The Health Impact Fund and Traditional Medicines

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The Health Impact Fund and Traditional Medicines*

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Abstract: The therapeutical potential of traditional medicines (TMs) is not fully exploited because the patent system provides insufficient incentives to conduct randomized controlled trials on these medicines. This paper argues that the Health Impact Fund (HIF) can help incentivize investment into randomized controlled trials for TMs. The HIF offers a mechanism for rewarding investment in clinical trials without requiring exclusivity of supply and therefore may enable a much wider, and more rational, use of TMs. In addition, more extensive testing of TMs could reveal interesting opportunities for further research into active compounds, resulting in even more medical progress. Patients, suppliers, and insurers could then benefit from better use of TMs.

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1. INTRODUCTION

Traditional, mostly plant-based, medicines (TMs) have enormous therapeutic potential, but are typically overlooked in orthodox Western medicine. The key reason is that few of these medicines have been subject to randomized controlled trials (RCTs) in order to prove their safety and effectiveness. Our global systems of intellectual property, which are intended to incentivize innovation, fail to incentivize RCTs for traditional medicines because no firm is able to benefit from exclusive use of innovations in traditional medicine. Patients therefore do not benefit from potentially useful therapies, and suppliers of traditional medicines fail to achieve their potential sales volumes.

Randomized controlled trials are used to test the efficacy of medical interventions. The double-blind RCT is the most common of these methodologies. In this type of trial, random allocation of different interventions, or allocation of an intervention and a placebo, is made to two groups of participants. Neither the participants nor the researcher are aware of which intervention they are receiving. Statistical significance is achieved by ensuring adequate numbers of participants are included in the trial.[1]

This paper argues that the Health Impact Fund (HIF) can help incentivize investment into RCTs for TMs. As described below, the HIF offers a mechanism for rewarding investment in clinical trials without requiring exclusivity of supply and therefore may enable a much wider, and more rational, use of TMs. In addition, more extensive testing of TMs could reveal interesting opportunities for further research into active compounds, resulting in even more medical progress. Patients, suppliers, and insurers could then benefit from better use of TMs.

The following section introduces TMs and reviews both some of the important clinical advances achieved because of TMs as well as some of the literature that has been critical of TMs. Section 3 reviews the reasons that patents do not serve as an effective mechanism for incentivizing investment into RCTs for TMs. The ineffectiveness of patents might suggest that government-funded RCTs could be relied on as an alternative to patents. However, while government funding may be able to

[1] See Stolberg, Norman and Trop (2004).

provide for clinical trials that would not otherwise occur, governments are subject to corporate influence and lack the incentives that private firms have to ensure wide uptake of their products. Section 4 introduces the Health Impact Fund and its application to TMs. Section 5 introduces some obstacles to using the HIF to reward investment in clinical trials of TMs. Section 6 briefly concludes.

2. AN INTRODUCTION TO TRADITIONAL MEDICINES

There are many different types of "traditional medicine," a term which encompasses modes of treatment, therapies and systems of practice. In this article, we focus on traditional medicines that are consumed, such as plants and plant products. Common examples include ginseng and wolfberry. The use of these types of traditional medicine is extremely widespread. In some cases, and particularly in Chinese practice, several products may be consumed together.

TM systems often make use of whole plants or mixtures of plants. A number of whole plants have been supported by sufficient evidence to allow them to gain acceptance as treatments in mainstream medicine. These plants include *Ginkgo biloba* in the treatment of Alzheimer's type dementias, *Hypericum perforatum* (St John's wort) in mild to moderate depression, *Aesculus hippocastanum* (horse chestnut) in Chronic venous insufficiency, *Crataegus spp*. (hawthorn) in cardiovascular disease and *Serenoa repens* (saw palmetto) in benign prostatic hypertrophy.[2]

