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TISSUE BANKS: IS THE FEDERAL GOVERNMENT'S OVERSIGHT ADEQUATE?

HEARING

BEFORE THE

PERMANENT SUBCOMMITTEE ON INVESTIGATIONS

OF THE

COMMITTEE ON GOVERNMENTAL AFFAIRS
UNITED STATES SENATE

ONE HUNDRED SEVENTH CONGRESS

FIRST SESSION

MAY 24, 2001

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TISSUE BANKS: IS THE FEDERAL GOVERNMENT'S OVERSIGHT ADEQUATE?

THURSDAY, MAY 24, 2001

U.S. SENATE,
PERMANENT SUBCOMMITTEE ON INVESTIGATIONS,
OF THE COMMITTEE ON GOVERNMENTAL AFFAIRS,
Washington, DC.

The Subcommittee met, pursuant to notice, at 9:30 a.m., in room SD–342, Dirksen Senate Office Building, Hon. Susan Collins, Chairman of the Subcommittee, presiding.

Present: Senators Collins, Levin, and Durbin.

Staff Present: Christopher A. Ford, Chief Counsel and Staff Director; Mary D. Robertson, Chief Clerk; Claire Barnard, Investigator; Eileen M. Fisher, Investigator; Barbara Cohoon, Staff Assistant; Linda Gustitus, Democratic Chief Counsel and Staff Director; Laura Stuber, Democratic Counsel to the Minority; Jennett Rona (Senator Lieberman); Anne Marie Murphy and Elissa Levin (Senator Durbin).

OPENING STATEMENT OF SENATOR COLLINS

Senator COLLINS. The Subcommittee will come to order.

Good morning. Today, the Permanent Subcommittee on Investigations is holding an oversight hearing to examine the practices of the tissue industry and the adequacy of the regulatory framework that governs this industry. This hearing will also look at procedures for obtaining the informed consent of families who contemplate the donation of a loved one's tissue. Senator Richard Durbin of Illinois was the first to recommend that the Subcommittee investigate these important issues.

While most people are familiar with the concept of organ donation, tissue donation is not very well understood by most Americans. Yet the tissue industry is very diverse and growing rapidly. The recovery and medical use of tissue, including skin, bone, cartilage, tendons, ligaments, and heart valves, are increasingly common and can play an essential role in improving the quality of recipients' lives.

Tissue donation is also on the rise. In 1994, an estimated 6,000 individuals donated tissue. By 1999, however, this figure had increased more than three-fold to approximately 20,000. Donors now make possible as many as 750,000 tissue transplants every year in the United States.

Nevertheless, the industry that carries out these tasks has received little public scrutiny. The organizations that make up the tissue industry are collectively referred to as tissue banks. Some

are engaged in tissue recovery, while others process, store, and distribute human tissue. Some tissue banks are nonprofits, while others are for-profit companies.

Unlike organ transplants, human tissue is not usually transplanted "as is" from the donor's body into that of the recipient. Rather, donated tissue frequently undergoes considerable processing before it can be used. Bone from a donor's femur, for example, may be completely reshaped into a component designed to give support to a recipient's spine. Technology that greatly reduces the risk of rejection now allows surgeons to use actual bone in their patients rather than metal or other synthetic substances. In addition, donated tissue, once it is reshaped, can frequently be stored for an extended period of time, unlike organs, which must be transplanted into the recipient's body within hours of their recovery.

Tissue donation can improve the lives of many Americans. Just one donor, in fact, can help a large number of people in various ways. Skin donations, for instance, can be used to help heal burn victims or aid in reconstructive surgical procedures. Ligaments and tendons can be used to repair worn-out knees. Bone donations can be used in hip replacements or spinal surgery, enabling recipients to regain mobility. Donated arteries and veins can restore circulation, and heart valves can be transplanted to save lives.

With the phenomenal growth and the new uses for tissue transplants have come some problems. Just over a year ago, the *Orange County Register* ran a series of articles on the tissue industry.[1] Several of these articles brought to light incidents in which tissue obtained from unsuitable donors entered the American tissue supply, raising questions about the adequacy of Federal regulation. Other concerns have been raised about whether the practices of some tissue banks are sufficient to reduce the danger of spreading such illnesses as the human variant of "mad cow disease."

Because communicable diseases such as HIV and hepatitis, among others, can also be transmitted through tissues, it is vital that tissues be tested effectively and that potential donors be properly screened for suitability. It is equally important to ensure that persons and organizations involved in the tissue industry follow good tissue handling and processing practices in order to prevent contamination, and that the industry employ sound tracking procedures so that if a problem develops, all of the affected tissue recipients can be promptly notified.

Toward this end, the Federal Food and Drug Administration has proposed new rules that would extend the FDA's oversight role in the areas of donor screening, tissue testing, and good tissue practices.

The FDA's current rules focus on screening potential donors for suitability, testing tissue, and keeping proper records detailing the screening process. The FDA verifies such records through periodic inspections of tissue banks. In addition, the FDA has begun to implement a new rule requiring the registration of all tissue banks. Although the FDA has inspected only 118 tissue banks since 1993, we have recently learned that at least 350 tissue banks of various types have now registered with the FDA. These statistics suggest

[1] See Exhibit No. 11.a. which appears in the Appendix on page 189.

that many tissue banks may have been operating with little or no Federal oversight.

The tissue bank industry would not exist without the generous individuals who decide to donate tissue from the bodies of their loved ones. Of particular concern to me, therefore, is whether or not accurate and appropriate information is provided to the families of potential donors during what is always a very difficult time.

Only with adequate information can families make the right choice for them. Potential donor families want to be assured that their loved ones' tissues will be used to help others. They also expect that their loved ones' bodies will be respected throughout the tissue recovery process and that the tissue will be treated with the dignity and respect reflecting the generous gift that it is.

The process by which tissue banks obtain consent, unfortunately, has not always worked well. For example, a tissue recovery technician in Arizona removed a deceased donor's leg bone without obtaining consent and then falsified the records to cover it up. While this may be an extreme case, there are other troubling examples of inadequate information being provided to donor families.

As a lucrative tissue market has developed with medical breakthroughs making possible new ways to use tissue, competition for tissue has increased dramatically. By some accounts, a single donor can yield more than $200,000 in revenue to tissue banks. Tissue banks make this money not by selling human tissue, which is illegal, but by charging processing fees to the recipients of this material. Some tissue banks have charged others with making misrepresentations and with concealing information from potential donor families.

In response to these concerns about safety, oversight, and consent, last year, my Subcommittee colleague, Senator Durbin, and I asked Health and Human Services Secretary Donna Shalala to undertake a review of the tissue industry. Today, we will hear from the HHS Office of Inspector General about the results of that investigation.

This morning's hearing will examine many complex issues related to the tissue bank industry and to the adequacy of current and proposed regulatory oversight. We will hear from representatives of the FDA and a private accreditation organization working to ensure the safety of our tissue supply. We will also hear from experts who have firsthand knowledge of tissue banks and their operations. Finally, we will discuss ways to improve the tissue bank industry so that tissue recipients can have confidence that the tissue supply is safe and donor families can be assured that their concerns are respected.

I look forward to the testimony of all of our witnesses today and to learning more about this very important issue.

I would now like to recognize my colleague, Senator Levin, for any opening remarks that he might have.

OPENING STATEMENT OF SENATOR LEVIN

Senator LEVIN. Madam Chairman, thank you. Today's hearing will address a sensitive and important subject: Human tissue banking and the regulation, or the lack of regulation, of the tissue bank industry.

First, I want to thank Chairman Collins and Senator Durbin for their leadership in this area. We are here today because of their initiative and I think the Nation is in their debt because of it.

Human tissue is an important resource for medical treatment. It is used, for example, for reconstructive surgery, cancer care, cornea transplants, burn treatment, and heart valve replacement. Recent strides in medical technology have expanded the use and value of human tissue, and as the demand for human tissue increases, we must ensure that appropriate safeguards are in place for humane and safe handling.

Today's hearing will address some of the problems that have arisen in the tissue bank industry, which has been subject to only limited regulation. The lack of regulation is surprising to me, since organ donation is significantly regulated and since both organ donation and tissue banks involve the handling of human bodies.

Moreover, unlike entities involved in organ donation, which are non-profit, tissue bank recoverers use for-profit tissue processing companies to process the human tissue. There are reports that some of the non-profit tissue banks may be receiving money from the for-profit processing companies in order to get exclusive rights to the tissue from a particular tissue bank.

The last thing we want is a bidding war for human tissue. Apparently, the processing of the tissue and the development of the technology for the processing of the tissue requires for-profit participation, or at least it has done so up to now, and the result is a tension between the concerns about the appropriate treatment of human tissue and the for-profit incentives of the companies involved. To date, the FDA has not directly addressed this potential problem.

A number of other disturbing stories involving tissue banks have been reported in the press recently. One witness testifying today, the medical examiner for Lake County, Florida, said she cut ties to a non-profit tissue bank with ties to a for-profit company in Florida because she was disturbed by the financial issues and the way the bank's technicians treated donors' bodies.

Concerns have been raised over the possible transmission of communicable diseases through tissue banks. Some news reports have indicated that human tissue with CJD, or what we call "mad cow disease," imported into this country from Germany, was transplanted into U.S. patients in the early 1990's.

In another instance, after a 19-year-old Arizona woman died in a car crash, the family agreed to donate body parts to a tissue bank but expressly refused to authorize bone removal. The tissue bank admitted in court records to altering documents, making it appear as if consent to take bone from the woman had been given. The bones were returned after a 2-year legal fight, and her father said the following: "Instead of having some closure after her death, it just became an unending saga. It was like she was dying over and over again."

The Los Angeles County Coroner's Office was found to be giving away or selling hundreds of organs and tissue from accident and homicide victims. The body parts were sent to researchers without ever seeking the consent of the families. As a result, in September 2000, California enacted legislation which bans county coroners

from giving researchers body parts from accident and homicide victims without family permission.

The FDA has reacted by proposing two new rules governing tissue banks, one which mandates increased disease screening and testing for tissue donors, and one which requires that tissue banks follow a good tissue practice standard. The FDA also finalized a rule in January of this year which requires the registration of all tissue banks. Prior to that registration rule, which was initially proposed in 1998 and was not finalized until this year, we had no idea how many tissue banks existed. I am hopeful that the FDA will expedite the two proposed rules so that it will not take as long as the registration rule, and today one of the questions we are going to ask is: Why has it taken the FDA so long?

My own State of Michigan appears to have a good system in place that could serve as a model for the rest of the Nation. Instead of competing tissue banks in our State, Michigan has one federally-designated Organ Procurement Organization, the Gift of Life Agency, which also recovers tissue. The non-profit Gift of Life Agency is affiliated with the non-profit Michigan Eye Bank, which recovers only eye tissue, so that these entities work together and do not compete with each other. In many States, there are numerous tissue banks which end up competing for human tissue, and it seems to me that this is a source of a problem. I think we should be looking at ways to encourage States to move towards the Michigan model.

One thing this hearing should not do, and must not do, is discourage people in any way from becoming tissue and organ donors. Organ and tissue donors provide the most important gift in the world to their recipients—the Gift of Life. A half-million people or more each year rely on tissue transplants. A few unscrupulous tissue bank businesses should not be allowed to harm a life-giving and a life-improving medical therapy. Today's hearing can show us how appropriate regulation can inspire confidence in the public, and hopefully inspire more people to offer life-preserving tissue and organs after their own deaths.

Again, I want to commend our Chairman and also Senator Durbin, whose leadership in this area has brought us to this point today and hopefully will lead to some additional advances in this important area.

Senator COLLINS. Thank you, Senator Levin.

I am now pleased to call upon Senator Durbin. As I mentioned in my opening statement, it is in large measure through his interest in the oversight of the tissue industry that the Subcommittee has begun its investigation in this area, so Senator Durbin, I am pleased you can join us.

OPENING STATEMENT OF SENATOR DURBIN

Senator DURBIN. Thank you very much. I want to thank Senator Collins. When I raised this issue with her, she was immediately interested in it and looked into it and shared my belief that this is something that we need to address in Washington. Her staff has done an excellent job putting together the hearing on this topic today.

I am concerned about the safety and the ethical oversight of the tissue donation system. It should be of interest to every single one of us.

