

**HUMAN-TISSUE RELATED INVENTIONS:  
OWNERSHIP AND INTELLECTUAL PROPERTY RIGHTS IN  
INTERNATIONAL COLLABORATIVE RESEARCH IN  
DEVELOPING COUNTRIES\***

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**Abstract**

There are complex unresolved ethical, legal and social issues related to the use of human tissues obtained in the course of research or diagnostic procedures and retained for further use in research. The question of intellectual property rights over commercially viable products or procedures that are derived from these samples and the suitability or otherwise of participants relinquishing their rights in the samples needs urgent attention. The complexity of these matters lies in the fact that the relationship between intellectual property rights and ownership or rights pertaining to the samples on which the intellectual property right is based may either be overlooked or taken for granted. What equally makes the matter complex is that samples may be obtained from participants in developing countries and exported to developed countries for analysis and research. It is important for research ethics committees to tread carefully when reviewing research protocols that raise such issues for purposes of ensuring that appropriate benefit sharing agreements, particularly with developing countries, are in place.

This paper attempts to analyse the key questions related to ownership and intellectual property rights in commercially viable products derived from human tissue samples. Patent law is used as a point of reference as opposed to other forms of intellectual property rights such as industrial designs because it is the right that most inventors apply for in respect of human tissue-related inventions. The key questions are formulated following a systematic analysis of peer reviewed journal articles that have reported original investigations into relevant issues in this field. Most of the cases and reported studies that are referred to in this paper do not directly deal with HIV/AIDS research but the underlying principles are helpful in HIV/AIDS research as well. Pertinent questions, which members of ethics review committees should focus on in this regard are discussed and suggestions on appropriate approaches to the issues are proposed in the form of specific questions that an ethics review committee should consider. Specific recommendations regarding areas for further research and action are equally proposed.

**Keywords:**

Collaborative research, developing countries, human tissue, intellectual property, HIV/AIDS

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## **1. Introduction**

Current literature has focused more on the issue of property rights that the donors may have in tissue samples.[1] It is quite evident from the reported studies that were analysed for the purposes of this paper that little attention has been paid to the issue of ownership/intellectual property rights in clinical research generally and collaborative international research specifically, for example, a study of public opinion on use of tissues for research purposes failed to address this issue.[2] A survey of surgical patients' opinions omitted this issue as well.[3] It is equally worth noting that major concerns in this field have focused more on the nature of consent and the possibility of blocking important research such that little attention has been paid to ownership and intellectual property rights.[4] The Nuffield Council's discussion paper however alluded to this issue but set it aside as being beyond the scope of its workshop.[5] There is equally a glaring omission in the World Health Organisation's report on public health innovation and intellectual property rights.[6] The report appears to be focused more on the effectiveness of intellectual property regimes, other incentives and funding mechanisms in stimulating research and the creation of new medicines and other products against diseases of public health importance. Before commencing a detailed discussion, it is helpful to contextualise the issue in terms of HIV vaccine trials with a view to isolating the unique challenges that are involved in this field.

### **1.1 Human-tissue related inventions in the context of HIV/AIDS vaccines research**

The development of effective HIV vaccines is "the world's best long term hope for bringing the global HIV epidemic under control." [7] The development of such vaccines however remains an enormous challenge for reasons related to, *inter alia*, intellectual property issues and scientific challenges.[8] The unique challenges to HIV vaccines research, which are related to intellectual property rights, are extensively discussed in the Aids Vaccine Advocacy Coalition's (AVAC) 2005 Report.[9] One major concern in this context is the fact that a candidate AIDS vaccine may require the use of technology or biological materials which are subject to dispersely owned rights. Eventually the researchers may be constrained by "what they

are easily allowed to use, rather than what is best from a scientific point of view.” It is correctly concluded in the report that “making vaccines involves numerous overlapping thickets of patents and rights”.<sup>[10]</sup> A remarkable recommendation, which is made in the report, is that researchers should be given the freedom to use intellectual property rights that they need and appropriate arrangements should be put in place for compensating the owners of such rights.

The Global HIV/AIDS Vaccine Enterprise has recommended that an intellectual property framework that facilitates the creation of an enabling environment where there is stronger collaboration, data and material sharing is crucial for the success of HIV vaccine.<sup>[11]</sup> Prospects of creating such an enabling environment depend on the intellectual property framework in the respective collaborating countries. Most developing countries don't seem to have such frameworks in place yet samples from these countries may be transferred to collaborating developed countries without an appropriate legal regime to govern tissue transfer and ownership of the products that may be derived from the tissues.

