

Regulating the Human Tissue Trade

By Bradley Merrill Thompson and Leah R. Kendall

Over the past several years, the media has reported about the sale and processing of human skin, tissue, and bone. Not surprisingly, the most scintillating of these articles describe practices that are clearly illegal, such as obtaining human tissue by forging medical and death records. But what about the more common situations that are not as well publicized? For example, when families agree to donate a deceased family member's tissue – hoping or thinking that it will be used as a gift to save lives or benefit science -- only to have the tissue “sold” within an industry that has revenue reaching into the billions and that's driven by highly profitable biotech companies. Or, when a patient undergoes a surgical procedure, presuming that their tissue will be discarded as biomedical waste, only to have it eventually become a medical product. Certainly, this trade in human tissue raises complex moral and ethical questions, but what is its legal status?

The answer is frustratingly complex. Although there are some laws and regulations on the books for obtaining consent, prohibiting payment, and ensuring safety, the government has enforced those requirements sporadically, if at all. In other cases, such as state law, the legal requirements are neither comprehensive nor uniform. Taken as a whole, the current framework for regulating the human tissue trade seems to have done little to address the public's or even the government's concerns. More must be done to create a comprehensive system of regulation that will ensure the tissue recipient's health and safety, while also protecting the rights and dignity of the donor and the donor's family.

1. The Legal “Floor”

Currently pending litigation reveals the legal theories that form the “floor” of regulation and enforcement with respect to egregious cases in the tissue trade. These cases include the now-infamous Biomedical Tissue Services (BTS), a tissue procurement organization that allegedly forged death and medical records in order to obtain body parts from various funeral homes around the U.S. In turn, BTS sold the parts to tissue processors and manufacturers that used the stolen and sometimes contaminated tissue in their medical products. Ultimately, this scheme culminated in a recall of medical products and recommendations by the U.S Food & Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) that recipients of those products be tested for HIV, hepatitis B virus, hepatitis C virus, and syphilis.

The BTS case has spawned both criminal and civil litigation. The principal criminal case consists of a 122-count indictment that includes charges of enterprise corruption, body stealing, opening graves, unlawful dissection, and forgery. On the civil side, plaintiffs

have sued the companies involved on the basis of negligence, product liability, and infliction of emotional distress, among other causes of action.

These charges are examples of the legal floor for the “worst of the worst” cases – where parties obtain tissue in a clearly unlawful fashion. Though necessary to punish the worst offenders, such legal theories are clearly inadequate as a system for ensuring that human tissue is rightly – and safely -- obtained. Other areas of the law touch on this type of systemic and comprehensive regulation of the tissue industry, although they, too, ultimately fall short of what is needed.

2. Obtaining Consent from Donors and Families

One such area is the consent process, which the law addresses in a few respects.

Common Law Duties

In the context of living donors, courts have recognized the duty to inform patients of potential conflicts of interests and how their tissue may be used. For example, in the well-known case of *Moore v. The Regents of the University of California*, the court agreed that the patient’s doctors had a duty to inform the patient of his financial interests when the doctor took certain tissues with the intent of developing them into a valuable product.¹

In addition to obtaining consent from a living patient, certain common law theories speak to obtaining consent from a deceased donor’s family. For example, black letter law defines fraud or misrepresentation as the knowing concealment or failure to reveal a material fact in order to induce someone to act to his or her detriment. Notwithstanding that duty, tissue procurement organizations have said they do not want to reveal certain information (for example, the for-profit status of a tissue processor) to donor families for fear of decreasing donations. Yet if the organization does not want to reveal certain facts for fear of discouraging a donation, then it would seem that by definition such information may be material to the family. This commentary also suggests that the procurement organizations realize the family would perceive certain donations to be to their detriment.

The theory of unconscionability, which generally is defined as extreme unfairness as demonstrated by a party’s lack of meaningful choice and contractual terms that unreasonably favor the other party, also is relevant. In that regard, consider this description of the potential unfairness involved:

There is the bed-side or in-home solicitation of grieving family members, who do not seek out an opportunity to

¹ *Moore v. The Regents of the Univ. of Cal.*, 793 P.2d 479 (Cal. 1990). The court also ruled, however, that the patient had no property interest in his discarded body parts and thus no right to profits from the ultimate commercial product.

make a deal, and may not even know that they are being asking to negotiate. Add to this the imbalance of information, the time-pressured nature of the decision families are asked to make, and the fact that they are not in a position to investigate the meaning or validity of the [procurement organization's] agent's disclosure of the possible end uses of the tissue, and it is hard to image that the resulting deals would withstand legal scrutiny.²

Although these common law theories offer some initial approaches for assessing the consent process in the context of tissue, it is unlikely that they can provide a comprehensive, efficient, and workable method of ensuring adequate consent.