Last year, 6,000 people died while waiting for an organ donation. There are over 75,000 on a waiting list for possible life-saving organ transplants. While 6,000 people donated organs, another 20,000 tissue donations were obtained. The public and donor families do not usually differentiate between the two. They expect that both donations will serve a medical or a medical research purpose and will enhance, or in the case of organ donations, possibly even save, a recipient's life.

My attention to this issue was called by a series in the *Chicago Tribune,* and then I read subsequent to that a series in the *Orange County Register.* In each case, they outlined some very serious policy concerns. I am going to submit my entire statement for the record, but I want to make this point as clear as I can.

A decade ago, the tissue industry's revenues were $20 million a year. By 2003, they are expected to reach $1 billion. I think we have a special responsibility in Washington, when it comes to setting down rules, to make sure that there are no abuses in this industry. I cannot even express strongly enough my concern if we undermine the integrity of organ and tissue donation by not accepting our Federal responsibility. People need to understand that when they are making these selfless gifts, that they are not doing it for a commercial purpose unless they expressly make that decision, and to do otherwise is, I am afraid, to discourage exactly what we should encourage, namely organ donations. I hope that the results of these hearings and some of the things that are brought forward will help us reach some changes in policy.

I was happy last year when this first came up to call in then-Secretary Shalala and she agreed to take a look at this issue as quickly as possible. It was a bipartisan request. This should be a bipartisan issue. I do not think there is a Democratic or Republican approach to this. Any single one of us, Independents alike, could end up needing a tissue or organ donation and we have to make certain that we have policies that serve this country.

I want to thank again the Chairman of this Subcommittee for her response to this issue. It is going to be something, I think, of great value in years to come. Thank you.

Senator COLLINS. Thank you, Senator Durbin.

[The prepared opening statement of Senator Durbin follows:]

PREPARED OPENING STATEMENT OF SENATOR DURBIN

I want to start by thanking my colleague, Senator Collins and her staff for putting together a hearing on this topic today. Both the safety and ethical oversight of the tissue donation system is clearly of great interest to many including myself. It is essential that the public have faith in the integrity of this system.

Last year more than 6,000 people died while waiting for an organ donation and there are more than 75,000 on a waiting list for a possibly life-saving organ transplant. While 6,000 people donated organs, another 20,000 tissue donations were obtained. The public and donor families do not generally differentiate between organ and tissue donation. They expect that both donations will serve a medical or medical research purpose and will enhance, or in the case of organ donations, possibly save a recipient's life.

My interest in the tissue industry originally stemmed from some news articles I read last year in the *Chicago Tribune.* The articles show the ever increasing com-

mercialization of the tissue industry. What for donor families is an altruistic "Gift of Life" has become for others a multimillion dollar business.

A decade ago, the tissue industry's revenues were $20 million a year. By 2003, they are expected to reach $1 billion. While it is illegal under Federal law to buy or sell either an organ or tissue for transplantation and it is illegal to buy or sell fetal tissue for any purpose, a tissue bank or processor may make a profit on ancillary services such as transportation, processing, etc. The *Chicago Tribune* and *The Orange County Register* reported that the tissue from one body could yield up to $230,000 in revenue for a company.

Because of the profitability of tissue, a fierce competition has broken out between companies seeking access to donated tissue. Some of the methods used to, in essence, steer donations to a given tissue company, I believe, make many of us very uneasy. For instance, according to the *Chicago Tribune,* the head of the University of Wisconsin Hospitals, Robert Hoffmann, was found to have been paid by a company called Allograft, a tissue bank that Hoffmann helped create and that received donated tissue from the university hospital. In 1996, Hoffmann arranged to have the tissue harvested from hospital patients delivered to the American Red Cross. In return, the Red Cross paid him personally for those services. Two years later, several Red Cross employees, aided by Hoffmann, set up their own non-profit tissue bank, Allograft Resources. The hospital's donated tissue was then sent to Allograft rather than the Red Cross and Hoffmann continued to receive a fee. When this information was made public, Hoffmann eventually agreed to pay his $86,000 in fees to the university for "organ donation education."

Other examples reported in the media tell of medical examiners receiving large sums of money in exchange for directing donations to a particular tissue business. For example, a second *Chicago Tribune* article reported that a Texas medical examiner was receiving $47,000 a year from tissue banks and his assistants also received $50 from the tissue bank each time they obtained a family's consent to harvest tissue. These payments basically are like "bounty payments."

While donor families believe, in general, that the donations will go to medically necessary transplantation, the profitability of cosmetic uses is often higher and so a significant quantity of tissue is instead being processed for cosmetic uses such as lip enhancement, penile implants and face lifts. Donor families do not generally receive an opportunity to direct the donation to medically necessary uses including reconstructive uses, rather than cosmetic uses.

At the same time, both the *Chicago Tribune* and *The Orange County Register* suggest that there have been shortages of skin for burn victims. In fact, the American Association of Tissue Banks and the American Burn Association surveyed their members involved in burn repair and found that shortages do exist, with surgeons sometimes having to delay surgery or to modify it to accommodate a smaller tissue sample.

While we have, as a Nation, an allocation system for organs based on medical necessity, we have no similar system for tissue distribution.

Likewise, we require that all organs be procured by non-profit Organ Procurement Organizations and we also require them to have representatives of transplant centers, voluntary health associations, and the general public on their board of directors. No such requirement exists for tissue procurers.

As the Inspector General will, I believe, talk about in his testimony, tissue donation is often solicited by phone and the requesters tend to be far less trained than those used by Organ Procurement Organizations. Donor families often do not receive much information about the uses that the donation will be put to, nor do they receive information about the companies who will be getting the tissue and the financial arrangements of those companies. This lack of transparency, can undermine the public trust.

Donated tissue can provide a fantastic therapeutic value to patients, whether it be for repairing burns, or for reconstructing those who have been injured or who have congenital problems. Many in the industry work extremely hard to ensure that they meet the highest standards. The American Association for Tissue Banks has a voluntary accreditation process that sets a high standard and it has also developed in collaboration with the Eye Bank Association of America and the Association of Organ Procurement Organizations, a model for appropriate informed consent.

Unfortunately, only 40 percent of the tissue banks or processors are members of AATB. Many of the largest for-profit companies choose not to be members.

In fact, FDA does not even know who all the companies are that are involved with tissue processing. FDA clearly cannot be inspecting those whose existence they are unaware of. When FDA has done inspections, in some instances, it has found very serious deficiencies in the areas of screening for diseases such as HIV and Hepatitis.

It seems likely that those who are not inspected may well also have similar deficiencies.

All of these problems led me to invite the previous Secretary of HHS to meet with me and several other Senators last year. Secretary Shalala met with Senators Wyden, Santorum, and me. After that meeting, the Secretary directed the Inspector General to perform the two investigations that the IG is discussing today.

Those meetings also led the Secretary to direct the FDA to speed up the implementation of its new regulations. One regulation requires all tissue companies to register with the FDA and to list the types of products that they process. This will allow the FDA finally to be in a position to inspect all facilities with some regularity. The other rules that are in varying degrees of implementation will require increased scrutiny regarding donor suitability and, for the first time, "good manufacturing practices."

All of these new rules cost money. Currently, the FDA has been using money from other programs to pay for these new rules. It seems unwise to be robbing one good program to pay for another. Therefore, I asked FDA in January to provide me with budget details regarding how much money will be needed to implement these new rules. It is now late May and I still have not received an answer. It is difficult to help the agency get the resources it needs if it does not respond in a timely manner.

I agree with the Inspector General's recommendations that FDA needs to move forward more aggressively to inspect all facilities and to establish a regular inspection process.

I also have been concerned with the issue of prion diseases and have been working in the food safety area to minimize the likelihood of transmission of "mad cow disease" and the human counterpart, vCJD.

Similar issues arise in the tissue field. Twelve years ago, Japan had a terrible problem with the transmission of CJD due to the mixing or pooling of tissue samples. This led AATB to prohibit pooling or batching for its members. Given that there is no known effective manner to deactivate prions, I am glad to see that the new FDA rules prohibit pooling or batching. Clearly mixing tissue samples from multiple donors significantly increases the risk of disease transmission.

Since tissue transplantation is generally not done in a medically urgent setting and is life-enhancing rather than life-saving, it is very important that it not put a patient at additional risk for a horrible and ultimately lethal disease such as CJD.

The only reason to batch-process tissue is to save money by using economies of scale. There is no therapeutic value to batch processing.

I hope the FDA will remain firmly opposed to pooling or batch-processing and will not get pressured by any company looking at its bottom line into sacrificing human health and safety.

The issues involved in this area are very complex but it is now abundantly clear that business as usual is undermining the public's trust in the donation system. We need to move forward quickly to develop solutions to restore that trust.

This hearing should provide a good start for the Subcommittee to examine the issue and get input from those familiar with the tissue industry, so that we can make improvements in the upcoming weeks.

I want to thank again, my colleague, Senator Collins, for arranging this hearing and starting this very important dialogue. Our offices are currently working on legislation to encourage organ donation and I hope that we will also work together to craft solutions to improve the tissue system.

Senator COLLINS. I would like to inform all of our witnesses that we will be using a timing system today. Your complete written statements will be placed in the hearing record. You will be given 10 minutes for your initial presentation and there will be a light system. When the light turns to orange, you have only 1 minute to sum up.

I would now like to call upon our first witness this morning, who is George Grob. He serves as the Deputy Inspector General for Evaluation and Inspections of the Office of Inspector General within the Department of Health and Human Services. Mr. Grob has been with the Office of Inspector General since 1988 and he will testify regarding the findings in the Inspector General's reports on the tissue industry, which are entitled, "Oversight of Tissue Bank-

ing and Informed Consent in Tissue Donation."[1] We are very pleased to have you with us this morning. We look forward to your testimony.

Pursuant to Rule 6, all witnesses who testify are required to be sworn in, so at this time, I would ask that you stand to take the oath.

Do you swear that the testimony you are about to give to the Subcommittee will be the truth, the whole truth, and nothing but the truth, so help you, God?

Mr. GROB. I do.

Senator COLLINS. Thank you.

TESTIMONY OF GEORGE F. GROB,[2] DEPUTY INSPECTOR GENERAL FOR EVALUATION AND INSPECTIONS, OFFICE OF THE INSPECTOR GENERAL, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, WASHINGTON, DC

Mr. GROB. Good morning, Madam Chairman and Senators Levin and Durbin. It is a pleasure to be here, and I must begin my remarks by saying that the opening remarks of all the Members have covered all the ground that I was going to speak to today in a very thorough way, so if you do not mind, I will repeat to emphasize some of the points that you made and keep my remarks short, hoping that we can cover more ground in the questions and answers, which then may be more penetrating.

Human tissue in the form of skin, bone, heart valves, eyes, cells, and the like, is an important source of treatment, benefitting thousands of Americans every year. For example, donated skin can save the lives of burn victims. Donated bone can replace cancerous bone and be used in knee and hip replacements and for spinal surgery. As noted by the Chairman, there has been a very rapid growth in this industry, which is fortunate. The availability of these tissues is increasing year by year.

But there are other changes underway, as well. Processing has become more sophisticated and tissue is being put to new uses. At the same time, the field is becoming more entrepreneurial. For-profit firms are increasingly entering an arena that was once dominated by nonprofit agencies. I wish to emphasize that I do not intend this last remark to be taken negatively. In fact, this may account for and contribute positively to the development of new products and treatments.

However, as promising as these new trends are, the standards of practice have not kept pace with the growth and development of the industry. As a result, some donor families have been confused and disappointed by the treatment and disposition of the remains of their loved ones, and questions have been raised about the quality, safety, and supply of human tissue.

When these issues emerged last year, Secretary Shalala asked the Office of Inspector General to examine the oversight mechanisms and the processes whereby donors and their families are approached for donation. We issued two reports in January, and I believe you all have copies. At the time of our study, the fall of the

[1] See Exhibits No. 9 and 10 which appear in the Appendix on pages 135 and 166 respectively.
[2] The prepared statement of Mr. Grob appears in the Appendix on page 49.

year 2000, we found shortcomings in both aspects of the service sector.