The extent to which concern over intellectual property and other rights may affect HIV vaccines research may be gleaned by considering the experience in some international collaborative research with some developing countries, such as Kenya. Two different disputes arose in respect of clinical research into potential HIV/AIDS vaccines in Kenya. The first dispute was between the Department of Microbiology at the University of Nairobi and the Human Immunology Unit of Oxford University. The two institutions were collaborating on vaccine development for AIDS based on the finding that some commercial sex workers from Majengo Slum in Nairobi had an immune response to HIV that protected them from the disease. The finding was used to develop a DNA based vaccine. “Disagreement arose when the university of Nairobi scientists protested that their partners at Oxford had patented the HIV vaccine development process without giving them sufficient acknowledgement. The dispute was resolved by drawing up a memorandum of understanding allowing the research to proceed but it required several months of what one local newspaper described as ‘name-calling, resignations and agonizing moments that threatened the future of the vaccine and its patent ownership.’”<sup>[12]</sup>

The second dispute, which eventually ended up in a Kenyan court, involved a Kenyan researcher alleging fraud and theft of his research materials against eight Oxford University scientists.<sup>[13]</sup> The stolen material consisted of AIDS orphans’

blood and tissue materials, which were allegedly taken from a Nairobi orphanage's laboratory.[14] For the purposes of this paper, it is interesting to note that while this dispute was going on one of the researchers was quoted as registering a concern that "just 10 millilitres of blood can give massive information if one has access to it. Therefore, the blood should only leave the country under tight agreements." [15] The envisaged agreements are not commonly used in Kenya, unless collaborating parties take the initiative to sign a memorandum of understanding.

The two cases that arose in the course of HIV related research are quite instructive in terms of the common types of tissues that may be required for developing tissue related inventions. A detailed discussion regarding other types of tissues that might have been used in the past to derive patent rights is however beyond the limited scope of this paper.

## **1.2 The unique challenges**

The Nuffield Council acknowledged in its report that human tissue-related inventions "raise[s] ethical and moral questions that have not been encountered to the same degree (or at all) with other technologies [and]... this poses a challenge to patent law." [16] The challenge lies in the fact that two competing interests are involved: "On the one hand, there is a need to satisfy legitimate public concern about the ethics of these inventions - while on the other hand; there is a political and economic need to do so in a way that does not inhibit innovation and discourage economic investment." [17]

It will be argued in this paper that the role of balancing the above interests partially falls on the shoulders of research ethics committees (RECs). This is so insofar as the determination of ethical and moral questions does not fall within the domain of patent law. This position may be attributed to the fact that "the image of patent law is understood and explained in positivist terms and thus is logically premised on the absence of morality." [18] Although calls to a return to ethical values in patent law have been prompted by developments in genetic engineering, the relationship between ethics and law, in this regard, remains an uneasy and uncomfortable one because the present law lacks the necessary resources or will to accommodate ethical concerns. [19] This relationship probably accounts for the existence of diverse legal frameworks and the manner in which legal systems have addressed the issue of human tissue related inventions and patent rights.

The Nuffield Council Report aimed at clarifying the legal status of human body parts and tissues. In this regard, it has been noted that the report provides a starting point for future policy formation.[20] Commentators on the Report however noted that it failed to address the crucial issue as to whether morality should be considered relevant to the grant of patents and resulting intellectual property rights.[21] These observations on the shortcomings of the report essentially mean that more work needs to be done to ensure that conventional research ethics principles, which are aimed at fostering respect for human dignity, are carefully considered. The appropriate stage for such reckoning should be during the approval of the research, and possibly, monitoring of the ongoing research is equally advisable. This is a unique challenge because monitoring ongoing research, particularly with a view to ensuring fair dealing when it comes to filing a patent application, may be expensive, time consuming and in direct conflict with the legal requirement of novelty when assessing the patentability of the subject matter. The first recommendation in this paper sets out how this challenge can be addressed.

The key questions that were isolated from the analysis of relevant publications are: First, is it acceptable to have a dichotomy between ownership of tissue samples and intellectual property rights in the products derived from the samples? Second, is the legal regime that governs the patenting and ownership of the commercially viable inventions that are derived from human tissues adequate? Third, if there are inadequacies in the legal framework, what are the possible remedies for such inadequacies and what strategies can RECs use in addressing them? Each of these questions is discussed below.

## **2. Ownership of human tissues versus ownership of human tissue-related inventions**

Ownership of human tissues or organs is a matter that each legal system should clearly provide for because the generally established legal principle is that “a thing which the legal system does not recognise as susceptible to ownership (a thing which is *res extra commercium*) will not be deemed as an asset in that legal system.”[22] In line with this principle, most states prohibit the sale of corpses, or parts of them or parts of a living person. Sale of such parts may only be allowed as an exception. [23] The fundamental question with regard to this issue is: can tissues and cells be considered as property and if so, what right does a patient or research

participant have in such materials? The inconsistent manner in which this question has been addressed in some jurisdictions has led to public mistrust in view of the related socio-economic question: “Why donors should be excluded from profits associated with their unique and valuable tissue?”[24] Proposals have been put forth to compensate donors but counter arguments have been raised against this proposal viz economically disadvantaged populations may be encouraged to donate their tissues, the researcher-participant relationship may be turned into a commercial one and donors may conceal important health information in order to become or remain eligible for study.[25]

It is important to note that “patent law is bound to its own version of traditional ‘proprietary’ distinction between law and nature.”[26] The object of a patent is to exploit a technical disclosure; it does not transmit the proprietary rights of physical objects for example tissues, human organs or parts. Given the very clear position on the scope of patent law, a detailed discussion on the dichotomy between ownership of tissue samples and ownership of the inventions derived from such samples is beyond the scope of this paper. This is not to say that individual countries cannot take steps to ensure a proper management of this dichotomy. As will be noted in the next section, countries such as India seem to be blazing a trail which other countries may follow with regard to this issue.

