Ownership of Biological Materials and Sharing of Benefits from their Development: A Few Points for Consideration from the Perspective of Traditional Knowledge Providers and Indigenous Peoples

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A LARGE proportion of important drugs now in use were either derived from natural compounds such as plants, fungi or microorganisms, or else such natural products provided important clues how to make entirely synthetic (human-made) drugs. Similarly, natural compounds have been the basis for pesticides and other agricultural chemicals, energy production, ways to break down environmental contaminants, and industrial catalysts. Occasionally, the plants, fungi or microorganisms that give rise to these useful products are found only in isolated regions of the world, and sometimes traditional knowledge is helpful in indicating where to find and how to use such organisms. Such traditional knowledge sometimes is part of a well developed body of knowledge widely known in a particular culture (such as *Aryuvedic* medicine in South Asia) and sometimes it is knowledge known only to a local population which may be an indigenous, minority population whose numbers are dwindling and whose culture and economic survival is threatened.

When traditional knowledge plays an important role in finding or developing a useful natural compound, what rights does the source country or the local population have to control the development of useful products or to share the benefits that may arise from successful development? Even if such rights are limited, what options do the source country and local population have in negotiating conditions under which they will let outsiders use such knowledge? Where finding such organisms or developing useful products from them involves international collaboration (either with foreign

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universities or companies) how does the situation differ? Finally, how does the situation differ when human tissues (blood, excised tumor samples, etc.) lead to the isolation of particular substances that form the basis of potentially useful products? In such cases, the issue is not the contribution of traditional knowledge, but rather the rights of the individual tissue donor and whether he or his community should control the development of such products or share in the benefits that may arise from their development.

These are the questions at the heart of this paper. The purpose of this paper is to provide general answers. Another purpose is to offer some suggestions how representatives of (a) providers of traditional knowledge, (b) source communities and (c) persons who donate body tissue, can negotiate to ensure some degree of compensation and benefit for those whom they represent. It is not a comprehensive, scholarly overview of the literature on this subject nor does it provide new research findings. It does, however, draw upon my work as a cancer researcher in the National Cancer Institute (NCI) of the US National Institutes (NIH), during which time I was deeply involved in cooperative epidemiology field research with Chinese scientists into the causes of cancer in Chinese villages. Later I worked in the technology development office of the NCI, where I was responsible, along with the Director of the Natural Products Branch of the NCI, for negotiating agreements with source countries for the collection of natural products by NIH scientists. These agreements, which I will return to later, are intended to comply with the letter and spirit of the International Convention on Biodiversity (ICBD) and to ensure that source countries will share in the benefits from the development and commercialization of any drugs to be derived from natural products collected under such agreements.

To put the issues of this paper in concrete terms, I next present five hypothetical cases:

Case 1: A US patient with a rare form of leukemia seeks surgical care. His surgeon thinks that the patient's tissues will be useful for developing a test to diagnose this disease and maybe also to discover a new drug treatment. Some of the patient's cancerous cells are analyzed after they are removed during surgery. The doctors form a venture company, which develops a successful test to diagnose predisposition for the disease. Unexpectedly, the company also has promising early results developing a drug to treat this form of leukemia.

Case 2: A UK woman with family history of lung cancer is asked to take part in large-scale epidemiology survey.

Her blood is collected for genetic and other studies. Family history and lifestyle data are also collected, so that these data can be compared to the genetic data to determine the relationship between genes, environmental factors and disease. Although it is highly unlikely that a commercially valuable gene, protein, etc. will be discovered, researchers find a gene and

protein from this woman that predisposes her to leukemia. These become the basis for a commercially successful test to diagnose this predisposition in many other persons. Furthermore, the protein becomes the basis of a new drug to treat the leukemia.