Many practitioners of TM claim that the therapeutic effect of a whole plant used as a medicine is likely to be a result of a synergy between compounds within the specific plant or combination of plants in a mixture.[3] Some practitioners of TM have resisted scientific testing of their medicines because they fear the products will be used or tested in a way counter to the product's intended use; testing is generally done on isolated components, while traditional medicine combines many components of the organism. TM is practiced within a non-reductionist, holistic framework.[4] While it is

[2] Mills and Bone (2000). See also Hoffman (2007, p. 18).
[3] Williamson (2001).
[4] Spelman et al. (2006 p. 475) state that medicinal plants may never be completely understood by analyzing their component parts. The therapeutic properties of plants arise from interactions between multiple constituents. "Chemical synergy exists when the action of many chemicals is greater than the arithmetical sum of the actions of individual components." These concepts are in direct opposition to reductionist science.

possible for a plant, as a whole entity, to be subjected to an RCT, science has traditionally focused on reducing organisms and other substances to a molecular level for the purpose of testing those molecules in isolation. Although paradigmatic and political tensions exist between TM practitioners and scientific medicine, there is no reason, from a scientific perspective, why whole plants, plant mixtures and isolated parts of plants cannot be studied using standard scientific methodologies. In fact, many TMs would appear to be ideally suited to testing in RCTs.[5]

Organisms other than plants are also a reservoir of untapped therapeutic potential. Marine life has been targeted by drug researchers in only a small way and remains largely unexploited. Similarly, insects are thought to contain many potentially therapeutic compounds.[6] Micro-organisms, the source of penicillin, a range of other antibiotics, and some anti-cholesterolemic drugs,[7] also deserve further research.

While TMs often consist exclusively of unprocessed plants or plant parts, many pharmaceuticals in use in modern medicine were derived directly from plants. It has been estimated that up to 25 percent of prescription drugs in common use have at least one component that has been synthesized from original molecules and compounds isolated from plants.[8] Several naturally occurring, non-synthetic plant-derived drugs have seen relatively long-term use, such as aspirin, morphine, colchicine, ipecac and atropine. Newer non-synthetic plant-derived drugs include important anti-cancer agents vinblastine, vincristine and taxol and a variety of drugs with specific effects on various body systems. See Table 1 for a list of drugs that are essentially non-synthetic plant isolates.

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[5] Bone (2000, p. xiv) views the application of herbal medicines within an orthodox medical context as somewhat problematic from the perspective of TM practice. The need for a middle ground that respects the value of science but does not regard traditional assumptions about treatment is proposed. Evans (2008, p. 5) argues that there is a concern in relation to the use of evidence-based medicine as a treatment rationale for herbal medicine on the part of some herbalists. She argues that evidence-based medicine is paradigmatically incongruous with TM philosophy. She further argues that herbal medicine cannot be practiced appropriately using the strategy of (orthodox) medicine.

[6] Aylward (1995, pp. 104–105).

[7] Ibid., p. 104.

[8] World Health Organisation (undated); Sheinand Maehira (2002, p. xi).

Table 1. Source, medication and action of conventional pharmaceuticals derived directly from plants

Plant Name	Species Name	Medication	Action
Autumn crocus	*Colchicum autumnale*	Colchicine	Anti-gout
Belladonna	*Belladonna atropa*	Atropine	Anticholinergic
Camptotheca	*Camptotheca acuminata*	Topotecan	Antineoplastic
		Irinotecan	Antineoplastic
Ephedra	*Ephedra sinica*	Ephedrine	Antiasthmatic
Foxglove	*Digitalis purpurea*	Digoxin	Cardiac
Hemp	*Cannibis sativa*	Dronabinol	Antiemetic
May apple	*Podophyllum peltatum*	Etoposide	Antineoplastic
		Teniposide	Antineoplastic
Periwinkle	*Catharantus roseus*	Vincristine	Antineoplastic
		Vinblastine	Antineoplastic
Poppy	*Papaver somniferum*	Opium (morphine)	Analgesic
Senna	*Cassia italica*	Senna	Laxative
Willow bark	*Salix alba*	Salicin	Analgesic
Yew, English	*Taxus baccata*	Docetaxel	Antineoplastic
Yew, Pacific	*Taxus brevifolia*	Paclitaxel	Antineoplastic

Based on information from Indiana University Biotech Project. cited in J. Myers. *Herbal Medicine*.