First, with respect to oversight, the Food and Drug Administration focuses on preventing the transmission of communicable diseases by requiring donor screening and tissue testing. We found that the FDA had designed and was implementing an oversight system that was fundamentally sound. However, due to resource constraints, it was unable to sustain its program. Since 1993, it had inspected 118 banks. During this period, 68 had only been inspected once instead of every 2 years, and we found another 36 that had never been inspected. Late-breaking developments show us that there were perhaps twice as many who were totally unknown, and, in fact, we found that at that time, the number and location of all tissue banks was unknown.

Also because of resource limitations, several key regulations which were under development had not been finalized.

The American Association of Tissue Banks conducts a voluntary accreditation program. In addition to screening and testing, it addresses operational practices and organizational aspects of tissue banking, including safety, equipment testing, labeling, and quality assurance programs. However, at the time of our study, it had accredited only 58 tissue banks. Another 90 that we knew of at that time were not accredited.

Florida and New York are the only two States that inspect tissue banks. Their requirements address a broad range of practices and also require that banks report adverse incidents. However, they only inspect those banks that do business within their jurisdiction.

With respect to donor concerns, the expectations and altruistic motives of donors and their families are the foundation of tissue banking. There would be no tissue transplantation without them. Their concerns, then, are vitally important. Their assumptions and desires are that donated tissue will enhance the lives of others; the donor will be respected throughout the process, from recovery to use; the gift will be recognized as coming from donated human tissue; family emotional needs will be respected; the tissue banking industry can be trusted and will act as stewards of the gift.

The reality of tissue banking raises some underlying tensions with regard to these assumptions. These arise from the commercialization of the service sector, the appearance of tissue being treated as a commodity, and the use of tissue for cosmetic purposes.

The key to meeting the donors' concerns is information and their informed consent, but the circumstances during which the request is made present fundamental obstacles to this. It is the generous gift of these donors that makes it possible, but it occurs within hours of the death of a loved one.

We found shortcomings in the oversight of requesters and in the written information provided to families. More importantly, at the time of our study, there were no standards or written principles governing the manner in which the request is made and informed consent obtained. Also, at the beginning of our study, there was no knowledge of the adequacy of supply of tissues, particularly of human skin. Subsequently and during the course of our study, we

learned that the supply of skin for burn victims was somewhat tight.

Our reports include recommendations to address the shortcomings that we found. During our study and since then, progress was made in addressing them. FDA is now beginning to inspect all known tissue banks. The regulation requiring the registration of banks and their products was issued in January, and since then, identification of a large number of tissue banks previously unknown has occurred. A draft regulation on good tissue handling practices was issued for comment, and comments on a draft regulation on donor suitability and tissue testing are now under review.

Both industry groups and donor family groups have issued statements of principles to govern the informed consent process. The American Association of Tissue Banks and the American Burn Association have conducted surveys to determine the adequacy of the supply of skin.

In short, progress is being made, but gaps remain. The tissue banking and transplantation industry has moved from its infancy to its adolescence. It is full of promise, but it is experiencing some significant growing pains. I hope our studies will be helpful in getting it through the stage, and I will be happy to answer your questions.

Senator COLLINS. Thank you very much, Mr. Grob.

In one of your reports, you noted that at least 36 tissue banks had never been inspected by the FDA, is that correct?

Mr. GROB. That is right.

Senator COLLINS. Now, what universe of banks were you dealing with at that point? How many, about 118 or so?

Mr. GROB. About 150.

Senator COLLINS. A hundred-and-fifty?

Mr. GROB. Yes.

Senator COLLINS. We have recently learned that more than 350 tissue banks have registered with the FDA pursuant to the new regulation.

Mr. GROB. Yes.

Senator COLLINS. So what does that suggest when you were looking at 150 tissue banks, which presumably were all the tissue banks that you were able to locate by using various sources, like the FDA, the two States that regulate, is that correct?

Mr. GROB. Yes, and a few other States that license them, wherever we could find it.

Senator COLLINS. And you came up with a universe of 150, about.

Mr. GROB. Or so, yes.

Senator COLLINS. And yet out of those, you found that there were at least 36 that had never been inspected. Now we find out that there are something like 350——

Mr. GROB. Yes.

Senator COLLINS [continuing]. Tissue banks. Does that not suggest that there are literally scores of tissue banks that have been operating with no Federal oversight whatsoever?

Mr. GROB. Or State oversight, or any oversight by the industry accreditation group. And the significance of that, if I could point out, is that when the Food and Drug Administration conducts its

inspections, and when the American Association of Tissue Banks conducts its accreditation reviews, they do find problems and some of them are significant. So we have to assume that if they find problems in the banks that they inspect, then there are probably those same problems, if not more of them, in the banks that have never been inspected.

Senator COLLINS. I think that is an excellent point, and that is what troubles me, as well, is that it appears that there are scores of tissue banks that have been operating with no oversight whatsoever, not by the FDA, not by the States, and not by the private accreditation group, and yet in those tissue banks that were known to FDA, there were still problems. It seems to me it is more likely that there will be even greater problems in the ones that no one was really aware of or watching over. Could you tell us about some of the inspections that the FDA has conducted and what they revealed?

Mr. GROB. Where they found problems—they found problems in about half of the banks that they reviewed, and some of these were serious problems that required official action. Examples of that might have been cases where contamination had been noted, a bank that might not have been able to successfully recall tissue that needed to be recalled. There might have been some problems where they could not track the tissue back to the source, which, of course, is necessary to ensure that it is safe. And then a couple of cases where we had what you might call repeated testing to come up with the right result. In other words, if the testing is positive——

Senator COLLINS. Can you explain that?

Mr. GROB. The testing might be positive for some contamination. What you might then do is try to keep testing it until the result is negative, and then at that——

Senator COLLINS. Let me stop you here to make sure I understand. This case, this repeating testing, where the first test of the tissue indicates that there is a problem.

Mr. GROB. Yes.

Senator COLLINS. It is contaminated or there is some other disqualifying result that has occurred in the testing.

Mr. GROB. Exactly.

Senator COLLINS. So instead of that tissue being discarded and taken out of the tissue supply, are you telling us that what happens is the technician just repeats the test until they get the result that they want?

Mr. GROB. Yes, exactly.

Senator COLLINS. That strikes me as an extremely dangerous practice.

Mr. GROB. I would think so, yes.

Senator COLLINS. Could you tell us, also, were there cases of tissue banks that failed to assure sterility of the tissue and lacked operating procedures to prevent cross-contamination?

Mr. GROB. That is probably true. Now, the Food and Drug Administration's inspections are primarily related right now to the transmission to HIV and hepatitis, and their inspections then would look at such things as whether there are records that enable the tissue bank to be sure that the donor had been properly

screened, and then whether there had been proper testing for those diseases, and, of course, for the general handling of the tissues to prevent their further contamination in the tissue bank.

So some of those general things that they would have to look at would apply to other diseases, as well, but their look right now is limited only to those two. The good practices regulation, which has recently issued in draft form, would provide additional protection for a variety of ways the tissue is handled and the way the tissue bank is run and things of this nature.

So right now, the Food and Drug Administration's inspections are more limited. For example, they are more limited now than the kind of review that is done by the accreditation association or by the States of Florida and New York, which have a broader set of requirements. Now, the requirements of the Food and Drug Administration will catch up with those and probably surpass them in detail when their new regulation is issued in final.

Senator COLLINS. How extensive is the accreditation process by the American Association of Tissue Banks?

Mr. GROB. Well, at the time we did the study, I think it was 58 banks that were accredited out of what we now know to be more than 350 tissue banks.

Senator COLLINS. So while those 50 to 75, let us say, because I think it has gone up recently, banks may be held to higher standards——

Mr. GROB. Right.

Senator COLLINS [continuing]. Than even with the FDA standards——

Mr. GROB. Yes, right now.

Senator COLLINS [continuing]. There is still a vast universe of banks that are not accredited by the private organization, is that correct?

Mr. GROB. Yes. If we were doing our study today, the finding would have been that we found that FDA had inspected 118 banks but there were 350 total. I mean, the numbers would be very different, because at that time, the numbers were simply not known. The same thing is true for the accreditation. The accreditation is purely voluntary and there are lots of issues about that in the sense that you have to look to the motives of the banks to see if they have any motivation to become accredited.

Senator COLLINS. Should the Federal Government or State Governments be encouraging accreditation by this private organization?

Mr. GROB. It is my opinion that there should be an encouragement for accreditation by any suitable accreditor. The American Association of Tissue Banks certainly is doing that. Others could do it as well, or could be formed to do it.

But I do think it is important to point out the differences between the FDA review and the accreditation. While they currently do not overlap, they both serve important purposes. For example, the accreditation association cannot do things like force a recall, take action against someone who has not been performing properly, things of this nature. So it does not have that enforcement authority that the FDA has.

My own opinion is that some combination of the two is always better than just doing one, and to that extent, then I believe that it should be encouraged. Accreditation is used in many other health care sectors effectively, but I do not think it would be a substitute for the FDA inspection in this case.

Senator COLLINS. I agree with you. You found tissue banks that had been refused accreditation by the American Association of Tissue Banks, is that correct?

Mr. GROB. That is correct. Right.

Senator COLLINS. Did anything happen to those banks that were turned down? Was there any sort of referral to FDA? Does FDA place those banks that were denied accreditation under more scrutiny?

Mr. GROB. No, I do not think so. I think that—although you might want to check with your FDA witness on that particular point. But as a general rule, the answer to your question is that those banks that are not accredited are free to operate without having to follow any of the rules that they would have had to follow had they been accredited.

Senator COLLINS. So there are no restrictions or they are allowed to engage in the same kind of practices as those that successfully sought and obtained accreditation.

Mr. GROB. Right, only if they were violative of the FDA communicable disease standards.

Senator COLLINS. In your judgment, to ensure public safety, how often should the FDA be inspecting a tissue bank?

Mr. GROB. I would leave that up to FDA. Now, they have told us and in various places they have suggested every 2 years, which is why I referred to that. Other inspection programs or accreditation programs, if you look at hospitals and home health agencies and nursing homes, range from 1 to 3 years. So 2 years certainly seems to be well within the range of practice in the health industry.

Senator COLLINS. And of the inspections that you found that FDA had done, I think it was 188 inspections of 118 tissue banks——

Mr. GROB. Yes.

Senator COLLINS [continuing]. What kind of time cycle were those banks on? Were they being inspected once every 2 years, or did it vary greatly?

Mr. GROB. It varied greatly, and as I said, only 68 had ever been inspected more than once, and that was data that went back to 1993.

Senator COLLINS. Mr. Grob, is there a difference between the informed consent procedures for organ donations versus tissue donations?

Mr. GROB. I think in principle, they are very similar, but in practice, there are some significant differences. For organ donation, all the requesting must be done by the organ procurement organizations who do this constantly or by a hospital or other personnel whom they train, whereas in the tissue business, some OPOs may be involved sometime, but in many cases, and probably more commonly, the requesting would be done by representatives of the tissue banking industry or different groups that work for them for

this purpose. So the requesting that is done by different groups and the level of training, therefore, would be very, very different and not as consistent in the tissue banking industry at this time.

Another difference, I think that is central here, has to do with the circumstances. Generally speaking, for an organ transplant, the patient would have had a close connection to the hospital right before the time of the consent, because, generally speaking, we are talking about a patient who is brain dead and so they are under the close supervision of the hospital. And so as a result of that, the organ procurement organization may have had communication with the family for several days or even a longer period of time before the actual consent is reached, whereas for the tissue patient, that is not limited to brain death. It could be a car accident or something and the family must be approached within hours of the death.

I must say that the tissue banking has quite a challenge in this respect, to balance the desire of the family for some privacy or information and the circumstances. Often they, for example, will make the request by telephone instead of at the hospital, and that may be out of the respect for the family, who may want to get back to its home setting before they are asked.

So there is not an easy answer to that, but because it has to occur within hours of the death, it makes it difficult, and that also causes some of the difference.

Senator COLLINS. Thank you. My time has expired. Senator Levin.

Senator LEVIN. Thank you, Madam Chairman.

The National Organ Transplant Act forbids the selling of organs and tissues. However, the Act does permit a reasonable payment which is associated with the removal, transportation, implantation, processing, preservation, quality control, and storage.

Mr. GROB. Yes.