Case 3: A member of a small tribe in a developing country, whose members are at high risk for developing a rare form of leukemia, seeks medical care for this disease in a hospital run jointly by doctors from Japan and from the developing country. The patient's cancerous tissue is removed and some of his cells are sent to a university hospital in Japan. The cells are transferred to a pharmaceutical company, which develops a successful test to diagnose predisposition for the disease. The company also has promising early results developing a drug to treat this form of leukemia.

Case 4: A member of a small tribe, whose members are susceptible to lung cancer, is asked to take part in a co-operative study on the causes of this cancer – a study that involves leading scientists in this developing country and Japanese scientists. Samples of the patient's blood and sputum are collected for genetic and other studies. Unexpectedly, the Japanese researchers find a gene and protein from the donor that predisposes her to leukemia. These become the basis for a commercially successful test to diagnose this predisposition in many other persons. Even more fortuitously, the protein becomes the basis of a new drug to treat the leukemia.

Case 5: The same situation as case 4, but this is a small collaborative study focusing on this tribe and an unusual type of lung cancer. Information from tribal members is valuable for determining the hereditary pattern and other information related to the disease. Tissue samples from other tribal members help determine which genes are unusual in this tribe and which are related to cancer. In addition, traditional medicines and dietary supplements known only to this tribe appear to protect some people from disease and to make the progression slower in others.

With respect to each of these five cases, please consider the following questions:

- According to current laws, who probably owns the patent on the key genes and proteins identified by using these patients' tissues?
- Who ought to own the patents?
- What would be a practical and fair way to allocate rights and benefits?

In all cases, the most likely answer to the first question is that the researchers or their institutions own the patents. In Case 1 and probably also Case 3, the reasoning would rely partly on the precedent of a 1990 decision of the Supreme Court of the US State of California that held that a patient has no right of ownership over tissues removed from his body during normal medical procedures. (The basic facts of this case, *Moore* vs.

Regents of the University of California are the same as Case 1.) However, the court did rule that the patient's doctors owed him a fiduciary duty to disclose that they may have had a financial interest in the collection of his tissues. Although this case is binding only in the State of California, it has been cited by scholars and commentators the world over. At least in the US today, most hospitals and state and local governments regard human tissue collected during the course of normal therapeutic medical procedures to no longer belonging to the patients.

However, in the case of participants in research projects (cases 2, 4 and 5), the transfer of ownership to the researchers is not so automatic. At least in the US under the Department of Health and Human Services's *Regulations for the Protection of Human Research Subjects*, research subjects have to give full, voluntary and informed written consent before they participate in any government supported research. Thus, in theory, participants can refuse to participate unless special provisions are made to allow them to maintain ownership or control over their tissues. In practice, such special provisions are rarely made. In addition, many informed consent documents now explicitly require participants to acknowledge that their tissues may be used for commercially relevant research and development (R&D), and to agree that they will have no ownership over removed tissues and no right to share in commercial benefits arising from R&D using their tissues. Examples are the recent informed consent guidelines issued by the UK's Medical Research Council that are being applied to large scale epidemiologic studies of the type summarized in Case 2.

As for the ICBD, the consensus among the persons who negotiated the Convention, scholars and commentators is that it does not apply to human tissues. Therefore, the ICBD does not give tissue donors any rights of ownership or any rights to share in the benefits arising from R&D using their tissues. Moreover, although the ICBD emphasizes benefits sharing, most of its provisions refer to benefits to the source country or its agencies. None of its provisions directly give providers of traditional knowledge or source communities any rights to share in benefits.

As for intellectual property rights, to my knowledge, under all major patent treaties and the patent laws of all major countries, patent rights arise from inventorship. In some cases, governments that sponsor research or the inventors' employers have the right to claim (apply for) patent rights, and of course inventors can license or assign their rights to other parties. But initially the right to receive a patent depends upon inventorship and the existence of an invention. The conditions for the latter are the same in almost all countries. An invention must be (a) new, (b) non-obvious (i.e., inventive), (c) useful and (d) sufficiently disclosed in the patent application. Human tissue donors usually fail the non-obvious (inventive step) and disclosure conditions, while providers of traditional knowledge usually fail

the novelty and non-obvious (inventive step) conditions. Within some countries including the US, there have been efforts to change national patent laws to require that the front page of a patent certificate acknowledge the source of an invention (including providers of traditional knowledge or source countries of natural products that lead to the invention), but at least in the US these efforts have not succeeded.