Artemisinin, a plant-derived drug isolated from *Artemisia annua*, has recently had a major impact on the global burden of disease resulting from malaria. The plant has been described in Chinese medicine texts over many centuries as an antipyretic (fever-reducer), and an antimalarial.[9] The discovery of artemisinin's value in *Plasmodium falciparum*–related malaria was timely. At the time evidence of its effectiveness against *P. falciparum* was emerging, the parasite was demonstrating increasing resistance to other antimalarials in common use. *P. falciparum* has shown little resistance to artemisinin, notwithstanding a recent report indicating that it may be losing some effectiveness in Cambodia.[10] In addition, artemisinin is safe for use with children and

[9] Subhuti Dhamananda (2002). *Artemisia annua* (syn Ching Hao, pinyin qinghao) has been used in traditional Chinese medicine in over 2000 antipyretic and anti-malarial formulas. Klayman (1985) states that *Artemisia annua* has been used as an antimalarial agent in China for several centuries. The first recorded use as an antipyretic was in AD 340, when Ge Hong's Zhou Hou Bei Ji Gang (Handbook of Prescriptions for Emergency Treatments) stated that fevers could be reduced through the use of *qing hao.* Klayman points out that there is some disparity among ancient texts about the identity of the herb, which was also known as "the green herb."

[10] Noedl et al. (2008, pp. 2619–2620).

pregnant women and has minor, manageable side effects.[11] These qualities give artemisinin significant advantages over other antimalarials. Artemisinin combination therapy (ACT) is now the preferred therapy for malaria. Currently, artemisinin and other compounds from *Artemisia annua* are under investigation in RCTs on the basis of a substantial body of literature reporting antineoplastic qualities.[12] While there has been, and continues to be, considerable research being conducted on *Artemisia annua,* this species is among only a few from a TM system that have undergone investigation of their therapeutic potential in contemporary times (see Table 1 for further examples).

It is interesting to note that many promising leads in TM remain incompletely investigated. Even in cases where plants have been researched using the scientifically preferred paths of drug development through isolating compounds with therapeutic potential, there are still avenues for further exploration. This is of concern given the thousands of published early-stage research studies that have identified biologically active plant isolates. A substantial number of these isolates have also undergone in-vivo studies in animals to confirm their therapeutic potential. *In vitro* and *in vivo* studies, while often revealing the therapeutic potential of a TM, fall short of meeting the standards of pharmacological safety and efficacy. Such data only becomes available through the conduct of RCTs involving humans. Unfortunately, RCTs are rarely applied to TMs, even where therapeutic potential is evident in preliminary studies.

There is widespread cynicism among medical experts about the value of many TMs. In part, this cynicism is nourished by the lack of clinical trials of RCTs. Without clear evidence of effectiveness and safety obtained in RCTs, anecdotal evidence from satisfied patients carries little weight with many experts, who are well acquainted with the placebo effect. Even widespread usage cannot serve as evidence of effectiveness, as shown by Tanaka, Kendal, and Laland (2009). Without RCTs, TMs are unlikely to achieve success in mainstream medicine, although they may achieve limited commercial success. Failure to demonstrate effectiveness, however, may lead to a long-

[11] World Health Organisation (2006).

[12] Rowan (2002) reports on the use of artemisinin in Vietnam and China for approximately 30 years. Given its chemical properties, it is thought that the drug could be an effective chemotherapeutic agent and add to the effectiveness of existing chemotherapy regimes. Rowan gives several case reports in which cancer regressed after artemisinin was used. Another compound from *Artemisia annua,* artesunate, is also thought to be effective against cancer. Studies into the value of *Artemesia annua*–derived molecules as chemotherapeutic agents for cancer are currently progressing.

term erosion in the currently substantial levels of TM sales in developing countries. This possibility should not be dismissed: TMs were the dominant form of therapy in Europe in the past, but have now been largely replaced.