The prevailing situation is that “there still remain unsettled questions concerning the ownership of biological materials taken from humans by researchers.”[27] English courts have, for example handed down inconsistent judgements on this issue. In the case of *R v Kelly*, the court of Appeal held that parts of a corpse are capable of being property under section 4 of the Theft Act 1968. The qualification that the court gave in this case is that such parts should have acquired different attributes by virtue of the application of skill such as dissection or preservation techniques.[28] The court had earlier rejected a claim of ownership in body parts that had been altered by the application of special skills.[29]

Ownership of human biological materials is an issue that is rarely accorded adequate attention, particularly in developing countries. Some protocols that were reviewed in Kenya, for example, show that participants were informed “that they would relinquish all rights to any preparations from their samples that would have commercial applicability.”[30] It is equally interesting to note, as the study established, that investigators do not see the need to seek consent for storage, reuse

and exportation of samples. This is evident from protocols that seek the ethics review committees' permission to store or export samples yet such information is not contained in the informed consent forms.[31]

A recent study, which was done in Uganda, however concludes that the interviewed respondents were willing to allow their samples “to be used for future research based on Institutional Review Board (IRB) approval, rather than their own additional consent.”[32]

### **3. Legal frameworks**

In view of the scope of this paper, the legal frameworks in place are viewed from the perspectives of available international legal instruments and regional as well as national legal frameworks that have attempted to address the issues under discussion. The discussion in this section is limited to the legal frameworks that provide for patent applications related to human tissues. The relevant region in this regard is Europe, while the selected developing country is India.

#### **3.1 International regime**

The international regime in place consists of treaties and conventions, which as may be expected, do not specifically address the issue of intellectual property rights in human tissue related inventions. They however provide a broad outline, which regions and national states may use to deal with the issue. The international Declaration on Human Genetic Data, though not legally binding, sets ethical standards for collecting, processing, storing and using human genetic data contained in biological samples. Article 16 of the Declaration provides that biological samples collected for one of the purposes set out in Article 5 should not be used for a different purpose that is incompatible with the original consent unless the prior, free, informed and express consent of the person concerned is obtained or unless the proposed use, decided by domestic law, corresponds to an important public interest reason and is consistent with the international law of human rights. [33]

The ethical standards that are enshrined in the Declaration are quite relevant because, as indicated in Article 6, where two or more states are involved in the collection, processing, use and storage of samples, the ethics committees in the states concerned should be consulted, where appropriate, and their review should be based on the principles set out in the Declaration and ethical and legal standards adopted by

states concerned. It is quite clear from this Article that the respective countries' legal standards play an important role and where no such legal standards exist; an ethics committee can use the ethical standards, which are set in the Declaration.

Article 18(a) provides that states should regulate the cross-border flow of biological samples in accordance with their domestic law and international agreements. Since this paper focuses on the ownership of human tissue related inventions, the relevant laws and international agreements should be those that address this issue. Notably, that there are no legally binding international treaties that specifically deal with human tissue related inventions. The relevant international documents are: Patent Law Treaty [34] and Patent Cooperation Treaty. [35] The Patent Law Treaty's aim is to harmonise procedures for application, acquisition and maintenance of patents. The Patent Cooperation Treaty's Clauses 5 and 6 (of Article 27) are quite relevant insofar as they emphasise the key role of national laws in the evaluation of patentability of inventions. Clause 5 provides that each contracting state is free to determine the criteria of its national law in respect of prior art and other conditions of patentability while Clause 6 provides that the national law may require that the applicant furnish evidence in respect of any substantive condition of patentability prescribed by such law. The broad framework provided by these treaties is useful for harmonising the diverse legal frameworks in different jurisdictions.

A study commissioned by the World Intellectual Property Organisation however established the absence of a perfect international system "that can satisfy all the needs and interests of inventors, investors, users and the general public within and between developed and developing countries." [36] It is argued in the study that the situation may be attributed to the fact that "an international patent regime operates within the complex economic, political and social sub-systems of each country." The current position with regard to the international legal framework does not seem to augur well for the need to develop an effective HIV vaccine. Nderitu succinctly captures the resulting scenario as follows:

"The present international IP [intellectual property] system suggests the existence of one interpretation of IP that is applicable to all nations of the world, whatever their social or economic status. This leaves developing countries especially in sub-Saharan Africa burdened with the onus of changing their legal systems and incurring huge financial costs in implementing the IP system." [37]

It should however be appreciated that within the broad framework, which is provided for in the international patent system, it is possible for developing countries to devise strategies of proactively dealing with patent related issues that are derived from human tissues. The specific strategies are discussed in part four of this paper.