Senator LEVIN. We have heard stories, however, that there have been grants that have been made to some of the tissue banks that do the recovering of the tissue, that some of the profit-making processors that seek that tissue for processing have made some form of grant to some of the tissue banks that have done the recovering, which are usually not-for-profit in theory. Have you also run into those kind of stories?

Mr. GROB. This issue of the profit making and the place at which there is a transaction of anything of worth was one of the issues that we struggled with more than any other, and I think I would have to report to you right now that the struggle continues, because I do not think that there is a consensus on exactly what should be done with regard to trying to govern in any way the transactions that occur during this period. So if I may, in this case, what I would prefer to do would just be to share with you some thoughts or ideas that we have talked about among ourselves and that might shed some light on this.

Certainly, the intention of that Act was to prevent any individual from offering his or her tissue for sale or for anyone to approach an individual and offer to buy it from them, and in our discussions, there has been almost universal agreement on that point. What happens after that, though, is that the tissue needs to be handled

in various ways, and I think that as the Act is written, certainly allows, as you said, for the reasonable payment of almost anything that occurs after that point in the sense that there is a storage or a handling or a transportation that occurs at almost every level there.

So really, in terms of the law, the issue turns to the question of what is reasonable. How much is a reasonable amount? In talking to donors, we found that they were not upset, generally speaking, many of them, with the notion that a profit could be made in those middle transactions or that money should be paid, but they certainly did not want excessive profiteering. But there was no way for any of us to get a handle on exactly what is excessive. One could look at the profits that a company makes, but big companies make a lot more profit than small ones do, for example, and it is very difficult to second-guess the cost that a company incurs because of all the overhead that goes into the company's operation.

We could think of no practical way to track that. We do not even know where the tissue goes right now. There is not even a way to sort out and track what happens to the tissue. And with the modern tissue banking industry, there are so many new processes coming into play all the time that it is difficult to even define the stages through which the tissue is going. And if one were to try to track it and consider what the price for that would be, any system you put into effect would probably be inaccurate within a few months of your doing it because of the changes that are occurring in the industry. And furthermore, there has been a long tradition of not establishing price limits for most products in the United States, including in the health care industry.

So we were unable to come up with any practical way to deal with what I think is a very fundamental concern, and I think Senator Collins referred to this in her opening remarks, about the expectation that the tissue would not be used for commercialization, that it would be donated for the benefit of someone else, a very difficult thing.

As far as we were able to take it in our own thinking, the key to it was information. Now, we think that the donors can make up their own minds about what to do, or at least could do that better, if they had more information than they have now, and we believe that information should occur at two times, once when the donation is being requested. The donor at that time may not be interested in those details, but there certainly is nothing wrong with providing written information that could be considered later, or perhaps in some cases it could be considered somewhat in advance if death is imminent.

But above and beyond that, a more general form of information to inform the public about the donation process in general and perhaps about the companies involved in particular would be useful, perhaps an annual or periodic statement by these companies indicating their sources of revenue, the uses to which they put the tissue, things of this nature that could be out there, so that as people become more informed about tissue banking and tissue donation, they could look to those documents, much as they look to the annual statements of nonprofit agencies who produce an annual statement of what happens to their funds, and then they can decide

whether they want to donate to a particular agency or not. Perhaps a similar thing could be beneficial in this industry, as well.

So I am sharing with you a long journey of trying to come to grips with that one.

Senator LEVIN. Well, there is another possibility, and it is what is in place in my home State of Michigan, which is that we have one organ procurement organization, one organ and tissue procurement organization——

Mr. GROB. Yes.

Senator LEVIN [continuing]. So that you do not have competition among different organizations for the tissue.

Mr. GROB. Yes.

Senator LEVIN. And it is that competition which then can precipitate grants, however you want to call them, monies going to various nonprofit recovering entities in order to get the tissue into the hands of the people who are making profit here.

Now, one thing we could do would be to modify the Federal law, which is to say that there is one organ procurement organization responsible for organ and tissue donation activities per region. Right now, we do that with organs, but not with tissue. Why not do that with tissue and take away some of that competitive activity which exists which could precipitate the commercialization of tissue donation, which is what we want to avoid?

Mr. GROB. I think there are lots of possibilities. If I may, I would like to speak as an analyst, so I will give you what I regard as the pros and cons of those kinds of arrangements. This is a difficult policy choice to make.

I think I can preface it by saying that, recently, organ procurement organizations have become more visible and active in tissue requesting and recovery than they were in the past. One reason for that seems to be that a couple of years ago, a law was passed that the hospitals must inform the organ procurement organizations of the death of patients in the hospital. The idea was so that they would be more alert to the possibility of organ donation. But what happened was as a result of that was that the organ procurement organizations became more alert for tissue recovery, as well, and as a result, their role in tissue recovery has greatly increased. And so that certainly is very much of a possibility.

However, it still is not the case that the organ procurement organizations are the ones who do it all, and if one were to switch over to that right now, then what would happen would be those tissue banks that have been involved, including many who have been involved for many years and are actually pretty good at it, then they might lose ground and then we may lose a resource in there for the tissue.

Now, another thing I will just have to say is that different people will have different opinions as to the usefulness of the competition. I think in an ordinary business world, the competition is always valuable. Now, when there are questions that come up about the allocation of important life-saving tissue, then those things can be set aside, as they are for organs.

Another difference, though, is this, that for organs, the gap between what is available and what is needed is very severe. The number of organs that are needed to save lives are several times

more that are needed than are available. As far as we can tell, with tissue, while there is probably a gap at times for skin, there certainly is not a gap of that magnitude as there is for organs. And furthermore, for other tissue types, there is not necessarily a gap. For example, for eyes, we are not aware of any particular gap. So the tissue industry is more diverse and the needs are different in terms of allocations here, if you will.

So, again, I think that the ideas you are presenting need to be on the table, as well as all kinds of other ideas. I do not think we see a clear shot to the goal line on this one.

Senator LEVIN. Your report does not get into pooling.

Mr. GROB. No, it does not.

Senator LEVIN. I am just wondering why not.

Mr. GROB. The pooling at that time was simply not one of the things that we were looking at as part of the general oversight of the industry. At the time that we did our report, there was no rule against pooling as such. The rule against pooling will occur when the new regulations are issued. Then it will certainly be a rule. Now, FDA has always looked at pooling, but it really was not on the table of the oversight system that we were looking at at the time. The States, like New York and Florida, have rules against pooling, and I believe that the American Association of Tissue Banking has, as well.

Senator LEVIN. You indicated a lack of resources, I believe, for the inspections.

Mr. GROB. Yes.

Senator LEVIN. Is that still true? Does the FDA have inadequate resources?

Mr. GROB. FDA has made it clear what their budget needs are for the inspection program that they design. Now, those numbers may be modified in light of the doubling of the number of known tissue banks that have come out of the recent registration of tissue banks. These budgets for this were recently proposed and I do not know the disposition of them. Any additional resources for this which FDA, I believe, says is in the order of $3 or $4 million a year for what they knew of at the time they made those budgets, were made in the current budget session, and I do not know what the disposition of that is in the current budget.

Senator LEVIN. We will find out later today. Thank you. Thank you, Madam Chairman.

Senator COLLINS. Senator Durbin.

Senator DURBIN. Thank you very much, Madam Chairman, and let me follow up on that question.

For a number of years, I have been keeping a close eye on the Food and Drug Administration. I cannot imagine how they can keep up with all of the responsibilities we send their way.

Mr. GROB. Exactly.

Senator DURBIN. An agency which spends roughly $1 billion a year is just being overburdened with all sorts of new responsibilities——

Mr. GROB. Yes.

Senator DURBIN [continuing]. All legitimate, as far as I am concerned——

Mr. GROB. Yes.

Senator DURBIN [continuing]. But certainly beyond their capability with current staffing.

Mr. GROB. Yes.

Senator DURBIN. We have to get honest about this. If we want the Food and Drug Administration to perform valuable oversight, they have to be given the resources. Otherwise, I do not think it is fair to hold them accountable for too few inspections if they do not even have the inspectors, and you certainly spell out in your report to us about the inadequacy of the inspection of these tissue banks, since 1993.

Mr. GROB. Yes.

Senator DURBIN. Let me ask you to comment on a couple of things, if you might. I want to get into the issue of informed consent in a moment, but first, an article in the *Chicago Tribune* last year[1] suggested that in San Antonio, Texas, the medical examiner's assistants were receiving $50 from a tissue bank each time they obtained a family's consent to harvest tissue. The same article also alleged that county supervisors took bids from tissue banks on the right to bodies collected by medical examiners. The winning bidder, South Texas Blood and Tissue Center, agreed to pay $180,000 annually. Do you think such payments are legal under our law that prohibits the sale of organ and tissue?

Mr. GROB. We have not considered the question you are asking, but we certainly can consider that. One of the things that happened during the course of our study was that we became more aware of the role of medical examiners, which was not on the table at the beginning of the study, but it was one of the things that we began to find out more and more about as the study progressed. So one of the things we have done is that we have decided that we will be conducting a study that examines the role of the medical examiners.

Senator DURBIN. But in terms of the payments, did you take, in the course of your survey, did you review the law as it relates to the sale of organs and tissues and whether or not you can receive compensation?

Mr. GROB. We did examine the law quite carefully when we began our study, and I had summarized earlier some of the complexities we had in trying to come to grips with that law and define exactly what is legal. Once the tissue leaves the donor family, in other words, there is no question that at the point where the donation is being made by the family, that there should be no transaction from the individual to offer a tissue or organ for sale or to be offered any money for donating either, but after that point, then the money can be legitimately used for almost any aspect of the handling of the tissue. But, I guess——

Senator DURBIN. I want to make sure it is clear, if I can.

Mr. GROB. It is only in exchange for the business.

Senator DURBIN. I want to make sure this is clear.

Mr. GROB. Yes.

Senator DURBIN. So that the family's decision to donate——

Mr. GROB. Is not affected——

Senator DURBIN [continuing]. Cannot be compensated.

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[1] See Exhibit No. 11.b. which appears in the Appendix on page 220.

Mr. GROB. Exactly.

Senator DURBIN. But beyond that, once the donation has been made——

Mr. GROB. Right.

Senator DURBIN [continuing]. There can be other intermediaries who start to put price tags on the tissue involved.

Mr. GROB. Exactly.

Senator DURBIN. Is that correct?

Mr. GROB. That is correct. The current law, basically, it actually has a list of what you can do more than that which you cannot, and that list, just superficially, would seem to cover almost all the products of tissue.

Now, an interesting question you are raising that I do not have any immediate answer for, and I would not want to venture one without consulting with others, is whether—say if the $50 were given, if that were covering a legitimate cost of the other agency, then the law would allow it.

Senator DURBIN. Yes.

Mr. GROB. But if it was simply an inducement for business, I do not think that that is one of the things that the law allows.

Senator DURBIN. Right. That is an important distinction.

Mr. GROB. Yes.

Senator DURBIN. Cost of transport and transportation, I think that is allowed.

Mr. GROB. Exactly.

Senator DURBIN. But it really does get to the heart of an important issue here, and that is if there is a feeling that somehow this selfless act of a family in donating tissues or organs will relate in some commercialization, I think it is going to inhibit a lot of people from even considering that possibility, and I think that we have to be very honest about that.

Now, you really address that from another angle, too, when you talk about the consent forms.

Mr. GROB. Yes.

Senator DURBIN. That is something that I think bears a little bit of scrutiny here, as well.

Mr. GROB. Yes.

Senator DURBIN. You were suggesting that the consent forms be more complete in terms of telling people what is actually going to happen to the tissues——

Mr. GROB. Right. Exactly.

Senator DURBIN [continuing]. Donations from their loved one.

Mr. GROB. Yes.

Senator DURBIN. You also note, though, that some people have said, I do not want to know too much about this.

Mr. GROB. Exactly.

Senator DURBIN. This is a very sad moment in a life, when someone is dying——

Mr. GROB. Yes.

Senator DURBIN [continuing]. And you can tell me something, but please——

Mr. GROB. Yes. Do not bother me with that.

Senator DURBIN [continuing]. If you get into graphic detail here, I cannot absorb all of this and handle it.

Mr. GROB. Right.

Senator DURBIN. I might just walk away from the whole idea.