Enhanced investment into clinical testing of TMs, of course, presents the possibility that the product will fail to demonstrate efficacy. In this case, the RCT could result in reduced sales of a product with limited or zero effect on health. While not desired by producers, such an outcome would benefit consumers.

In the following section, we explore the commercial rationale for limited investment into clinical testing of TMs, and we then proceed to examine how the Health Impact Fund can help to rectify this situation.

3. TMS, PATENTS, AND GOVERNMENT-FUNDED TRIALS

For orthodox medicine, the lack of scientific evidence of the effectiveness of traditional medicines is a critical problem. Despite considerable evidence of effectiveness arising from historical use, there have been relatively few RCTs, which, as noted above, are normally required by regulatory agencies to demonstrate safety and effectiveness. The lack of clinical trials is not an accident. Running clinical trials is both risky and extremely expensive, and these trials may cost millions of dollars. For most TMs, it is very unlikely that a firm investing in such a trial would recoup its costs.

Patents

For most pharmaceutical innovation, the patent system is relied on to create incentives to develop and test medicines. Patents, unfortunately, are not a solution to the problem of incentivizing investment into clinical trials for TMs. Even if the clinical trial of a particular traditional medicine successfully showed it to be both safe and effective, the firm that paid for the trial would not likely to be able to claim any effective property rights, such as through a patent, to help it to earn profits from the exploitation of the TM. There are two reasons for this. First, living organisms, such as plants, are generally viewed as being part of the commons. This means that they are available for exploitation by anyone who finds a use for them. The nature of TM is that there are typically many pre-existing producers and users of the medicine. This makes it next to impossible to claim patent rights over the product itself, although it may be possible to

obtain a patent for a previously unrecognized use of the plant to treat a particular condition or disease. If the use is not new, then no patent can be claimed or enforced, since it fails the patent requirement of "novelty". Even if the use is new, enforcing the patent would likely be extremely difficult, since it would require the patentee to observe how people use the TM. As noted by Roin (2009), difficulty in enforcing patent rights on medicines will inhibit investment into RCTs.[13]

Although a firm may be unable to obtain a patent over a use of an existing TM, it may in some situations be able to obtain a patent for an isolated molecule found within the TM. This process will not necessarily be easy. To enable the enforceability of the patent, the innovator may need to synthesize a molecule, changing the natural molecule in some non-obvious way to improve the therapeutic properties of the medicine. In these cases, the firm would have incentives to conduct RCTs for the patented medicine. These cases, however, clearly deviate from the historical use of traditional medicines and the use of active ingredients that are neither novel nor non-obvious.

Incentivizing RCTs for TMs in the absence of an altered synthetic molecule is the core problem. Examples of products that are in this situation include:

- *Buchanania lanzan* (common name: char): This plant has been used in Ayurvedic Medicine. Various parts of the plant are used in different types of cancer including skin, blood, and lung cancers. It has been over-exploited in the wild, which may indicate that people are finding it effective. The use of this plant for these purposes cannot be patented because there is sufficient prior use to demonstrate a lack of novelty. A MedLine search reveals no clinical trials involving humans.
- *Leonorus Cardiaca* (common name: motherwort): This plant has been used to reduce systolic blood pressure and uterine cramping. Numerous herbal medicine practitioners have written about its value over many hundreds of years, so that there is extensive "prior art." As a result, this plant has not been the subject of clinical trials involving people.

[13] According to Roin (2009, p. 520) "…the novelty requirement takes on great importance in the pharmaceutical industry, where new drugs can cease to be 'novel' inventions long before they have undergone the clinical trials needed to establish their medicinal value, and thus can become unpatentable before the public ever gains access to them."