### **3.2 Regional regime: European Union**

The relevant framework is enshrined in the European Patent Convention.[38] Article 52(1) provides that patents shall be granted for any inventions which are susceptible to industrial application, which are new and which involve an inventive step. This is essentially the substantive patent law in most jurisdictions. There is no provision which expressly prohibits patenting of human tissue related inventions in the Convention. This appears to be the position because Article 53(a) only prohibits ‘inventions the publication or exploitation of which would be contrary to "ordre public" or morality’.

For the purposes of the European patent office, morality is determined according to European culture such that “inventions whose exploitation does not comply with the presently accepted standards of attitude concerning European culture must be excluded from patent protection since they are contrary to morality.” A clear illustration of this position is the European Patent Office’s decision in the *Relaxin* case which states that patents relating to DNA encoding from any human gene do not grant any right to the patentee to human beings or their parts. [39] The opponents in this case argued that it was immoral to exploit a human state (pregnancy) for purposes of gaining profit because it violates human dignity. It has been argued that neither morality nor ‘ordre public’ are precisely definable notions and that it is not a patent office’s work to determine their nature since they are not patent-law notions.[40] The meaning of these notions can be determined by other legislations or by the moral judgment in the given country. This implies that in terms of patent law, the exploitation of an invention is only contrary to ‘ordre public’ if it is prohibited by law. The limits to morality in patent law context are however set by ethical norms which are established in the individual professional fields.[41] This position clearly shows that the role of balancing competing interests in human tissue-related inventions partially falls on the shoulders of RECs. The specific ways in which RECs can play this vital role are discussed in the fourth part of this paper.

The Nuffield Council proposed a complete removal of the immorality exclusion from patent application process under the European Patent Convention (EPC). The argument in support of this proposal is “to obviate the need for patent examiners to decide complex ethical issues for which their training has left them unprepared.”[42] The Council concluded that it would then be for national courts to resolve ethical questions. Two disadvantages were however noted for removing this exclusion: “First, removing the immorality exclusion would require amendments to the EPC and the harmonising [of] national legislation such as the UK Patent Act 1977. Secondly, national courts might differ in their determination of ethical issues—just as they have already been observed to do in their approach to other patentability issues.”

### **3.3 National regime: the Indian guidelines**

India’s Ministry of Health published Guidelines for Exchange of Human Biological Material for biomedical research purposes. [43] The guidelines are quite comprehensive insofar as they address some of the pertinent issues of concern in this paper. A brief summary of the key points that are provided for in the guidelines suffices since one of the recommendations in this paper is that India’s guidelines should serve as a model for developing countries that do not have any similar guidelines in place.

The following points from the guidelines are worth noting:

- a) Human biological materials with potential use in biomedical research are clearly defined to cover various types of biological materials that may be obtained from patients following diagnostic or therapeutic procedures, autopsy specimens, donations of organs or tissue from living or dead persons, fetal tissue, body wastes or abandoned tissue.[44]
- b) Clear guidelines for the exchange and transfer of biological materials are provided for. This is a good means of averting a possible loss of control over the use of such materials once they leave the local regulatory authority’s jurisdiction. [45]
- c) The guidelines require the signing of memoranda of understanding or agreements on material transfer between the Indian and foreign collaborating partners. The specific terms to be contained in such memoranda/agreements depend on the requirements of the case under consideration but generally, these include: the identification of the collaborating or sending/receiving parties’ background, the

material to be transferred and its quantities, purpose of transfer, the research to be carried out using the material, confidentiality, intellectual property rights, filing of patents, arrangements for future commercial exploitation, reporting, publication rights, indemnification, termination of the agreement, assignment or transfer of agreement/rights; safety norms to be observed, shipping arrangements.

The guidelines are commendable because they cover issues related to intellectual property rights as well.[46] Clause 4 of the agreement prohibits filing of patent/intellectual property issues on any product or process so developed with the biological material without the written consent of the collaborating scientists. Such a prohibition would be a good safeguard for averting complex disputes that may arise in the course of the collaboration such as the Nairobi/Oxford universities' dispute that was earlier mentioned.

### **3.4 Deficiencies in the legal frameworks governing ownership of tissue samples and patenting of products derived from research with human tissues**

Two main deficiencies are lack of harmonisation and lack of focus, particularly with regard to HIV vaccines research. The regulatory regimes that govern ownership of tissue samples and patenting of products derived from research with human tissues are quite diverse. The common sources of human tissue used for research are post-mortem examinations, surgical operations and bodies bequeathed to anatomy departments. [47] The only source that seems to be properly regulated is bequeathed bodies. In the United Kingdom, tissues and organs are expected to be treated with respect and according to society's expectations. In USA, research on already existing unidentifiable specimens are not classified as research on humans and as such, neither informed consent nor ethics review is required.[48] In some developing countries, different communities attend to the excised body tissues differently such that it may not be easy to draw a distinction between social and biological issues.[49]

The existence of diverse regimes may be illustrated by the controversy relating to the export of human biological material from India, which renewed the debate on the need to regulate the flow of human material from the country. [50] The Indian scientists accused foreign researchers of violating national guidelines and argued that this showed the Indian government's inability to enforce existing guidelines. The Indian scientists' concern was that "India's large and diverse population might serve as a source of valuable genetic information that could be of potential commercial

value.” The foreign scientists’ defence was that informed consent was procured from the donors of samples and that the university’s ethics committee approved the study and that, besides, none of the foreign researchers was aware of the violated guidelines.