Regulatory Oversight

Under the authority of the National Organ Transplantation Act³ and other federal statutes, the Centers for Medicare & Medicaid Services (CMS) recently issued a regulation for obtaining informed consent for organ and tissue donation. This regulation requires organ procurement organizations (OPOs) to provide the following to the individual(s) responsible for making the donation decision:

- A list of organs and tissue that may be recovered.
- The most likely uses for the donated organs or tissue.
- A description of the screening and recovery processes.
- Information about the organizations that will recover, process, and distribute the tissue.
- Informed regarding access to and release of the donor's medical records.
- An explanation of the impact the donation process will have on burial arrangements and the appearance of the donor's body.
- Contact information for individual(s) with questions or concerns.
- A copy of the signed consent form if a donation is made.⁴

If an individual consents to donation before death, an OPO must only provide information about the donation to the donor's family *if* the family requests it.

In response to comments, CMS scaled back this regulation from its original proposal. For example, the proposed regulation would have required procurement organizations to give donor families information on the for-profit or non-profit status of the organizations that will recover, process, and distribute the tissue. However, after receiving significant objections to such disclosure – including that “disclosing profit status is not relevant or

² Michelle Oberman, *When the Truth is Not Enough: Tissue Donation, Altruism, and the Market*, 55 DePaul L. Rev. 903 (2006).

³ 42 U.S.C. § 273 *et seq.*

⁴ 42 C.F.R. § 486.342.

meaningful information for the donor family”⁵ – the final rule omitted this language. Further, the proposed version would have required OPOs to inform donor families about the right to limit or restrict the use of tissue. Ultimately, though, CMS decided that “it should be up to each individual OPO if and how the right to limit or restrict the use of ... tissue should be handled.”⁶ In explaining why the agency removed this requirement, CMS said:

[T]here is no reason to introduce unnecessary information that may adversely affect the donation decision. The disclosure of the decision maker’s right to limit or restrict the use of ... tissue could result in unreasonable or unnecessary limitations on donated ... tissue. Since this could have an adverse effect on ... tissue donation and availability, this requirement has been removed from the final rule.⁷

The regulation also has important limitations in its scope. In particular, it applies only to OPOs, which are entities that the government has designated as being responsible for all organ recovery in the United States. OPOs can also recover tissue, but because the government does not designate tissue recovery entities, others are free to enter into the tissue recovery business without being subject to the regulation. These parties may include tissue banks, coroners, or really anyone who wants to get into the business.

The final rule does say that OPOs must *cooperate* with tissue banks with which a hospital has an agreement in obtaining informed consent for tissue donation, but the preamble to the rule also explains that the OPO is not required to *request* tissue donation on behalf of such tissue bank. The rule also does not require OPOs to cooperate with tissue banks whose agreement is not with the hospital, but is instead with a medical examiner or coroner. Further, while OPOs must “ensure” that the consent of individuals responsible for making the donation decision is informed, this requirement applies only when the OPO requests the tissue. Thus, the regulation does not include within its scope the other entities that may seek tissue donations. To complicate matters further, no one yet has assessed the degree to which OPOs are complying with the regulation, and it is too early to determine how effectively CMS is enforcing this requirement.

State statutes establish an individual’s right to donate and the right of an individual’s family to donate in the absence of evidence of a decedent’s intent otherwise. Nearly all states’ laws are based on The Uniform Anatomical Gift Act (UAGA), which requires organ and tissue procurement organizations to seek the consent of a potential donor’s family members if the donor has not already issued a specific and uncontested donation of tissue. However, the model law does not set forth the form or content of an “informed

⁵ 71 Fed. Reg. 30982, 31020, *Conditions for Coverage for Organ Procurement Organizations (OPOs); Final Rule* (May 31, 2006).