For these and other similar plants, patents do not provide sufficient incentives for a firm to invest in clinical trials.

As a partial exception, a patent may be granted for a specific new, or novel, use of a product, provided that the use differs from the traditional use of the medicine. Holding a patent of this nature, however, cannot prevent someone else from selling the TM for a different use. Thus, such a patent does not give a company exclusive rights to market the product. So the patent system provides very weak incentives to undertake clinical trials for TMs.[14]

Government-sponsored Clinical Trials

Government-funded trials are an important alternative, but they may not substitute for privately funded clinical trials. First, governments may lack the appropriate mechanisms for determining which clinical trials to fund. Second, if governments run clinical trials and successfully demonstrate the safety and effectiveness of a given TM, providers of the TM will have limited willingness to engage in the promotional activities that are necessary to effectively increase the use of the product. We discuss these two points below.

Governments make poor decisions about funding clinical trials for several reasons. First, clinical trials are very expensive. Second, as public officials, government decision-makers typically have only a very limited financial stake in the outcome of a funding decision. As a result, the incentives to make good decisions are weak.

Third, the problem of deciding which clinical trials to run is compounded by the considerable expense involved in clinical trials and by the riskiness of these trials. Conducting RCTs, even where preliminary data is available from pharmacological and animal studies, is risky. At any stage of the trials, the test substance may be proven unsafe or inefficacious in humans. If a government agency runs ten clinical trials on different products, of which only one trial is successful in demonstrating safety and effectiveness, how is the government to assess whether it has succeeded? In a commercial environment, this assessment process is straightforward: trials are

[14] Many of these points, in a more general context, are discussed by Syed (2009), who observes that a patent is a very imperfect instrument for incentivizing investment into clinical trials in a variety of circumstances. Simmonds and Howes (2006, p. 63).

successful if their contribution to profitability is positive. The government, which earns no profits from the trials, has the more difficult weighting decision of comparing health gains to the cost of trials.

Fourth, governments are notoriously subject to lobbying and responsive to political pressures. For example, a government will almost certainly be strongly focused on domestic opportunities. It is therefore likely that governments will greatly prefer to run clinical trials on products that naturally occur in their own country and are used within that country's TM systems, rather than on products which are likely to have the greatest impact on *global* health.

The argument that governments are ill-equipped to decide when and how to invest into clinical trials does not imply that private corporations are better able to make such decisions. Private companies may have inferior information, and they may have incentives to hide negative trial results and to inflate positive results. Undoubtedly, there is a place for government-sponsored trials. The question is whether there is also a place for privately sponsored trials.

Even if governments make good decisions about clinical trials, and they are able to obtain marketing approval from regulatory authorities, this may be inadequate to ensure optimal use of the medicine. Generally, it takes some time for clinicians to become familiar with a medicine, which slows take-up of the product. Promotion by pharmaceutical companies crucially accelerates take-up of new drugs, as pharmaceutical representatives inform clinicians about the characteristics and features of newer products. In many cases, continuing clinical trials (sometimes called Phase IV trials) are important in demonstrating clinical benefits over alternative treatments, which may not have been shown in the clinical trials necessary for regulatory approval. Without post-approval clinical trials, the evidence base may be inadequate to justify large-scale take-up of the medicine. In other words, simply getting a medicine to the stage of being approved for sale may not be sufficient for ensuring widespread usage of the medicine. (For more on this important point, see Kieff 2001 and Berwick 2003.)

Governments have typically invested little in promotion of drugs to physicians, perhaps owing to the absence of a profit motive.[15]

These two important objections to relying exclusively on government-funded clinical trials to achieve commercialization of TMs do not constitute an argument against all government involvement. Government-funded trials can and will continue to be important tools for the increased realization of the potential benefits of TMs. But alternative mechanisms are also clearly desirable. The Health Impact Fund, as described below, presents such an alternative.