The Indian controversy highlights the need for RECs to play a vital role in the implementation of these guidelines and regulations that may be in place. The regulatory framework was put in place in India following the exportation of blood and tissue samples (obtained from people with genetic disorders and HIV) from India. The controversy equally serves as a reminder that obtaining consent and REC’s approval alone is not sufficient; compliance with national regulations is equally important. Possible remedies and the role that RECs can play in the implementation process are discussed in the next section.

A study, which examined how the regulatory framework affects incentive for research and development recommended harmonisation at the sub regional level, based on a SADC harmonisation initiative. Specifically, the study suggests that the AFRO region can be divided into various sub regions in order to reduce regulatory capacity problems and pool expert knowledge and resources for developing countries.[51] This seems to be a very viable proposal that should be considered alongside the third recommendation that is made in this paper, below.

With regard to lack of focus, it has been correctly argued that invoking international treaties or laws in discussion of AIDS drugs “may have little or no effect on the current need to open up the creativity to experiment or bring in all stakeholder participants.”[52] The inappropriate focus seems to be on the long term goal of access, which undermines the opportunities that ought to be utilised to invent the drugs. One interesting solution put forth in the AVAC report [53] is the use of preclinical covenant not to sue and later handling of intellectual property issues. [54] The terms of such a covenant are aimed at accelerating the development of an AIDS vaccine. Its salient features are: First, an agreement by the patent holder to grant the researching institution access to its patents for purposes of reducing freedom of operation problems in the early stages of vaccine development without raising the issue of infringement of its patent rights and second, free transfer of the rights under the covenant to other parties without the consent of the other party to the covenant.

The proposed solution is viable but the following weaknesses are worth pointing out: First there is no alternative dispute resolution procedure that is provided for in the covenant. An agreement not to sue does not guarantee that parties may not encounter

disagreements. Second, a variation clause should be included in the covenant because vaccine research is an activity that may raise new issues, which were not envisaged at the time of signing the covenant. A clause to this effect should be included to cater for such contingencies. Third, a clause should be included to provide for filing of further patents in respect of further development in the course of research. With these suggestions in place, the solution could be worth testing to establish its viability as proposed in the sixth recommendation in this paper, below.

#### **4. Possible remedies and the role of RECs**

The crucial role of RECs cannot be refuted because, one of the factors that influences the degree of vulnerability of prospective research participants, identified by the joint United Nations Programme on HIV/AIDS's (UNAIDS) consultation process, is "insufficient formal experience with, or capability to conduct ethical or scientific review of proposed research." [55] The ethics review process should ensure that the two competing interests: 1) Satisfying legitimate public concern about the ethics of these inventions; and 2) Not inhibiting innovation and discouraging economic investment are adequately catered for. The specific ways in which RECs can perform the suggested roles are discussed below.

##### **4.1 Recasting the doctrine of informed consent**

Following the US case of *Moore v Regents of the University of California* [56], it has been argued that "the right to self determination encompasses more than just the narrow interest in bodily integrity, but rather a broader dignitary interest in one's body and extracorporeal body parts." [57] The court's rejection, in Moore's case, that a patient retains an ownership interest in excised human tissue sparked much debate. Within the context of patent law, it is more plausible and practical to base patients' claims on dignitary interest in the excised tissue, which is independent of property interest as earlier explained. It has thus been suggested that the doctrine of informed consent be recast such that the right to self determination must be interpreted as protecting not only an individual's interest in bodily integrity, but in dignity. The two models that are proposed at the end of this paper would be a starting point towards recasting the doctrine of informed consent insofar as benefit sharing and granting of subsidies would ensure that the donors of tissues are accorded due recognition for their role in the research without too much emphasis on patent law. [58] It has been

argued, and rightly so, that an interest in one's dignity extends beyond the physical integrity of the body itself to the values that an individual holds. Consequently, "failing to inform an individual regarding what will happen to her removed body part, therefore violates her right to self determination, for it deprives her of the right to choose whether or not she wishes her body parts to be used for that purpose." [59]

In terms of the right to self determination, it has been suggested that every consent form should allude to the possibility of future research though this does not mean that RECs are exempt from requiring specific consent. [60] In jurisdictions such as the UK, it has been argued that research may proceed without consent if it is impractical or unethical to trace the patient and procure consent. Incidentally there are no UK guidelines to assist RECs in determining when it may be impractical or unethical to insist on procurement of consent. A study that considered practical issues related to obtaining explicit consent is however instructive in this regard. The study reports that two international studies had to be abandoned in the UK due to demands of explicit consent while the same studies went ahead in other countries without a similar requirement.[61] The investigators in the study encountered a very embarrassing situation where they inadvertently sent a letter requesting explicit consent to a patient who had died. The deceased's family members "sent an anonymous reply expressing considerable anger and distress and issued a specific instruction that they should not be contacted again..."