Mr. GROB. Exactly.

Senator DURBIN. This is a tough balancing act, is it not?

Mr. GROB. It is a tightrope, and if you fall off the left side of that tightrope or the right side, you are going to be in trouble. So as far as discouraging donation, it is a hard one.

I think that one idea here is, and I think that the statement of principles that were subsequently developed by the industry are somewhat promising in this regard because of the flexibility they provide. They sort of show that here are things that you definitely ought to—information that ought to be provided to a donor, and now here are some other things that you may want to raise, depending on the interest of the donor. And that is exactly what we found. I think in our study, we quoted an individual who said, "I do not want to know any more about it."

We also found mixed reaction to the point you raised about the commercialization. There was not such a strong reaction to the idea that profit would be made or that prices would be charged. There was concern about whether those profits would be excessive or not, whether there would be profiteering. But there was no practical way to define it and everyone had a different idea.

If I could just give you an example, no one objects to the fact that the surgeon who implants a tissue should get a salary, and then similarly, you could take that concept and just work it back through all the other parts of the processes. People do seem to understand that.

But what concerned them more is if the tissue were being used for some commercial purpose that they did not have in mind. If they thought, well, this skin will be used for burn victims, for example, or medical research, or even the training of surgeons or hospital personnel, they might say that is fine. But they probably might not have been thinking that it might be used for some form of purely cosmetic or voluntary——

Senator DURBIN. That is an important distinction.

Mr. GROB. Yes.

Senator DURBIN. It is one that I have really tried to grapple with here, because if you are talking about a tissue donation that is going to be used by a plastic surgeon to make an actress more beautiful, puff up her lips or whatever happens to be the fashion statement of the day, as opposed to skin that is being used in a transplant for someone who has been a victim of a burn, I mean, totally different world, but both commercial in nature.

Mr. GROB. Yes.

Senator DURBIN. And drawing that line honestly so that people know what they are getting into makes a big difference.

Mr. GROB. Yes.

Senator DURBIN. I was shocked when I read the series in the *Orange County Register.*[1] It had never crossed my mind as I got into this about the use of cadavers for test purposes. I just never thought about a cadaver being used as a test dummy, and yet it has been done.

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[1] See Exhibit No. 11.a. which appears in the Appendix on page 189.

Mr. GROB. Yes.

Senator DURBIN. I am virtually certain that the person who made that donation, signed that consent, did not have a clue that that is what might happen. They were donating for scientific research.

Mr. GROB. Right.

Senator DURBIN. How much should they have known about what was going to happen? I will not go into the graphic details from that series. I invite those who are interested and have not read it to read them——

Mr. GROB. That is right.

Senator DURBIN [continuing]. Because they are troubling, to think that people made these donations unaware of the lengths to which that donation might go.

Mr. GROB. That is why I think that there really needs to be two ways in which the information is provided, one at the point of donation, but the other one more generally. I think that, for example, if I could just reflect with you for a moment, there are other donations we are more accustomed to. For example, I think most of us understand the donation of blood.

Senator DURBIN. Yes.

Mr. GROB. And even of eyes. And over the years, we have been inculturated to accept this and to understand it and know about it, and that has grown up and we are all trained from the time we are very young. We are all trained about this and we understand this.

The tissue that we are talking about here, though, we have not been inculturated about as much and there are these expectations or these surprises, as you were describing them, of what people's expectations are.

So what I think is that we need to very gradually, but very concretely and very deliberately, begin to get people to understand that. I think there needs to be much more openness about all these things. Perhaps some people would be content if their tissue were used for cosmetic purposes. For example, for skin surgery, they largely need very large pieces of skin, and some of the smaller bits of skin may not be useful for that purpose but could be used, for example, for repairing blemishes or for some constructive type surgery of the face or other things and people might be totally content with that.

So it is a complex matter and I do not think there is a clear rule or a clear principle, but I think what we need is more understanding and something that can be done to get that out there so people can gradually learn about this. Then they can make more informed decisions, I think.

Senator DURBIN. Let me ask you this. Is it true that current law prohibits the sale of fetal tissue for any purpose, but only prohibits the sale of adult tissue for transplantation?

Mr. GROB. I would rather not answer because I did not prepare for that at all and——

Senator DURBIN. That is a fact. It raises some interesting questions.

Mr. GROB. We did not—and it was with great deliberation—did not take on anything related to reproductive tissue at all. The

issues that were raised in the newspapers and elsewhere dealt with what we would call conventional tissue for transplant, and at the time, we were all trying to learn so much, just to come to grips with all of this, that it seemed better at the time just to keep it narrower.

Senator DURBIN. Well, thank you for your report. Thanks, Madam Chairman.

Senator COLLINS. Thank you very much, Senator Durbin.

Thank you, Mr. Grob. Your testimony and your work in this area has been very careful for the Subcommittee's analysis, and as we go forward, we will be in touch with you, so thank you.

Mr. GROB. Thank you.

Senator COLLINS. I would now like to welcome our second panel of witnesses this morning. We are pleased to have with us Robert Rigney, the Chief Executive Officer of the American Association of Tissue Banks; Dr. William Minogue, the Chairman of the Board of the Washington Regional Transplant Consortium; and Dr. Valerie Rao, the Chief Medical Examiner of the District Five Medical Examiner's Office in Lake County, Florida.

Mr. Rigney was appointed as the first CEO of AATB in June of 1999. He has over 20 years' experience in health care legislation and regulation in both the public and private sector, and I understand actually began his career here on Capitol Hill, so we welcome him back to the Hill.

Dr. Minogue began his distinguished career in private practice, specializing in internal medicine and cardiology, having served previously as the Director of Medical Education and then Vice President for Medical Affairs at Overlook Hospital in Summit, New Jersey. Dr. Minogue is now the Senior Vice President for Medical Affairs at Suburban Hospital in Bethesda, Maryland. He has also served as Chairman of a Joint Commission on Accreditation of Health Care Organizations task force.

Dr. Rao currently serves as the Chief Medical Officer for several counties in the State of Florida, a position she has held since April of last year. She is board certified in both clinical pathology and forensic pathology and has 20 years of experience in this field. She is also now the President-Elect of the Florida Association of Medical Examiners.

As I explained earlier, pursuant to the Subcommittee rules, all witnesses are required to be sworn in, so I would ask that you please stand and raise your right hand.

Do you swear that the testimony you are about to give to the Subcommittee will be the truth, the whole truth, and nothing but the truth, so help you, God?

Mr. RIGNEY. I do.

Dr. MINOGUE. I do.

Dr. RAO. I do.

Senator COLLINS. Thank you.

Mr. Rigney, we are going to start with you this morning, so you may proceed.

TESTIMONY OF P. ROBERT RIGNEY, JR.,[1] CHIEF EXECUTIVE OFFICER, AMERICAN ASSOCIATION OF TISSUE BANKS, WASHINGTON, DC

Mr. RIGNEY. Thank you. Senator Collins and Members of the Subcommittee, my name is Bob Rigney. I am the Chief Executive Officer of the American Association of Tissue Banks. I am accompanied here today by our President, Dr. Richard Kagan. Dr. Kagan is the Medical Director of the Ohio Valley Tissue and Skin Center. He is also Assistant Chief of Staff at Shriners' Burns Hospital in Cincinnati and the Director of the University Hospital's Burn Special Care Unit. On behalf of our members and the people we serve, I want to thank you for the invitation to appear here. We welcome the opportunity to comment on this rapidly changing and critically important field of tissue banking and tissue transplantation.

Today, human tissues are used in a host of medical procedures and new clinical applications are constantly being developed. In the past two decades, human cellular and tissue-based products have improved and saved the lives of millions of our fellow citizens. It is imperative, therefore, that we do nothing to discourage Americans from donating their organs and tissues.

Let me address the items on which you asked us to comment, first, the role of the AATB and the tissue banking industry. The AATB is a voluntary nonprofit professional scientific and educational organization. Our mission is public health. We are dedicated to ensuring that human tissues intended for transplantation are safe and free of infectious disease, of uniform high quality, and available in quantities sufficient to meet national needs.

To further our mission, since 1984, we have published the only private "Standards for Tissue Banking." This document is recognized as the authoritative source for the industry.

For more than 15 years, we have also operated our own voluntary accreditation program to ensure compliance with our standards. All of our institutional members must be reaccredited every 3 years. Accreditation includes, among other requirements, an onsite inspection by independent inspectors, most of whom are former Food and Drug Administration compliance officers and none of whom are affiliated with any tissue facility. We offer a certification program for tissue bank personnel, and we also operate a tissue network and hotline to help tissue banks and hospitals in emergencies, locate musculoskeletal allografts for orthopedic surgeons, and skin needed to treat burn victims.

The Association's membership currently includes nearly 1,200 individual members and 74 accredited tissue banks engaged in the recovery, processing, storage, and distribution of human tissue. Not every tissue bank is a member of the AATB, but most of the major tissue banks have obtained AATB accreditation. In fact, we believe that at least a majority of the tissue banks in the United State are AATB accredited.

With the exception of ocular tissue, we also believe that AATB members provide most of the commonly used structural tissues for clinical use in the United States. In 1999, the year for which the most recent data is available, the number of bone allografts distrib-

[1] The prepared statement of Mr. Rigney Jr. appears in the Appendix on page 58.

uted by AATB accredited tissue banks totaled almost 524,000, more than double what was distributed 5 years ago.

In addition, tissue donations to our accredited banks are increasing significantly. AATB accredited banks recovered tissue from more than 17,000 donors in 1999. This represents a 274 percent increase in donations in the last 5 years.

It is important to recognize that for nearly a decade following publication of our first edition of our Standards in 1984, the AATB was the only organization overseeing tissue banking in the United States. Today, 17 years later, our Standards are still the most comprehensive and authoritative source in tissue banking, and over those years, we have compiled a remarkable record of donor service and patient safety.

Second, you asked us to comment on the instances in which AATB has denied accreditation to tissue banks. At the outset, I want to make clear that the philosophy of our accreditation program is education, not regulatory enforcement. Our goal is to bring tissue banks into compliance with our Standards, not to penalize them for being out of compliance. We, therefore, allow for corrective actions to be taken, but we also provide for suspension, denial, and revocation of accreditation.

Since the AATB's accreditation program began in 1986, a total of 116 tissue banks have been accredited. Of that number, 43 banks are no longer accredited. Approximately 23 of the 43 banks have either closed, merged with other banks, or for whatever reason did not seek reaccreditation. The remaining 20 banks failed to demonstrate compliance with AATB Standards. Of these 20 tissue banks, 14 were denied accreditation following reinspections.

Inspections of four banks were terminated because of obvious noncompliance at the time of the inspection and these banks withdrew from the accreditation process. Two additional banks would have been recommended for denial. Because their current accreditation was about to expire, they withdrew from the process and let their accreditation lapse. There have also been approximately ten other banks that applied for their initial accreditation but were denied or dropped out of the process.

Third, you requested our views on the roles of for-profit and not-for-profit tissue banks. AATB accreditation is open to any tissue bank that, one, voluntarily agrees to abide by the policies and procedures of the Association, and two, demonstrates adherence to the Standards by successfully completing the AATB's accreditation program. To ensure compliance with our Nation's antitrust laws, we do not now, nor have we ever, differentiated between for-profit or not-for-profit tissue banks.

Next, you wanted our opinion regarding pooling tissue. In all the private and public reporting about tissue banking and tissue transplantation, the greatest untold story, in our opinion, is safety. During the past 7 years, for example, tissue banks accredited by the AATB have distributed more than two million allografts to surgeons without a single reported case of disease transmission from donor to recipient.

For the past 12 years, AATB Standards have prohibited the pooling and commingling of tissues to prevent infectious disease contamination and cross-contamination. This requirement was adopted

because of safety concerns after reports in the 1980's that linked transmission of Creutzfeld-Jacob disease, or CJD, in Japan to human tissue that had been processed in batches in Germany. There has never been a case of CJD transmission from tissue processed in the United States. We believe that this safety record is due, at least in part, to the prohibition on pooling contained in our standards.