However, patent laws suggest one way for local/indigenous peoples and providers of traditional knowledge to obtain ownership over new inventions. That is for them to be working in key research positions, often alongside scientists from developed countries and sometimes in laboratories in developed countries, so that they will likely be co-inventors on inventions made using traditional knowledge or based on natural products from their communities. As will be discussed later, research organizations in developed countries can make this process easier by providing opportunities for scientists from source countries and even source communities (including persons familiar with traditional knowledge) to work in their laboratories.

Contracts offer another way for providers of traditional knowledge or donors of human tissue to have a legal claim to compensation or to share in commercial benefits – contracts either between the providers and the persons collecting samples or conducting research, or contract between the providers and their national or local governments who often (especially in the case of international collaborations) must issue permits for collection of samples.

A variation on such contracts involves organizations representing governments or collectors (in other words, the commercial, academic and/or international users of traditional knowledge or donated tissue) developing formal codes of conduct to apply when they use traditional knowledge or collect samples. The codes of conduct could incorporate standard contractual agreements to ensure benefits back to providers of traditional knowledge, source communities and individual donors – agreements that would be signed by representatives of the latter groups and the collectors and users of traditional knowledge, natural product samples and human tissues. Indigenous peoples, other providers of traditional knowledge and patient groups can have a significant voice in shaping these codes of conduct. *Indeed, without vigorous and coordinated, but also balanced and constructive, pressure from such groups, meaningful codes of conduct will not arise, and effective enforcement in courts of law will be unlikely.*

In the process of negotiating contractual agreements, the likely key needs of various parties (stake holders) should be considered. Let's briefly consider the key needs of the opposite party – the outside persons that collect samples and use traditional knowledge. In the five cases described above, ownership of materials isolated from the blood samples and ownership of patentable inventions are important for the outside

researchers. Ownership gives them freedom to do important research. Ownership allows them to sell or license the patent rights to a company that will develop a drug or diagnostic kit based upon the genes or proteins. Finally without exclusive ownership (i.e., exclusive patent rights or exclusive licenses), it is unlikely this company will obtain the outside private investment needed for its development work.[1] Finally, outside academic researchers want to be able to publish their results, although it would be entirely appropriate for the source communities to stipulate that information that affects the privacy of individuals or that reveals sensitive information about the community will not be published.

On the other hand, the key concerns of the individual tissue donors in cases 1-5 above are probably the following:

(a) safety and minimal disruption of normal life in the sample collection procedure (including no weaponization of biological materials and information),

(b) compensation for inconvenience and disruption involved in the collection procedure,

(c) increased access to medical care and information related to the disease under investigation,

(d) protection of privacy and prevention of discrimination arising from the study results,

(e) in some cultures, a near absolute prohibition against the alienation of blood or other tissue,

(f) even in the absence of such a prohibition, concerns related to respect for autonomy and dignity, including the desire to control former body parts or at least to ensure that they be treated with respect, and

(g) the concern that outsiders will not profit from the exploitation of one's body tissues, or if they do, there should be acknowledgement of the donor's contribution and some benefits to the donor or her community.