⁶ *Id.*

⁷ *Id.*

consent.” Although a few states have issued specific regulations for the informed consent process,⁸ many have not taken this step.

Considering both federal and state requirements, the question is whether this framework is sufficient to protect the rights of donors and their families. Unfortunately, the answer seems to be no.

In 2001 -- before the CMS regulation was in place -- the Department of Health and Human Services (HHS) Office of Inspector General (OIG) issued a report on informed consent practices in tissue banking. This report described several deficiencies with respect to obtaining consent for tissue donation, such as tissue banks requesting consent over the phone, lack of training and accountability for external parties who seek consent, and providing families with inadequate materials at the time of donation.⁹ Despite this well-publicized critique and the administrative record supporting the new CMS regulation, enforcement of both old legal authorities and the newly-enacted regulations has been rare. For example, a 2007 article on the tissue industry chronicled the consent practices of procurement organizations, calling them “famously aggressive” and describing their practices of “framing” consent language (e.g., “recovery”, not “harvest”) as “turning the lexicon of scandal into the preferred patois of altruism.”¹⁰

At the least, significant disagreement exists on whether procurement organizations are complying with current legal standards for informed consent and whether the current framework is adequate to protect the rights and integrity of donors and their families.

3. “Reasonable Payments” for Human Tissue

The law also forbids the sale of human tissue. More specifically, the National Organ Transplant Act (NOTA)¹¹ forbids knowingly acquiring, receiving, or transferring tissue or bone for “valuable consideration for use in human transplantation.”¹² However, the definition of “valuable consideration” excludes “reasonable payments associated with the removal, transportation, implantation, processing, preservation, quality control, and storage of a human organ.”¹³ The term “reasonable payments” is not defined and has rarely been enforced or interpreted by the courts.

⁸ See e.g., Cal. Health & Saf. Code § 7158.3.

⁹ U.S. Dep’t Health & Human Services, Office of Inspector General, *Informed Consent in Tissue Donation: Expectations and Realities* (2001). The report ultimately issued a number of recommendations to both the government and the industry for strengthening the informed consent process. Contemporaneously with this report, the OIG also issued a report entitled *Oversight of Tissue Banking*, which examined and identified several limitations in government and other external oversight of the tissue banking industry.

¹⁰ Kerry Howley, *Who Owns Your Body Parts?*, Reason, Mar. 2007, available at: <http://www.reason.com/news/show/118517.html>.

¹¹ NOTA provides a well-defined framework for the donation and distribution of major organs, such as the heart, lungs, or kidneys. Although NOTA touches on the donation of tissue and bone, the framework for these donations is somewhat less well defined than that for major organs, particularly with respect to payment issues.

¹² 42 U.S.C. § 274e(a).

¹³ 42 U.S.C. § 274e(c)(3).

Therefore, under the current framework, individuals and organizations harvest tissue and bone and provide it to other entities in return for “reasonable payments.” A key question, then, is whether such payment – and revenue for the industry as a whole – is consistent with the limitation on “reasonable payments”?

Although it is difficult to quantify the magnitude of such payments, some estimate the tissue industry as reaching upwards of \$1 billion in annual revenue.¹⁴ Moreover, the stock prices of companies that manufacture and sell medical products from donated tissue have marched steadily upward. Another piece of the puzzle is the “price per part”, which – depending on the type of tissue – is reported to range from tens of thousands to hundreds of thousands of dollars.¹⁵

Yet even in the face of these significant amounts of money changing hands, HHS has not defined a ceiling or even provided guidelines on what “reasonable payments” might be. Moreover, the government does not appear to be enforcing the “reasonable payment” provisions, and recent government issuances suggest that current industry compliance with the “reasonable payment” requirement has not been comprehensively reviewed.¹⁶ What is clear, though, is that the current approach has fostered a highly commercial market built on human tissue that may have been intended as an altruistic, charitable gift. At a bare minimum, current payment practices merit a close review in light of the current framework – a review that in turn may call for strengthening government oversight and increasing transparency of and limits imposed on “reasonable payments” that are made in connection with the removal, transportation, implantation, processing, preservation, quality control, and storage of human issue.