Fifth, you asked for our assessment of the current regulatory oversight of tissue banking. Tissue banks have been regulated by the FDA since the agency issued its interim regulations in December of 1993. The agency issued its final regulations in 1997. As detailed in our written statement, the 1997 regulations gave FDA the authority to inspect a tissue bank's facilities, equipment, processes, the screening and testing of donors, medical records, and products. The agency also possesses the police power to sanction tissue banks found in violation of the FDA regulations.

The FDA's current regulatory authority over tissue banks is considerable and the agency has been exercising that authority. We know, for example, that in the past few years, the FDA has inspected approximately one-third to one-half of AATB accredited banks each year. For us, the question is not that FDA has no authority to regulate tissue banks, but whether it has the resources to enforce its existing regulations.

Finally, you requested our opinion of the Food and Drug Administration's proposed rules to expand its oversight of tissue banks. The AATB has had a longstanding history of support for the FDA's goal of developing a balanced, effective, and reasoned program of tissue regulation. That support began with the FDA's first regulatory initiative in 1993 and continued with the 1997 final regulations.

We have also supported the FDA's concept for regulating human tissues that was published 4 years ago. Human tissues are not drugs, biologics, or devices, and they should not be regulated as such.

To implement this new regulatory framework, the FDA published its tissue action plan, the principal components of which were the three separate regulations covering registration, donor suitability, and good tissue practices. Since its first publication, the AATB has always supported the FDA's registration of tissue banks, and we are pleased that registration and product listing are now realities.

The AATB has also strongly supported mandatory donor screening and testing to prevent disease transmission, as outlined in the FDA's proposed donor suitability rule. Since 1979, the AATB has had published guidelines on donor selection criteria, and donor suitability requirements have been included in every edition of our Standards since they were first published in 1984.

In addition, the AATB has generally endorsed the provisions of the FDA's proposed current good tissue practices rule. They are specifically and directly designed to address the risk of disease transmission to patients. We have also submitted extensive comments to the FDA that included recommendations for changes in this regulatory proposal.

The AATB believes that the FDA has adequate regulatory authority at this time. The agency has proposed a regulatory frame-

work for human cellular and tissue-based products that is in keeping with the unique characteristics of human tissue. Once all three proposed rules are final, we believe that sound public policy dictates that the new regulations are given sufficient time to work before their effectiveness is evaluated.

In conclusion, let me simply reiterate that the principal focus of the AATB is the tissue donor, his or her family, and the recipient patients. We respect and honor our donors and their families for helping to ensure that patients receive their life-enhancing and sometimes life-saving gifts. We are the stewards of their gifts and we take that responsibility very seriously. We serve patients by helping to ensure the quality, safety, and availability of tissues and cells for transplantation. This is our public health mission and we are constantly reviewing and improving our standards, our programs, and our operations to address that mission.

I thank the Subcommittee for its time and attention and I will be happy to try to answer any questions the Senators may have. Thank you.

Senator COLLINS. Thank you, Mr. Rigney. Dr. Minogue.

TESTIMONY OF WILLIAM F. MINOGUE, M.D.,[1] CHAIRMAN OF THE BOARD OF DIRECTORS, WASHINGTON REGIONAL TRANSPLANT CONSORTIUM, WASHINGTON, DC

Dr. MINOGUE. Thank you. Good morning, Madam Chairman. I am Dr. William Minogue, Chairman of the Board of Directors of the Washington Regional Transplant Consortium. I would like to thank you for this opportunity to testify before the Subcommittee today. My goal is to share with the Subcommittee WRTC's experience with the tissue banking industry.

The Washington Regional Transplant Consortium is a federally-designated organ procurement agency for the Washington, DC area. We perform organ recovery services for 48 hospitals in Maryland, Virginia, and the District of Columbia, a responsibility we have had since 1988. As you are aware, all organ procurement agencies are required by Federal law to be nonprofit. Each OPO has regulated functions, responsibilities, reimbursement practices, and a board of directors or an advisory board with federally-mandated representation.

I think our Board of Directors illustrates this. It is an all-volunteer board which includes transplant surgeons, a liver transplant recipient, a donor family member whose wife was a donor and 4 years later, tragically, his daughter was a donor following a serious automobile accident, and a prominent biomedical ethicist, in fact, the senior ethicist at Georgetown University. I think the makeup of that board avoids any mischief that could possibly come in this industry. They give us such wonderful support. I am an internist.

Federal law makes one OPO responsible for organ recovery and distribution in a given geographical area and makes the OPO responsible for approaching families regarding the option of organ donation. This same arrangement does not exist in tissue donation, as the Subcommittee obviously is aware. We have chosen to offer

[1] The prepared statement of Dr. Minogue appears in the Appendix on page 74.

both organ and tissue recovery services for one purpose, to protect the integrity of both the organ and tissue donation processes.

To the public, organ and tissue donation constitutes the same activity. Families confronting the loss of a loved one do not make a distinction between a person who recovers a heart, lungs, liver, or kidneys and the person or organization that recovers skin, bone, heart valves, and corneas. Each time a family decides not to donate because of confusion or suspicion, then we risk the lives of several people waiting for organ transplants. We have one high standard for family approach, donor screening, and tissue recovery and we have through experience developed an approach to working with donor families that respects their grief while offering them the possibility of turning their loss into some greater good.

We are also responsible for the integrity of the organs and tissues that are recovered and are entrusted with protecting the recipient community from potentially unsafe organs and tissues. Moreover, we are accountable to the donors and their families to ensure that these gifts will be respected and utilized appropriately.

For these reasons, we endorse the recommendations brought forth by the Model Elements of Informed Consent for Organ and Tissue Donation developed jointly by the Association of Organ Procurement Organizations, the American Association of Tissue Banks, and the Eye Bank Association of America. We encourage its implementation industry-wide.

As you know, there are over 75,000 people nationwide waiting for life-saving gifts. Tissue donation is life-enhancing and improves the quality of life. However, there is no comparable shortage of tissue for donation or urgency for tissue transplants, so we impose stricter standards on tissue donor suitability. If tissue donor evaluation and recovery practices are unsafe, a recipient can be subjected to unnecessary risk. Organ donation procedures are regulated while tissue donation is not. This is why we support the Food and Drug Administration's proposed rules on donor suitability and good tissue practices.

WRT has chosen LifeNet, a federally-designated OPO in the Tidewater area of Virginia, as its tissue bank to process and distribute tissue recovered by us. Because of their high standards, they also recognize that tissue banking and organ donation are inextricably linked. We trust LifeNet as our partner because of their integrity, their commitment to quality products and services, and to donors and their families.

Regrettably, not all organizations involved in recovery processing and distribution of tissue share our concern to maintain and respect the integrity of the donation process and the sanctity of the donated gift. Consider, please, the following scenario: An elderly patient dies at a local hospital. In accordance with the Federal regulations, the hospital refers this case to the local OPO for potential donation. The OPO determines that this patient is not a candidate for organ or tissue donation and communicates this to the hospital and the family. The decision is based on the generally accepted suitability criteria for tissue banks.

Sometime later, the OPO receives an excited call from the local hospital, which demands to know why this patient is now being pursued for tissue donation. The OPO investigates this case and

determines the following: Another tissue recovery agency obtained confidential patient information without the knowledge of the hospital. They told the family that this patient's tissue could be recovered for transplant purposes. The family specifically stated they did not wish the tissue to be recovered for use in medical research. The second tissue recovery agency was pursuing the tissue for transplant even though the following medical conditions existed: The patient was outside the generally accepted age range for donation; the patient had a history of cancer that had rendered the tissue medically unsuitable; the patient had been dead for almost 24 hours; and there was evidence of a recent infection.

The investigation points to the following conclusions: The fact that the family had specifically stated they did not wish to donate for research indicates that this agency was either pursuing donation for transplant purposes or recovering tissue for research but not fully disclosing that intent to the family. They were recovering tissue in our region for a publicly-traded for-profit tissue bank. Neither the for-profit tissue bank nor their local recovery agency had a written agreement with the hospital to recover tissue at that facility, nor were they authorized to talk to the family about tissue donation.

Situations like this occur when organizations that lack sufficient experience in tissue recovery become involved. Furthermore, some of these organizations operate from profit motives that supercede the public interest. Our example illustrates the necessity for clear industry standards with regard to the safety and soundness of donated tissue.

There are an increasing number of for-profit tissue processing and distribution agencies entering the donation arena. These entities need access to human tissue in order to generate revenue and are under shareholder pressure to increase their market position to maximize profit. They are not required to take the overall donation interest of the public into account, and unlike OPOs, their boards have no requirement to represent the public interest.

In addition, we have seen for-profit tissue banks create nonprofit recovery agencies or use local nonprofit organizations as a conduit for human tissue into their processing and distribution facilities. These nonprofit groups usually have established relationships with hospitals outside of tissue donation, which gives them access to hospital facilities and patient information. Patients and their families, as well as members of the local nonprofit organizations themselves, are not aware that the donated gift will go to publicly-traded corporations as raw material, and these recovery agencies have also attempted to transfer bodies out of the hospital to locations where they are able to perform the recovery. We perform all of our recoveries in operating rooms under clean and sterile conditions.

Our recommendations, then, are that both donor and recipients must be protected, the former by implementing an approach such as the Model Elements of Informed Consent for Organ and Tissue Donation, and the latter by the swift adoption of the Food and Drug Administration's two proposed rules expanding donor screening and testing and on standards for good tissue donation practices. We also endorse the institution of an annual reporting mechanism

for all entities involved in tissue donation processes, both for-profit and not-for-profit, to ensure transparency.

We are pleased that tissue banks have begun registering with the FDA in accordance with its newly implemented rule and hope that comprehensive inspection of all tissue banks by the FDA will soon follow. Moreover, we agree with recent actions taken by the FDA in urging a tissue processing and distributing organization to stop its practice of pooling from multiple donors during processing. The experience with a CJD contaminated dura mater allograft is adequate evidence of a need to ban this practice.

WRTC would like to highlight two additional recommendations for consideration. First, we recommend giving OPOs oversight authority over all donation activities, including family contact, donor evaluation, recovery, processing, and distribution.

Second, ensure that tissue recovery organizations are nonprofit and that relationships with for-profit organizations are held at arm's length. It is neither wise nor possible to eliminate for-profit companies from all processing and distribution activities resulting from tissue donation. In fact, new patient care technologies based on donated human tissue may well be developed by for-profit or jointly between nonprofit agencies and for-profit companies.

In conclusion, society does not distinguish between organ donation and tissue donation. Organ donation is well regulated and closely controlled in the public interest. The task before us now is to ensure that the tissue banking industry is held to the same high standard. We look forward to the day when our citizens completely accept the benefits of organ and tissue donation as a common, dignified, and valuable contribution to the quality of life and to death with dignity. Thank you.

Senator COLLINS. Thank you, Doctor. Dr. Rao.

TESTIMONY OF VALERIE J. RAO, M.D.,[1] CHIEF MEDICAL EXAMINER, DISTRICT FIVE, LEESBURG, FLORIDA

Dr. RAO. Good morning, Chairman Collins and Members of the Permanent Subcommittee on Investigations. My name is Dr. Valerie Rao. I have been appointed by the Governor of the State of Florida to hold this position as District Five Medical Examiner. The district involves five counties running from Central Florida all the way to the Gulf, so it is a very, very large area. I also sit on the Medical Examiner Commission, and that is also a Governor-appointed position. I have been there since April 2000, prior to which I was in Dade County for 18 years and 9 months.

I would like to thank you for inviting me to appear today before the Subcommittee and I am very pleased to discuss this most important issue to me. I believe that human donation is a selfless and invaluable gift, and as such, would like to see that all tissue recovery organizations are required to adhere to standards that promote safety and respect for donation. Unfortunately, my observations tell a very different story and I would like to share my experience with this Subcommittee.

The role of the medical examiner in organ and tissue transplantation results from government-mandated investigation into sudden

[1] The prepared statement of Dr. Rao appears in the Appendix on page 82.

and unexpected or traumatic deaths to determine the cause and manner of death. The manner includes natural, accident, suicide, or homicide. A medical examiner death investigation includes documentation and evaluating the scene of death or the injury as well as the body at the scene. Included is the determination of the terminal episode and the medical history of the decedent.