Several suggestions have been put forth to deal with this issue. Firstly, that consent forms be modified so that hospitals inform patients about future use of tissues. [62] However, in some studies, it has been established that the specifics for future use are unknown as at the time of procuring consent, consequently it is not sensible to seek consent for each specific use. [63] A solution that has been suggested in this case is that patients should be allowed to give conditional consent.[64] Other commentators have argued that any system requiring any kind of consent will take time and money that might be better spent on research itself.[65]

A recent landmark judgment in the US gives a glimpse of how impractical the above suggestions may be. In the case of *the Washington University v William J Catalona & others* [66] a number of tissue donors and a principal investigator claimed the right of ownership in tissue samples consisting of prostate tissue, blood and DNA samples, which had been donated for prostate cancer research. The principal investigator (who had left the university after more than two decades of

service) alleged that the tissues had been donated to him and that in terms of the Code of Federal Regulations the participants were entitled to have the tissues returned to them. The relevant regulations require that the research participants should be told that they can discontinue participation at any time without penalty. [67] The court held that this requirement does not imply any right to control the future use or disposition of the physical specimen. Withdrawal from participation was held to imply three things: the university may destroy the samples; the university may store the samples without using them any further in research protocol or the university may remove all personal identifiers from the sample and continue using them in exempt anonymised research.

The court's judgement is in accordance with Federal regulations, which prohibit the return of what may strictly speaking be deemed to be biological waste. Such biological waste should be destroyed and the university could not return them to the donors. Most countries have substantive laws that govern the disposal of biological wastes and a similar argument could be advanced to defeat a donor's claim for a return of the donated tissues on withdrawing from research participation. It is worth noting that the university's regulations provided that investigators who leave the university were prohibited from taking blood or tissue samples unless they had written approval from the vice chancellor. The issue of intellectual property rights and ownership of tissue samples was equally provided for in the university regulations in the following terms: "all intellectual property including...tangible research property shall be owned by the university if significant resources were used or if it is created pursuant to a research project funded through corporate, federal or other external sponsors administered by the university. Again, this is a typical clause that one may find in universities' and research institutes' regulations.

In view of the foregoing circumstances and facts, the court held that the tissue samples belonged to the university, not the principal investigator or the research participants. The court relied on two previous decisions where courts had denied that donors of tissues retained any rights in their tissues. The first case is *Moore v Regents of the University of California*, which has been alluded to in this paper already. In this case the California Supreme Court exhaustively reviewed the law relating to ownership and use of human tissues and held that a participant could not have an ongoing ownership interest in excised tissue because of the laws requiring the disposal of such materials as hazardous biological waste. The second case that the

court relied on is *Greenberg v Miami Children's hospital Research Institute Inc.* where the plaintiffs supplied blood and tissue samples to the defendant for research purposes and the court held that “the research participant’s property right in blood and tissue samples...evaporates once the sample is voluntarily given to a third party.” The court’s view was that “at the core, these were donations to research without any contemporaneous expectations of return.” [68] Much as the donors may not expect the tissues to be returned, it is interesting to note how the court, in this quoted statement, did not address the issue of these tissues being used for purposes that the donors may not have given the tissues for.

The donation in these two cases that the court relied on was implied as there was no express statement to this effect in the informed consent forms. The judgment has elicited mixed reactions. Some bioethicists and legal experts are reported to argue that people will be dissuaded from donating tissue samples while others argue that “the opposite decision would have been disastrous for tissue banks and tissue research.”[69] This case illustrates that the suggestions that are mentioned in this section may not be practically viable in view of the jurisprudence in existence and other substantive legal provisions in place that govern the use and disposal of human tissues. A more plausible proposal seems to be that each country should define its own limits in terms of policy. [70] The practical consequence of this last proposal would be lack of harmonised regulatory regimes that was mentioned earlier in this discussion. It is thus crucial for policy makers to consider circumstances such as the existing regimes in the collaborating countries before implementing such a proposal. Perhaps this would require a case by case assessment, which means that it is a task the RECs will need to perform in each application that is presented for approval.

#### **4.2 Catering for the tissue donors’ interests**

Investigations have established that most, if not all tissue donors are not interested in claiming ownership or sharing in the intellectual property rights that may be derived from their tissues. Most tissue donors simply want to have a say in how their contributions are used and they are also interested in ensuring that their cultural values are taken into consideration. This position was established in an interview with one of the parents involved in a legal battle with a hospital in USA over the way in which their contributions to research had been used. The parent clearly indicated that

the legal battle “is not about the Canavan families wanting a piece of the pie; it is about ‘having a say in how their contributions are used.’”[71]

It is not possible for the tissue donors to claim ownership of patent rights. The underlying reason for this position was succinctly explained by the Nuffield Council as follows:

“The right of ownership in a patent derives from the act of invention. In the case of inventions derived from human tissue, the act of invention is carried out by the person who extracted and purified the human tissue by some inventive means- and it is this intervention which confers the right to apply for a patent. It follows that the monopoly is not the donor of the tissue in question; he has played no part in the inventive act. Hence the donor has no right to interfere with the lawful owner’s exercise of his monopoly- irrespective of whether the tissue was obtained and/or experimented with or without his consent.”[72]

It is also important to note that current statutory and case law in the UK recognise the autonomy of patients’ decisions over their bodies, but not ownership of tissue.[73] The position is in line with traditional jurisprudence, which, as Tedeschi argues, recognises “two additional rights apart from rights in property: family rights and the rights of personality.” He appears to agree with the majority view that recognises the right of a person over his body as a personal right as opposed to a property right. [74] The distinction between property and personal rights is this; the term property introduces certain economic and market connotations, otherwise the law of torts/delict would still provide for certain rights such as privacy and adequate disclosure to give informed consent. [75] The personal rights in this regard are usually translated to the right to self determination, which requires the procurement of the donor’s informed consent.

Before concluding the discussion in this section, it is important to set forth some practical considerations on how tissue donors’ interests can be taken care of in view of the prevailing position on the ownership of tissue samples and intellectual property rights that are derived from them. One of the strategies that the joint UNAIDS consultation process suggested for the development of HIV vaccines and ensuring its availability in the populations is the use of effective incentives. One of such incentives is negotiation of intellectual property. Following the explanation of the current position relating to ownership of tissues and intellectual property rights in this paper, it is evident that the UNAIDS’s suggestion is not easy to implement in practice. This is because the collaborating developing countries tend to play the role of tissue donors who are not entitled to claim any intellectual property rights in the

inventions. As such it is important to think of other ways of catering for their interests.

The arguments that were earlier alluded to regarding the consequences of leaving the resolution of complex ethical issues for the national courts to contend with is a clear indication that RECs are better placed to delve into such issues. RECs, provided that they are well trained and competent, can play a vital role by declining to approve any proposed clinical research on human tissues that may breach ethical requirements. RECs could also help in the event that disputes concerning human-tissue related inventions were to be resolved by national courts. The RECs' role in this regard would be to adduce evidence in support of contentions that ethical requirements were breached. This obviously requires proper documentation of the relevant REC's proceedings, which can then be produced as documentary evidence to corroborate any oral evidence that may be adduced.

## **5. Conclusions**

From the key questions that have been discussed in this paper the following concluding remarks give an indication of what RECs should focus on when reviewing research protocols where human tissues are used.

- a) It is desirable, in appropriate cases, to include benefit sharing arrangements in the memorandum of understanding between collaborating institutions or countries. This would be an indirect way of contributing to the communities that are usually involved in the research. It is also a way of rewarding donor altruism and reducing public mistrust. Murray's congressional testimony with regard to this remark is quite thought provoking; "If biotechnologists fail to make provision for a just sharing of profits with the person whose gifts made it possible, the public's sense of justice will be offended and no one will be the winner." [76]
- b) There should be clear guiding principles on cases where it is deemed expedient and just to compensate tissue donors, using the model of subsidies on drugs.
- c) The scope of informed consent should be extended to take into consideration the tissue donor's dignitary interests.

Some relevant considerations that could help RECs are listed below.

- i. Are there aspects of the proposed study, which show that knowledge/expertise of local nationals is being exploited to access local biological materials?

- ii. Are there watertight procedures to ensure safe transfer of samples from one institution to another (particularly with regard to preservation of the tissue donors' confidentiality)?
- iii. Have the tissue donors relinquished all benefits/rights that they may derive from their samples' commercial applicability?
- iv. Was adequate time given to the tissue donor, when consent was procured, to consider the use of his/her tissues for research?
- v. Did the tissue donors give conditional consent?
- vi. What types of research are the tissues being donated for and are these specified in the Informed Consent form?

The above considerations are never delved into by patent offices. It is thus important for RECs to take care of these considerations because once patent rights have been granted, there are no prospects of relying on any of these factors to challenge the validity of the patent.

## **6. Recommendations**

The following recommendations follow from the issues that have been discussed in this paper:

1. Further research should be carried out to determine how effective the Indian guidelines have proved to be in terms of implementation so that they can serve as a model for other developing countries. In particular, material transfer agreements such as India's can serve as a good strategy of solving the complex issues that have been mentioned in this paper. The use of memoranda of understanding is equally recommended under the Indian guidelines. Using a memorandum of understanding can be a viable approach in countering the argument that monitoring ongoing trials particularly with a view to ensuring fair dealing when the collaborating parties decide to lodge a patent application may go against the patent law requirement for novelty. It is notable that the Nairobi/Oxford universities' HIV vaccine research dispute was amicably resolved by way of a memorandum of understanding. The particulars of the parties' agreement were never made public. Such lack of publicity confirms that it is possible to maintain the patent law requirement for novelty while at the same time setting out clear

terms on which the collaborating parties as well as research participants can deal with each other.