4. TMS AND THE HEALTH IMPACT FUND

The Health Impact Fund is designed to incentivize investments into the innovation and commercialization of medically valuable pharmaceutical products (especially where the patent system fails to provide any such incentive) and to enable the widest possible access to the resulting products. The HIF is a government-financed fund that would pay out rewards, on the basis of measured global health impact, for both newly approved medicines and new uses of existing medicines. In exchange for these rewards, registrants would agree to sell the registered product at the cost of production. In the case of products sold by competing producers, due to a lack of patent exclusivity, the registrant who had obtained the approval for a new product or new use would be rewarded based on the sales of the product by all suppliers. More details about the operation of the HIF are provided in Hollis and Pogge (2008) and at www.healthimpactfund.org.

Registering a product would be optional, and registrants would obtain a share of a fixed annual pay-out. Registrants with newly approved products would obtain 10 years participation in the pay-out, and registrants with newly approved uses would obtain five years of payments.

The annual pay-out is proposed to be initially $6 billion per year. This amount would be divided according to the assessed health impact for each eligible, registered product or new use for an existing product in each year. Thus, a product which had

[15] While it is clear that governments can invest in promotion to physicians (sometimes referred to as academic detailing), they have historically not performed this role with the same intensity as private, for-profit pharmaceutical companies.

produced 25 percent of the total assessed health impact achieved by all registered products would receive $1.5 billion. Health impact would be measured in a standardized unit, such as "quality-adjusted life-years" (QALYs) that, while imperfect, constitute the best available metric.

This mechanism of dividing rewards according to assessed health impact has important advantages, but it would also require a substantial investment in assessment of global health impact. Hollis and Pogge (2008) proposed an annual expenditure of approximately $600 million on health impact assessment.

There are three broad kinds of investments that may be stimulated by the HIF: investment in research into new drugs, investment in clinical trials, and investment in promotion of optimal use. The patent system, when it enables a stream of revenues from patent protection, can stimulate all these investments. However, in many cases patents do not provide effective protection or are not available. They may fail particularly to adequately incentivize investments into clinical trials and promotion of some valuable products. In other cases, market demand may fail to reflect clinical benefits in cases where patients are poor and cannot afford medicines. Here, although patent protection may be technically effective, it still fails to stimulate investments.

For TMs, the HIF presents unmistakable advantages. The HIF can effectively reward a firm for making investments into clinical trials and promotion, which will allow TMs to become commercially viable on a global basis. A product is eligible for registration with the HIF if it meets certain conditions: specifically, a product must qualify as a "new drug." For example, suppose that a TM qualifies as a "drug" under section 201(g)(1)(B) of the US Food, Drug and Cosmetic Act because it is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in people. If such a product were not "generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling," then it would qualify as a new drug.[16] In other words, a drug must not already exist as an accepted treatment. New drug status requires that the product meet stringent requirements under the Food, Drug and Cosmetic Act in order to demonstrate its safety and effectiveness.

[16] See Food and Drug Administration (2006).

With the HIF, the firm that develops the product need not sell the product itself; rather, it could promote the product actively to physicians, and earn rewards each year for ten years based on the assessed incremental health impact of the sales made by all suppliers of the product. The assessment of health impact would compare actual health outcomes to the expected counterfactual outcomes had the TM not received regulatory approval. Determining the counterfactual is complex: it would require the HIF to consider both alternative treatments for a given condition and the amount of the product that would have been sold in the absence of clinical trials and regulatory approval.[17] Consequently, the registrant of the product would not need exclusivity rights in order to be rewarded.

Like the patent system, the HIF mechanism imposes the risks of running clinical trials on private investors. If trials do not result in regulatory approval, or if a product is shown to be inferior or no better than other products treating the same medical condition, the HIF will not make any payments to the product's registering firm. This allocation of risks gives firms incentives to invest in the clinical trials that have the largest ratio of expected health effects to trial cost.[18] These incentives are economically efficient, and are similar to the desired effect of the patent system.