In Miami-Dade County, where I spent 18 years and 9 months as an associate medical examiner, when a case arrives, it is initially screened by a tissue bank coordinator for consideration as a potential donor. If the quality appears suitable, the next-of-kin authorization is received. In the meantime, the medical examiner performs a careful external examination. The body is transported to a sterile autopsy suite where a tissue bank pathologist participates in the tissue excision process. During this procedure, blood and lymph node tissue are retained for screening. The body returns to the medical examiner for an autopsy. For the non-medical examiner case, the tissue bank pathologist performs the autopsy. At any time during this procedure, should testing raise doubt, the donor material is removed from the preparation and distribution pipeline.

Most medical examiner donor cases are people of prior good health who experience violence, 24 percent; sudden, unexpected, non-infectious cardiac dysrhythmia or stroke, 76 percent. These are the statistics from Miami-Dade County, Florida, from 1995 through 1999. The very nature of such cases of previously healthy individuals with sudden death creates a donor pool where infection and malignancy are minimized.

The protection against transmittal of infection and malignancies must be the primary principle in all transplantation programs, and the shortage of donor materials and business pressures should not work against this principle. Therefore, it is recommended that tissue bank physicians and coordinators become aware of their own State medical examiner guidelines in order to understand the investigative process and its relationship to quality assurance.

As the medical examiner determines the cause of death, a complete autopsy and tissue for subsequent microscopic examination serves as a quality assurance step in the transplantation process. Medical examiners are charged, in addition to forensic investigation into death, also with public health issues, particularly with regard to the possibility of transmission of infectious disease. Autopsies are required for donor acceptance, and medical examiners believe that autopsies should be done routinely on all donor cases. Autopsies are the only means by which diseases such as tuberculosis, histoplasmosis, degenerative disease of the brain, unsuspected malignancy, viral myocarditis, non-A, B, or C hepatitis, diseases of unknown etiology, and other potential transmissible diseases can be detected and those donors excluded from the donor pool.

The entire issue of medical examiner participation in the acquisition of tissues from cadaver donors must also be considered in light of the recent developments. As I stated, medical examiners are the guardians of public health interest and should be in a position to make a determination which tissue bank serves both the interests of the recipient patient as well as to satisfy the medical examiner's statutory duties. Certainly, a trust in the professional competence

and reputation of the tissue bank personnel is an important factor in making such a determination.

Last April, I became concerned regarding several questionable practices by a tissue bank. My first concern was when Regeneration Technologies, Inc., through its association with the University of Florida Tissue Bank, would accept donors with non-metastasizing malignant tumors of the breast, colon, cervix, and lung. They also accepted donors with septicemia, pneumonia, and intestinal obstruction. To the best of my knowledge, they do not perform routine blood or bone marrow aspirate cultures, which is done to detect for possible disease. They do not require an autopsy and, hence, do not know the cause of death in the donor.

Tissue excisions are performed by technicians without physician supervision or participation, and the use of sterile precautions are not observed during the excision and the retrieval process. The technicians do not have sufficient training and knowledge to observe changes which would be noted by a pathologist, yet they performed an autopsy removal of the brain which would obviously impair further medico legal investigation into the death of the deceased. Finally, the customary care and respect for the body of the deceased are not observed. I believe that the dead have rights, too.

In contrast, the University of Miami Tissue Bank has demonstrated quite the opposite. All of their excisions are performed aseptically by trained physicians in an operating room environment. Blood cultures and bone marrow cultures are also routinely performed.

As I stated before, I believe that public trust in the professional competence and reputation of those involved in the donation process is vital to its continued success. Thank you very much, Madam.

Senator COLLINS. Thank you, Dr. Rao.

Mr. Rigney, I want to start by asking you some questions. You mentioned in your testimony that the Association has accredited 74 tissue banks, is that correct?

Mr. RIGNEY. That is correct. Our current membership is 74.

Senator COLLINS. And according to the FDA, we know that at least 350 tissue banks have registered to date under the agency's new mandatory registration rule, and perhaps your testimony was written before that fact became available. I am trying to reconcile your testimony saying that most of the tissue banks in the United States have obtained AATB accreditation. In fact, we believe that at least a majority of the tissue banks are AATB accredited. If you have accredited 74, yet we know that 350 have registered with the FDA, you are a long ways from accrediting the majority of banks, are you not?

Mr. RIGNEY. That would be correct, Senator. The testimony was written when the only figure we knew was what the OIG had reported. We received the list that the OIG reported and compared it against our own banks and our knowledge of the existence of other banks. What we found in our review was that of the 90 banks that were not accredited and cited in the OIG figures, about 30 of those, as we counted them, were either double-counted because they were listed both under a former name of the bank and their current name, or they had gone out of existence and closed their operation, or they had merged with another bank, or they were

now accredited by the AATB. Another third of that number were banks that we knew that did exist and were not accredited members. And the final third was a group of banks that we had never heard of before, quite frankly.

Senator COLLINS. But you are talking about the OIG's report.

Mr. RIGNEY. Right.

Senator COLLINS. Were you surprised to learn that there were 350 tissue banks that registered with the FDA?

Mr. RIGNEY. I just learned that yesterday, the number that had registered with the FDA. What I am told is that that number includes a number of reproductive banks, who are not required to actually register until the year 2004. It also includes a number of stem cell banks, a number of laboratories, and others that we would not necessarily consider a traditional type of tissue bank, but that would meet the regulatory definition under the registration rule.

Senator COLLINS. I would inform you that the Subcommittee staff raised that issue with the FDA and that was not the case.

Mr. RIGNEY. OK.

Senator COLLINS. The vast majority of these are tissue banks——

Mr. RIGNEY. Then that number would, indeed, surprise us.

Senator COLLINS. And one of my concerns suggests that there are an awful lot of tissue banks out there that have been operating without accreditation by your Association, without oversight by State regulators—very few States have an effective regulation of tissue banks—and flying under the radar of the FDA, as well. We did get a breakdown of the numbers and there were actually 368 banks. We took out those that were the stem cell ones that you mentioned or reproductive and you still get close to 350.

So it seems to me that the industry is far more extensive and there are far more organizations involved in the recovery and processing of tissues than any of us would have guessed, which is troubling to me in terms of proper oversight.

The HHS Inspector General's report mentioned that there are differences between your required standards for accreditation and the FDA's current requirements. Could you describe those differences for us?

Mr. RIGNEY. Let me describe them, if I can, Senator, in general terms. If you want a specific side-by-side, we will try to prepare that.

Senator COLLINS. Just general will be fine.

Mr. RIGNEY. Generally speaking, our current Standards are much more detailed and much more extensive than FDA's current final rule under which it is operating. That is sort of the long and the short of it. We go into many more areas in terms of accreditation of the tissue bank than FDA's current regulations would cover. Generally speaking, as a follow-on, their proposed rule, that good tissue practices proposed rule, is patterned in many respects off of our Standards.

Senator COLLINS. Do you require more testing than the FDA does for specific pathogens?

Mr. RIGNEY. We require basically the same testing, except one that immediately comes to mind in terms of living donors. We would also require a hepatitis B core antigen test.

Senator COLLINS. Do you require screening for CJD, because I do not believe the FDA does.

Mr. RIGNEY. We do have screening requirements for CJD in our Standards.

Senator COLLINS. Has the AATB ever suspended or revoked its accreditation of a tissue bank?

Mr. RIGNEY. Yes, and I cited some of those numbers in my statement.

Senator COLLINS. When that occurs, however, there is nothing that prevents that tissue bank from continuing to operate, is there?

Mr. RIGNEY. No. Our Association and our accreditation is voluntary. You submit to it. The only power we have, essentially, is to revoke one's accreditation once it is granted, or to deny it if they are applying for it.

Senator COLLINS. Do you know if any of the banks for which you have revoked or denied accreditation are still operating?

Mr. RIGNEY. I personally cannot answer that for you right now. I would be glad to check that out and report back to you.[1]

Senator COLLINS. I would appreciate your doing so. Based on our investigation, there are indications that some of the banks that have been denied or revoked accreditation by your organization are still operating.

When you do act to revoke an accreditation, do you report that action to the FDA or share that information with the FDA?

Mr. RIGNEY. Generally speaking, no.

Senator COLLINS. Do you think that would be helpful to the FDA in its inspection and evaluation of tissue banks that might be problematic?

Mr. RIGNEY. The problem we have, Senator, is that our accreditation program provides certain assurances of confidentiality as the bank is moving through the process.

Senator COLLINS. Do you believe that the FDA should prohibit pooling of tissues, as your members are prohibited from doing?

Mr. RIGNEY. Right now, based upon what we know, we have, as I noted, had standards prohibiting pooling for 12 years and think that the FDA should probably have the same standards——

Senator COLLINS. Thank you.

Mr. RIGNEY [continuing]. If they do not already.

Senator COLLINS. Dr. Minogue, your testimony is very interesting to me because you have tremendous experience in overseeing organ transplants in the donation process, which seems to me, as your testimony suggests, to be much more regulated, much better understood. Processes are far more established. One area that concerns me as I have been examining this issue is the differences between organ and tissue donation. Do you think that the procedures for obtaining informed consent for tissue donation should be more like those that are used for organ donation?

Dr. MINOGUE. Yes, I do. I believe that the organ procurement process has matured over time. I happen to have been one of the founding members of this board 14 years ago and it was pretty much made up of transplant surgeons and the hospitals they represented trying to get our act together. Now it is so wonderful and

[1] See Exhibit No. 19 which appears in the Appendix on page 251.

mature and it sounds to me, and I am learning more today than I ever did know about the tissue side, that tissue has to mature in a similar fashion. But it needs this oversight. I strongly favor the not-for-profit, altruistic model of my board. There is just no possibility for us to get into, as I mentioned before, some mischief of this type. There must be oversight. Also, of course, favor that there be one regional tissue procurement organization, whatever that may be, so that this competition goes away.

Senator COLLINS. Modeled on the OPO——

Dr. MINOGUE. Modeled on the OPO arrangement.

Senator COLLINS. I would like to talk to you further about a local nonprofit organization that you referred to in your testimony, because I think it illustrates some of the underlying issues that you have identified and that we are discussing today. It is my understanding that the organization involved is a local service club and that it provides tissue to a large for-profit tissue company called Regeneration Technologies, Inc., or RTI.

It is further my understanding that RTI uses tissue pooling, or has been using tissue pooling, which many experts tell me, and you have testified this way, also, that the risks far outweigh the benefits. Is that an accurate statement?

Dr. MINOGUE. That is a perfectly accurate statement, yes, ma'am.

Senator COLLINS. I would like to refer to a specific exhibit, which is Exhibit No. 4,[1] and I think you have it in the book before you, also. Now, as you probably recognize, this is a WRTC donor referral and tissue bank donor worksheet, and it is my understanding that this is used to establish the medical history of a potential donor in order to evaluate the suitability. I would note that we have redacted any personal information that could identify the individual involved. Is that what this is used for, to work up whether or not this person may be suitable as a donor?

Dr. MINOGUE. That is correct.

Senator COLLINS. Now, as I look at this worksheet, it seems pretty clear to me that WRTC rejected this individual as a donor for skin, bone, heart valves, and eyes, and the reasons why that the WRTC found the donor unsuitable were two reasons, primarily, one, that he was 82 years old, and second, that he had a history of prostate cancer. In your view, would those two factors make it too risky to transplant tissue from this donor to someone else?

Dr. MINOGUE. The age is problematic because of the suitability of the tissue and the likelihood of an effective transplantation later on. And as you have heard earlier, since there is not a great shortage of tissue, as there is with solid organs, why in the world take these risks, even if we do not have scientific evidence that prostate cancer, which may well be very localized, would be harmful to the patient or to the recipients downstream. This sort of case, and it sounds quite like the case that I illustrated in my testimony, was rejected by us and would continue to be.

Senator COLLINS. I would like to switch to Exhibit 5,[2] which—this is a worksheet that was produced by the local nonprofit organization that I mentioned that was acting as a tissue bank, and as

[1] See Exhibit No. 4 which appears in the Appendix on page 116.
[2] See Exhibit No. 5 which appears in the Appendix on page 118.

you can see in the first question, has the deceased ever had cancer, tumors, leukemia, lymphoma, received radiation therapy or drugs for cancer, and the answer is yes to that. It further goes on to ask some other questions, which also identify problems. But the very first question indicates that this tissue bank knew that the individual had prostate cancer, so there is no doubt that that was known to the tissue bank based on this document, is there?