4. The FDA Framework

Donated tissue and its use in the manufacture of medical products implicates critical health and safety issues, as demonstrated by reports of harm stemming from the use of diseased human tissue. FDA has developed and recently refined a regulatory framework that is intended to ensure the safety of human tissue and products made from tissue, but this framework seems to be inadequate in the face of the ever-increasing medical products that result from the tissue trade.

By way of background, the FDA regulates human cells, tissues, and cellular and tissue-based products that are intended for implantation, transplantation, infusion, or transfer into a human recipient, or so called HCT/Ps. This regulation occurs under a two-tiered, risk-based framework. Importantly, a major difference between the two tiers is that

¹⁴ Oberman, *supra* note 2; See also Robert A. Katz, *The Re-Gift of Life: Can Charity Law Prevent For-Profit Firms From Exploiting Donated Tissue and Nonprofit Tissue Banks?*, 55 DePaul L. Rev. 943 (2006).

¹⁵ Oberman, *supra* note 2. Note also that despite the extensive amounts of money changing hands, typically there are no property rights in a body part, whether the donor is living or dead. In this way, neither donors nor their families receive any payment or compensation for their parts, which may ultimately draw in hundreds of thousands of dollars after “donation.”

¹⁶ Katz, *supra* note 14.

HCT/Ps regulated under the “low risk” tier do not require any FDA review or approval before they can be marketed or sold, while HCT/Ps that fall under the higher tier do require premarket clearance or approval. The two tiers work as follows:

Tier 1: “Low Risk” HCT/Ps

The fundamental intent of the low risk tier is to prevent the transmission and spread of communicable diseases.¹⁷ Consistent with this, the requirements for HCT/Ps under this framework center on ensuring the safety of the HCT/P. In particular, key areas of regulation include: registration and listing requirements, donor eligibility standards, and “Good Tissue Practices”, which require facilities to use specific controls to prevent the HCT/P from becoming contaminated. The low risk framework does not require FDA premarket clearance or approval for an HCT/P and does not set forth advertising and promotion requirements for “low risk” HCT/Ps.

To be regulated solely under the low risk framework, HCT/Ps must meet all of the following criteria to qualify:¹⁸

- The HCT/P is minimally manipulated;
- The HCT/P is intended for homologous use only;
- With limited exceptions, its manufacture does not involve the combination of the cells or tissues with another article; and
- Either:
 - o The HCT/P does not have a systemic effect and is not dependent upon the metabolic activity of living cells for its primary function; or
 - o The HCT/P has a systemic effect or is dependent upon the metabolic activity of living cells for its primary function, and it is for autologous use, reproductive use, or allogeneic use in a first-degree or second-degree blood relative.

Tier 2: HCT/Ps that are also Drugs, Devices, or Biological Products

FDA regulates HCT/Ps that exceed the above-listed criteria as a drug, device, or biological product (whichever is most appropriate for the particular HCT/P), which means that the HCT/P must receive FDA clearance or approval before it can be marketed or sold. After such a product is FDA approved and hits the market, it is subject to restrictions on the medical claims that can be included in advertising and promotional materials. At a high level, these restrictions prohibit

¹⁷ See 69 Fed. Reg. 68612, *Current Good Tissue Practice for Human Cell, Tissue, and Cellular and Tissue-Based Product Establishments; Inspection and Enforcement* (Nov. 24, 2004); U.S. Food & Drug Administration, Compliance Program Guidance Manual, *Inspection of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)*, 7341.002 (2005).

¹⁸ 21 C.F.R. § 1271.10(a).

promotion exceeding the bounds of the FDA clearance or approval, which is commonly called “off-label” promotion.

Although on its face the FDA framework looks quite comprehensive, the actual promotion and use of certain products made from human tissue suggest that FDA enforcement and oversight is inadequate. In this regard, there are several problems.

First, some tissue products regulated under the “low risk” tier seem to meet the statutory definition of a medical device and are highly processed, manufactured, advertised, and sold to doctors, hospitals, and clinics just like any other medical device would be. For example, one of the most lucrative and prominent products made from donated human skin is promoted for “restoration of structure, function and physiology in abdominal wall repair” and “coverage, support, and stabilization of implant/expander in immediate breast reconstruction”. The definition of a medical device encompasses articles that are intended to affect the structure or any function of a patient, so it seems that if this product were not made from human skin, it would be a medical device and would require FDA premarket review, not to mention additional regulatory controls designed to ensure the safety, quality, and integrity of the product. If a product meets the statutory definition of a medical device, it should be regulated as such.