2. Two solutions can be proposed as models for catering for the interests of collaborating developing countries: benefit sharing arrangements and granting of discounts on drugs that may be developed using the patent rights. The benefit sharing model in this case, would entail utilising some of the profits derived from the patent to set up community development projects with a view to uplifting the living standards in the participating communities. The actual nature of such projects would be determined on a case by case basis depending on the particular community's needs. [77]
3. A study should be done to establish the plausibility or otherwise of implementing a system where each country determines the specific modifications that should be made to the standard consent forms. The purpose of such a study would be to ensure that implementing the proposed system does not lead to more diverse regimes.
4. In view of the argument that local RECs may lose control over exported samples, a precautionary approach that RECs ought to use in such situations would be to consider and detect possibilities of local knowledge and expertise of local nationals being exploited to access local biological materials as was alleged in the Indian controversy.
5. It has equally been suggested that "bioethicists should work to ensure safeguards other than informed consent." [78] A safeguard that has been proposed is the establishment of tissue-trustee infrastructure, rather than consent issues to ensure the confidence of the donating public. [79] Such an infrastructure is essentially similar to the Indian material transfer agreement system. In this regard, once a study has been done on recommendation 1 above then it may be viable to recommend the use of the infrastructure to other developing countries as well as other collaborators in international research projects.

6. The proposed use of covenants not to sue, which has been put forth by AVAC, should be tested in a selected number of international collaborative research projects with developing countries to establish its viability.

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### **Competing interests**

None

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  - <sup>5</sup> Nuffield Council on Bioethics. 'The ethics of research related to healthcare in developing countries. A follow up discussion paper'. London, March 2005, p.62. It is noted in the discussion paper, with regard to large scale studies in genetic epidemiology that are currently being conducted in several different populations, that there are a number of complex interacting factors involved such as the relationship

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between intellectual property protection and the ownership and the rights pertaining to the resources on which the intellectual property has been based.

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<sup>8</sup> Other challenges that are mentioned in the report are inadequate resources, clinical trial and regulatory concerns. UNAIDS/WHO (See reference 7, p.16).

<sup>9</sup> AVAC 'AIDS Vaccines at the Crossroads, (September 2005),

<[http://www.avac.org/pdf/reports/2005\\_Chapter4.pdf](http://www.avac.org/pdf/reports/2005_Chapter4.pdf)>

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<sup>16</sup> Nuffield Council on Bioethics. Human Tissue: Ethical and Legal Issues. April 1995, p.96.

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<sup>33</sup> International Declaration on Human Genetic Data. <[http://portal.unesco.org/en/ev.php-URL\\_ID=17720&URL\\_DO=DO\\_TOPIC&URL\\_SECTION=201.html](http://portal.unesco.org/en/ev.php-URL_ID=17720&URL_DO=DO_TOPIC&URL_SECTION=201.html)>. The uses of samples that are provided for under Article 5 are diagnosis and health care; medical and other scientific research; forensic medicine and legal proceedings and any other purposes that are consistent with the Universal Declaration on the Human Genome and Human rights and international law of human rights.

<sup>34</sup> <[http://www.wipo.int/treaties/en/ip/plt/trtdocs\\_wo038.html](http://www.wipo.int/treaties/en/ip/plt/trtdocs_wo038.html)>

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- <sup>39</sup> See reference 27. The Relaxin case concerned the patenting of genes isolated from pregnant women, which were encoded to produce Relaxin. The patent was granted to the Horward Florey Institute of Experimental Physiology and Medicine, of Melbourne Australia to cover the hormone relaxin, which relaxes the uterus during childbirth. The gene was obtained from a human ovary.
- <sup>40</sup> See reference 27. The notion of 'ordre public' includes the safeguarding of public security, the protection of the physical integrity of individuals and also the protection of the environment.
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- <sup>42</sup> See reference 16, p. 97.
- <sup>43</sup> Government of India, F.No.L.19015/53/97-IH(Pt.) Ministry of Health & F.W. Department of Health, Nirman Bhawan, New Delhi (19<sup>th</sup> November 1997) Guidelines for Exchange of Human Biological Material for Biomedical Research Purposes. <<http://icmr.nic.in/min.htm>>
- <sup>44</sup> The human materials that are listed in Clause I of the guidelines are: Organs and parts of organs; Cells and tissue; Sub-cellular structures and cell products: Blood; Gametes (sperm and Ova); Embryos and Fetal Tissue; Wastes (urine, faeces, sweat, hair, epithelial scales, nail clippings, placenta etc.) and Cell lines from human tissues.
- <sup>45</sup> See paragraph II of the guidelines.
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- <sup>63</sup> See reference 3.
- <sup>64</sup> See reference 2.
- <sup>65</sup> See reference 60.
- <sup>66</sup> US District Court, Eastern District of Missouri Eastern Division, Case No. 4:03 cv 01065 SNL. The judgment, which was handed down on 14<sup>th</sup> April 2006 is available at <[prostatecure.wustl.edu/pdf/findingsOfFact.pdf](http://prostatecure.wustl.edu/pdf/findingsOfFact.pdf)>
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