Assuming that a product is approved and marketed, the registrant may also wish to engage in promotion of the medicine to physicians by detailing, free samples, or other permitted activities. These kinds of investments appear to be important for enabling a rapid uptake of new medicines. The firm will find these activities profitable if they increase the product's effective consumption enough to make the increase in reward larger than the costs of promotion. As noted above, however, firms are generally unlikely to invest in promotional activities if they are competing against many other firms for sales of the product, as when there are generic competitors. With

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[17] The amount of sales that would have been made in the absence of the clinical trials and regulatory approval would have to be inferred. The most plausible inference is the amount of sales that occurred annually before the clinical trials and regulatory approval. Developing this kind of information may present considerable difficulties.

[18] It is economically efficient for firms to invest in those clinical trials that will show the largest health gains per dollar invested in a trial. In advance of running the trial, we don't know the actual health gains, and so we are interested in the health gains, weighted by the probability of actually achieving those gains. For example, suppose a trial for "A" is expected to be "successful" with probability 80%, and if successful the medicine will save 50,000 QALYs per year, then the expected impact is 40,000 QALYs per year. Suppose the trial costs $10m to run. Then, based on ten years of sales, the expected QALYs per dollar is 0.04, implying that the cost of the trials per expected QALY is $25.

the HIF, the registrant benefits not only from its own sales but from those of its rivals, so promotional investments can indeed be profitable. The firm might also engage in supplementary clinical trials to provide further evidence of the effectiveness of the registered product. Again, this kind of activity would be profitable if the clinical trial demonstrated a clinical advantage sufficient to increase the rewards enough to pay the costs of the trial.

Firms will also be more willing to invest in exploration of the chemical properties of TMs if they know which TMs are actually effective. It is likely that evidence from clinical trials of TMs would create more reliable information on new clinical leads. This would be an additional benefit generated by the clinical trials incentivized by the HIF.

5. OTHER ISSUES

Sustainability of Plant Resources

The sustainability of plant materials, particularly where they are taken from natural ecosystems, is a major concern. Significant increases in the use of TM over the past two decades have been described in the literature.[19] As a result, many naturally occurring plant species have become threatened through wild harvesting.[20] Over-exploitation is sometimes driven by extreme poverty, which encourages individuals to exploit any opportunity to benefit themselves and their families despite the larger ecological consequences.

The registrant of a TM with the HIF would have incentives to ensure that the plant harvest was sustained at least through the reward period of ten years. Within the ten-year window, it would most likely be necessary to secure supply through sustainable agricultural enterprises. Such endeavors could potentially benefit the developing world through providing a sustainable local industry. Beyond the reward period, the HIF would not have any effects on sustainability. The HIF does no worse than the patent system in this respect; firms have incentives to ensure the availability of patented products during the duration of their patents, but have no incentives once the patent expires.

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[19] See, for example, Eisenberg et al. (1998, pp. 1569–1575), MacLennan et al. (1996, pp. 569–572), and MacLennan et al. (2006, pp. 27–31).
[20] McGraw et al. (2005 p. 76).

Compensation for Traditional Knowledge

The Convention on Biological Diversity (CBD) is concerned with the conservation and sustainable use of biological resources. The rights of states to control genetic resources within their borders and the rights of original knowledge-holders to receive compensation for sharing their knowledge are supported under this agreement.[21] The TRIPS agreement, however, does not expressly recognize such a requirement, although it has been suggested that clause 27.3(b) of the document contains some recognition of the sovereign rights of states over biological resources.[22] The CBD supports the position that local communities have rights to compensation for knowledge of biodiversity which is used to develop products and acknowledges the right of indigenous peoples to protect their traditional knowledge from exploitation.[23]

The distribution of biological diversity in the world deepens the ethical case for compensation. The regions of the world with the greatest wealth of biological diversity happen to contain mostly developing countries.[24]