Second, many of the products on the market seem to exceed the required criteria under the “low risk” tier. For example:

- *Minimal manipulation* – For structural tissue, minimal manipulation is defined as processing that does not alter the original relevant characteristics of the tissue relating to the tissue’s utility for reconstruction, repair, or replacement. For nonstructural tissues, it means processing that does not alter the relevant biological characteristics of cells or tissues. Although FDA has issued some interpretive guidance and individual decisions on what constitutes minimal manipulation, the dividing line remains blurry. For example, as explained below, decellularization may or may not constitute minimal manipulation, depending upon how a company uses or promotes its product. As technology continues to advance, companies seem to be pushing the boundaries, particularly with respect to the requirement that minimal manipulation must not alter the biological characteristics of cells.¹⁹
- *Homologous use* – Homologous use means the repair, reconstruction, replacement, or supplementation of a recipient’s tissues with an HCT/P that performs the same basic function(s) in the recipient as in the donor. In other words, skin should be used as skin, bone for bone, etc. Current practices seem to have crept beyond these boundaries. One example is products made from skin promoted for the repair of internal body walls. Physiologically speaking, this practice seems risky in that skin – a highly elastic tissue – is being used

¹⁹ See e.g., U.S. Patent No. 5,336,616 (filed Feb. 2, 1993) (describing processing for human skin harvested from cadavers and sold as minimally processed products).

for a low elastic content location, and for internal rather than external use. This can cause recurrent hernias due to stretching of the graft site.²⁰

- *Either not dependent on the metabolic activity of living cells for its primary function, or, if it is so dependent, must be for autologous use, reproductive use, or allogeneic use in a first-degree or second-degree blood relative* – Currently, some manufacturers of tissue products made from donated skin promote how their products work and interact with the recipient’s living tissue in order to regenerate new tissue. Such promotion suggests that the product is dependent on the metabolic activity of living cells for a primary function and thus can only be used for first or second degree blood relatives under FDA’s low risk framework. However, these products are currently not limited in this manner.

Third, when FDA does initiate some type of enforcement, it may be woefully inadequate. This problem is also best illustrated by example. In 2006, FDA issued two “violative advertising and promotional labeling letters” pertaining to a product made from donated human skin. This letter said that, in order to meet the requirement for “minimal manipulation”, the product could only be marketed for wound covering of diabetic foot ulcers – not for the repair or healing of diabetic foot ulcers. The letter directed the companies to revise their websites and promotional materials to this end.

At a fundamental level, this enforcement approach can be problematic because it does not address the root problem of the company’s manipulation and processing of the skin. In effect, the letter suggests that by saying a product is used for wound “repair” -- as opposed to a wound “covering” -- somehow the extent of “manipulation” changes, which of course it does not. Either a product is “minimally manipulated”, or it is not – this is an objective standard that should not be changed by promotion. FDA’s approach could allow companies to circumvent the “higher risk” framework merely by tweaking their marketing materials, rather than addressing the fundamental issue of how the product is made and used. A recent review of some company websites also suggests that this approach may be ineffective.

Finally, another basic question is whether the FDA framework is adequate to ensure patient and public safety, given the way in which certain tissue products are promoted and used just as any other medical device would be. This seems to be a question of FDA enforcement – can and does FDA inspect often enough, and rigorously enough? The recent scandal over contaminated tissue obtained by Biological Tissue Services – and the resulting recalls and disease testing recommendations -- have heightened these concerns.

Conclusion

We have seen an incredible amount written about the tissue trade over the past decade, much of which has described the harm to donors, their families, and in some cases,

²⁰ See A. Gupta et al., *Vertral herniorrhaphy : experience with two different biosynthetic mesh materials, Surgisis and Alloderm*, Hernia, Vol. 10, No. 5, 419-425 (Oct. 2006).

recipients of donated tissue. While some regulations do exist that could be used to combat these problems, the public outcry and many of the problems with the regulatory framework continue: comprehensive informed consent requirements have not been enacted, the prohibition on “reasonable payments” lacks teeth, and current FDA oversight has limitations. In light of these issues, the government should address the lack of federal legislation and enforcement and begin a dialogue on potential solutions for solidifying the human tissue regulatory framework.