

V. Conclusion

Patent law does not provide sufficient protection to ensure that plant-derived drugs will be discovered, developed and brought to the market. Moreover, tropical rain forests are important sources for the plants from which many plant-derived drugs come. Because the rain forests are disappearing so rapidly, it is imperative that Congress take steps to protect the drugs that may be found in these vast chemical storehouses. Drug de-

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was "drafted by the students applying all of the standards and theories of international law." *Id.* at 6.

129 *Id.* at Part II, art. 19.

130 *Id.* at Part II, art. 18.

131 *Id.* at Part III, art. 26.

132 *Id.* at Part III, art. 30.

133 *Id.* at Part III, art. 31.

134 *Id.* at Part III, art. 38(c).

velopers should receive patent-like protection for plant-derived drugs; in exchange the developers should be required to return a percentage of the profits to the plant's country of origin. By allowing protection for "inventions" that would ordinarily be unpatentable, Congress would promote the same policy that underlies the patent law itself—the promotion of science and the useful arts for the public benefit.

Liz Hanellin