In certain cases, indigenous peoples have claimed that they should be able to share in profits arising from knowledge held in their traditional medicine systems. A typical situation related to intellectual property rights for indigenous people arose in the case of *Hoodia gordonii*, a cactus endemic to Southern Africa. The San people have traditionally eaten the cactus to prevent hunger and thirst on long hunting trips. According to the traditions of the San, food is eaten communally, so all game would be brought back to the tribe. Hoodia aids this tradition by curbing the desire to eat during a long hunting expedition. The cactus is now the source of the appetite suppressant bioactive compound "P57," patented in 1996 by the South African Council for Scientific and Industrial Research. At the time, however, the patentee did not consult with or inform the San that it had used and patented an element of their indigenous knowledge. When the San learned about the commercial exploitation of their traditional knowledge, they demanded compensation and have received a "benefit-sharing" package including

[21] United Nations Conference on Trade and Development (UNCTAD) and the International Centre for Trade and Sustainable Development (ICTSD) (2005, p. 403).
[22] Ibid., p. 391.
[23] Bodeker (2007, p. 420) and New (2006, p. 345).
[24] Convention on Biological Diversity (1994).

milestone payments and royalty payments based on commercial success of derivative products.[25]

The HIF does not provide a mechanism for ensuring an equitable distribution of benefits or compensation for the use of traditional knowledge. It somewhat mitigates the unfairness that the pharmaceutical that is developed is at least available at low cost universally, and the society which provided the traditional knowledge does not have to pay high prices for access to the resultant product. This is not necessarily the case under the patent system. However, like the patent system, the HIF does not provide an automatic solution for sharing the rewards of the exploitation of traditional knowledge.

Assessing Total Usage

A problem that may arise specifically in the context of the HIF is that in order to provide the correct amount of rewards, the HIF would require a reasonably accurate estimate of the number of people treated by a given traditional medicine. With ordinary pharmaceutical products, there is a well-established supply chain that can be followed to help track sales and usage of medicines. But with plant medicines, there may be many thousands of suppliers, who, for example, engage in wild harvesting. Obtaining reasonably accurate data about the amount of such medicines sold may be challenging and require government regulation of sales.

Attribution Issues

A clear determination of the rights to the rewards may be challenging to establish. One approach would be to use a mechanism similar to that used for granting data exclusivity in the US.[26] Syed (2009) discusses some of the possible mechanisms for determining attribution when unpatented medicines achieve regulatory approval.

[25] Kitua and Malebo (2004, p. 11).
[26] For example, under the US Federal Food Drug and Cosmetic Act (21 USC 355(j)(5)(F)(iii)), an applicant may obtain 3 years of Waxman-Hatch exclusivity if one or more of the clinical investigations was essential to approval of the application and was conducted or sponsored by the applicant.

Product consistency

TMs, to the extent that they are derived from natural products, may have properties that differ depending on the age of the product and its environment. For example, some plants are considered to have different therapeutic properties depending on the maturity of the plant, or the season in which it is harvested. This is one of the issues that could be addressed in the context of a clinical trial. However, if these differences exist, it might be quite difficult to ensure that the effectiveness of a registered product in practice corresponds to its assessed effectiveness in a clinical trial setting.

6. SUMMARY

Traditional medicines are widely used in much of the world. However, their usefulness is limited by a lack of clinical trials that would definitively demonstrate efficacy and safety. Without clinical trials, regulatory approval cannot be obtained, and the products cannot be marketed as drugs. As a result, these products face the limitations of dietary supplements. To the extent that some of these products are in fact clinically effective and safe, there are large potential losses in health from underuse of these products.

One reason for the lack of clinical trials for TMs is that clinical trials are extremely expensive and risky, and no single firm may be in a position to capture the full benefits of a successful clinical trial. Even if a patent on the use of the product could be obtained, it may not be possible to prevent other firms from selling the same product. Thus, firms lack incentives to invest in clinical trials.

The HIF, because it does not rely on the patent system to determine the allocation of rewards, could make investment into clinical trials and promotion of TMs commercially viable. This would benefit suppliers of TMs as well as patients.

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