In Case 5 and maybe also Case 4, where traditional knowledge and the cooperation of the local community is important to the study, the providers of traditional knowledge and the community as a whole probably have the same concerns as the individual tissue donor – but applied to the community and its knowledge as well as to the biological tissue samples. For

1. Such concerns about outside private investment are greatest in the case of venture companies, and probably of less concern in the case of established pharmaceutical companies that can finance development from internal funds. On the other hand, it is often easier to interest a venture company in developing an early stage new invention.

example, instead of simply expecting increased access to medical care or information for the individual donor (concern (c)), the community may try to receive benefits and augment its capabilities in the fields to which they contributed (for example medical care if their contribution was medically related, access to new agricultural technology and markets if their contribution was in the field of agriculture, etc.). In other words, the community may strive to maintain an active economic stake in the use and development of what it contributes. In this regard, the community will also be concerned that potential commercial opportunities not be permanently lost. For example, if the community that has knowledge how to cultivate particular medicinal plants lets an outside organization have unrestricted access to this knowledge, the outside organization might set up a plant breeding facility elsewhere, and the community would lose opportunities to exploit its knowledge. Instead, it might try to condition its co-operation on the outside organization helping it to establish its own plant breeding facility and to train local persons to staff it.

Organizations in developed countries can be constructive partners in achieving these objectives. A responsible organization will make sure to obtain all necessary permits before beginning to collect natural products or human tissues. These permits are a mechanism for the source country government and local governments to ensure that collections are made safely and that the source country benefits from the collection activities and subsequent R&D. To my knowledge, however, it is still rare for such permits to require compensation or benefits to the source communities or to providers of traditional knowledge. Requirements for benefit transfers are usually limited to institutions of the source country government. *Representatives of indigenous peoples and traditional knowledge providers should increase pressure on their own governments to try to ensure local community input into the permit granting process and to make compensation or benefits to the source communities a condition for outsiders obtaining collection permits.*

Developed country organizations can also take more pro-active steps to benefit source communities and providers of traditional knowledge. Research laboratories can require, as does the US NIH, that if their researchers collect natural products from foreign countries and then make an invention based on those natural products, before it licenses the invention to a company that will develop it, the company must work out an agreement with the source country under which the source country would share benefits from commercialization. (For example, the source country government will receive a percentage of worldwide sales of medicines based upon the natural products.) However, NIH does not require that the agreements include benefits to the source community or to providers of traditional knowledge. Foreign organizations funding research can organize consortia of developing and developed country academic laboratories and

for-profit companies to develop long-term sustainable uses of natural products, while at the same time building source country conservation and R&D capabilities.[2] Perhaps most importantly, developed country laboratories and research funders (such as the US NIH, UK MRC, UK Wellcome Trust and Japanese Ministry of Education (MEXT)) can promote the training of scientists from source countries, including scientists familiar with traditional knowledge. Such training will provide source communities with persons who can bridge to the outside world and also play a leading role in the development of source community knowledge and natural resources. They might even become (co-)inventors of key inventions, which will give them (and indirectly their communities) significant control over the inventions.[3] Training in contract negotiation and other legal and business issues should also be made available so that members of source communities can negotiate effectively. Finally, as mentioned above, representatives of developed country academic institutions and businesses can develop good practice guidelines that prescribe standards for negotiating with source communities and require compensation or benefits to source communities.

But ultimately it is primarily up to members of source communities and providers of traditional knowledge to take steps to empower themselves and their communities. For better or worse, their best hope lies in training and contract negotiations rather than in trying to change intellectual property laws. The ability to effectively negotiate and enforce contracts depends upon training (particularly in science, law and business), understanding the key needs of outside partners, setting realistic goals, building worldwide networks with other local communities, building networks with developed country organizations that are able to help their cause, building networks to their national and local governments, learning how to effectively influence mass media and public opinion, and deciding among them who should be their key representatives so that their communities can speak and act coherently.[4]

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2. An example of such a program is NIH's International Cooperative Biodiversity Groups.
3. The Natural Products Branch of NCI, NIH has provided funding for source country scientists to come to its laboratories to work on the development of natural products from their countries with precisely these objectives in mind.
4. One problem cited by outside organizations and source country governments is that it is not usually clear who are the key representatives of these communities and who are the key providers of traditional knowledge. Simply by clarifying who represents the communities and traditional knowledge, providers would resolve this problem and increase their bargaining power.