Dr. MINOGUE. None whatsoever.

Senator COLLINS. Do you know whether this tissue bank, despite this information, tried to persuade the donor family to give permission to recover various tissues from the body anyway?

Dr. MINOGUE. I do not, as personal knowledge, know. A colleague of mine, from WRTC, who directs all of this tissue donation process, is here today and he might be able to comment, if you wish, but I do not know.

Senator COLLINS. Is that individual available?

Dr. MINOGUE. Yes, he is.

Senator COLLINS. Would you like to consult and relay?

[Pause.]

Dr. MINOGUE. David DeStefano, my colleague, says he does not believe there was persuasion per se, and I believe that was part of the question, but they were indeed pursuing this patient for donation and the patient had already been rejected by WRTC.

Senator COLLINS. It is unclear to me why any tissue bank would pursue this individual as a potential donor—not pursue the individual, but discuss this with the individual's family. Do tissue banks face pressure to produce a certain amount of tissue?

Dr. MINOGUE. That is the perception that we are working on. Again, I do not have firsthand knowledge of that, but there seems to be quite a bit of aggressiveness in some parts of that industry and that is disturbing to us.

Senator COLLINS. And it is your opinion that the for-profit sector of the tissue bank industry is particularly subject to pressure to recover more tissue?

Dr. MINOGUE. It seems logical, particularly on the recovery side. As I mentioned in the testimony, the for-profit processing end of the equation and that whole industry may well do creative works and research and so forth if properly regulated and motivated, but to tie the donation itself to profit is very disturbing to us for the reasons I mentioned, that these are very delicate situations at the bedside, as you can imagine, and to have any suggestion of aggressiveness in this regard is just destructive to the whole process.

At our board, we look very carefully at all of our hospitals and do death review, for example, and any time we see that there was an opportunity missed for solid organ transplantation, we treat that and investigate it and encourage the hospital to investigate it, because as many as five or six lives could have been saved by that proper donation. Why did it go wrong? That is how seriously we take one single loss of an opportunity. So in any way tainting this terribly complex dynamic at the bedside is just wrong.

Senator COLLINS. What characteristics does WRTC look for when developing a relationship with a tissue bank?

Dr. MINOGUE. A high degree of integrity, that they have the same feeling and passion for protecting the donation process and

that they remain at arm's length as far as all of the business, if you will, of their organization, and just have the same philosophy of integrity and ethics.

Senator COLLINS. Do you at times refuse to do business with certain tissue banks?

Dr. MINOGUE. We do.

Senator COLLINS. Thank you. Just one final question for you. Do you believe that tissue banks—you have testified that there needs to be a better regulatory structure for tissue banks. Do you believe as part of that that there needs to be regular inspections of tissue banks to ensure compliance with good procedures?

Dr. MINOGUE. Absolutely.

Senator COLLINS. Thank you.

Dr. Rao, I would like you to explain further about your experiences with RTI and tell me more specifics on what troubled you about this particular tissue bank.

Dr. RAO. Yes. When I took the job initially, I had to find out what was going on in the district and there were several tissue banks that came in and were taking tissues and my technicians were telling me that there were some very strange goings on, and so I waited to see for myself, and the first case I saw, as soon as I saw the case, this was a lady whose upper extremities were taken and the incisions run all the way down the arm to take out the long bones and the incisions were not even closed and the body was—it just took me aback. I was not used to this. I just looked at them, like, no, these people are not coming back here. That was it. I had made my decision.

I received a lot of political pressure because of that decision, but I just could not be associated with that kind of business, because a medical examiner—what will happen is they will say it came from District Five and then it reflects on the medical examiner that was involved in that transaction. So I told all the tissue banks that there had to be a moratorium on tissue recovery in District Five until I could look at everything that was going on. That was one incident.

The other incident, they took bones prior to it becoming a medical examiner case. Initially, it was not a medical examiner case, and then the family called with some history which then brought it under the jurisdiction of the medical examiner. And the issue that was to be discussed by the medical examiner was did this lady have a stroke? So when I opened the body and the head, I found that they had taken the brain and they had placed the cerebral hemispheres in the chest cavity, and then they took a dowel to replace the spine that was removed and pushed it up into the foramen magnum, as a result of which the entire cerebellum was all squashed. So there was no way I could determine, did this lady have a stroke. But they did not realize it was going to come to the office.

So there was a second incident that I saw this happened, and after that, of course, I was determined not to allow them to come into the office.

The above examples all pertain to the University of Florida Tissue Bank, an affiliate of RTI.

Senator COLLINS. In the first case that you gave us as an example of inadequate respect for the dignity of the donor and, undoubtedly, the family would have been very upset to see the body left in that condition, and I want to indicate that is not typical, that most tissue banks do a very good job and are very respectful, as are the OPOs and those involved in organ donation, but that was an example where there was inadequate respect for the donor's body.

The second case sounds like the haste to recover tissue caused you to be unable to perform your duties as a medical examiner, is that accurate?

Dr. RAO. Exactly.

Senator COLLINS. Could I ask you about a third issue, and that is have you ever been concerned about whether there were sufficient screenings performed on tissue to make sure that they were safe for donation?

Dr. RAO. Yes. At one of the ME committee meetings I had, the director of the University of Florida Tissue Bank came to me and talked to me and asked if he could come back into the office, and I said to him, "If you agree to these standards and these tests, then yes." And he looked at me and he said, "Well, that will not be essential," and then I said, "Well, then you cannot come back." So he did not want to comply with what was required, as a result of which I thought even more that he should not be allowed to take tissue from District Five cases. So they do not want an autopsy on every case because it is expensive and it will cut into the profit margins, but I am not concerned about profit margins. I am concerned about the public health, safety in the recipients that get this bone donation.

Senator COLLINS. What kind of research can a family, which is considering donation of a loved one's tissues, do to ensure that they are dealing with a reputable tissue bank? Is there any advice you can give us? I actually think that is a very difficult burden to put on the family. I mean, the family is going through a time of incredible grief and difficulty, which is one reason why I think we have to look to the Federal Government to perform that kind of role.

But assuming we do not have a good regulatory structure in place right now, or a sufficient one, what kind of advice could you give to families that are considering donation, that very much want to make a gift that is going to enhance the quality of life for others, yet want to make sure that they do not run into the kinds of problems that you have identified?

Dr. RAO. Actually, to answer that, there was a letter received, which is part of your exhibit package,[1] from an elderly gentleman, and you can see that he is keeping up with the literature and with the press releases out there, and I was pretty surprised to get that letter from him. You see the giving nature of this individual. He is a pretty elderly man, 84 years old, and he still wants to give of himself but he is very concerned. Am I doing the right thing? How should I go about this?

Being unaware of the many agencies out there, my advice would be to do some research as to which bank is going to take this, what

[1] See Exhibit No. 3 which appears in the Appendix on page 114.

is their reputation out there, and research it on their own, then make a decision, hopefully they will talk to the medical examiner, if it is a medical examiner case, and think, am I comfortable with this tissue bank, and go from there.

Senator COLLINS. Thank you. I just have one final question for all three of you. This morning, we heard some very disturbing testimony from the Office of Inspector General on practices that the FDA had caught during its inspections, which we have learned have not been as frequent or as widespread as we would all like to see, which identified tissue banks engaged in the practice of repeat testing in which tissue is repeatedly tested until the tissue bank obtains the result that it wants of no disease, even after previous tests have identified problems.

Are either of you familiar with that and could you comment on that practice? Dr. Minogue, we will start with you.

Dr. MINOGUE. Certainly, I was as startled as you were to hear that today, and I am not aware of any test in medicine that goes from positive to negative just through repetition. So there is something very strange about that piece of information.

Senator COLLINS. I thought it was one of the most disturbing statements made at this hearing. It just seems to me that if a negative test, or a positive, in this case, a positive test indicating a problem is reached, that tissue should immediately be discarded. The idea that, instead, the technician just tests it again and tests it again and tests it again in hopes of getting an all-clear result is very troubling as far as the safety of the tissue in the system.

Dr. MINOGUE. Repeated testing, we will do confirmatory tests often. If we have a suspicion, let us say, and we get a negative, we might test to be darn sure. But to repeatedly, and that was the testimony, to repeatedly test until it is negative, that is just awful.

Senator COLLINS. Mr. Rigney, have you heard of this before?

Mr. RIGNEY. Certainly. Senator, every manufacturer's test kit, be it for living donor sera or for cadaveric sera, contains test kit instructions specifying how you are supposed to conduct that test. Without going into the details of how these tests are run, repeated testing that would in any way be different than what is in the manufacturer's instructions would be a violation not only of our Standards, but I think of FDA requirements. It would certainly, in our case, trigger a mechanism to suspend or revoke accreditation, or to deny it if it was somebody applying initially.

Senator COLLINS. Thank you. Dr. Rao, have you heard of that before, and given your extensive experience as a physician, could you give me your opinion of that practice?

Dr. RAO. I am not familiar. I was pretty disturbed, too, because in blood banking, we did blood banking during our training, if there was a unit which had anything, any little thing, the unit was discarded, and I think blood banking and tissue banking should both be on a similar par when you think of standards, because this is somebody's life one is dealing with.

Senator COLLINS. Thank you.

Mr. RIGNEY. Senator, I would simply note that the stories I have heard and the reports that I have seen of such cases would not be limited to tissue banking. They also involve blood banks, where

there have been a number of recalls precisely for those reasons, as well as other types of laboratories.

Senator COLLINS. Thank you. I want to thank all of you for your testimony and your assistance to the Subcommittee. Thank you.

Senator COLLINS. Our final witness today will be Dr. Kathryn Zoon, the Director of the Center for Biologics Evaluation and Research within the Federal Food and Drug Administration. She has been with the FDA since 1980. Dr. Zoon, we are very pleased to have you with us today. Before you get too comfortable, I do have to swear you in.

Do you swear that the testimony that you are about to give to the Subcommittee will be the truth, the whole truth, and nothing but the truth, so help you, God?

Dr. ZOON. I do.

Senator COLLINS. Thank you. Please proceed with your testimony.

TESTIMONY OF KATHRYN C. ZOON, PH.D.,[1] DIRECTOR, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, U.S. FOOD AND DRUG ADMINISTRATION, WASHINGTON, DC

Ms. ZOON. Thank you. Good morning, Madam Chair and Members of the Subcommittee. Thank you for inviting me to participate in this hearing concerning human tissue banking. I am Kathryn Zoon, the Director of the Center for Biologics in the FDA. My Center is responsible for the regulation of many different types of human tissues and cells used in transplantation. Today, I will provide background information on the regulation of human tissues for transplantation and FDA's current and future actions to help ensure the safety and availability of these important products.

No medical product is risk-free. The FDA regulates tissue under the authority of the Public Health Service Act and the Federal Food, Drug, and Cosmetic Act. Several categories of human tissue used for transplantation are being regulated as medical devices under the 1976 Medical Device Amendments. Many cellular and tissue base products are regulated as biological products under the Public Health Service Act and the Food, Drug, and Cosmetic Act, and other cells and tissues are regulated for communicable diseases under the PHS Act.

FDA's goals with regard to human tissues are to: One, prevent the spread of communicable disease; two, to ensure the safety and efficacy is demonstrated for cellular and tissue-based products; and finally, enhance public confidence in these products. FDA plans to accomplish these goals through implementing regulations in a manner that will not discourage the development of new products. Human tissues for transplantation include skin replacement for severe burns, tendons and ligaments for injury repair, and corneas to restore eyesight, as well as bone for replacement.

The increased use of human tissues has heightened public awareness of the need for appropriate regulation to minimize potential risks. Developments in the 1980's and 1990's prompted FDA to examine our approach to the regulation of tissue. Several incidents

[1] The prepared statement of Ms. Zoon appears in the Appendix on page 84.

illustrated the risks of disease transmission when adequate precautions were not taken.

In 1991, it was discovered that seven people had been infected with human immunodeficiency virus through the transplantation of organs and some tissue from a donor who tested negative for HIV. This led to intense discussions within the tissue bank community and the Public Health Service on how to reduce the risk of infectious diseases from transplanted human tissues, and ultimately to the comprehensive approach that I will describe.

In 1993, FDA learned that human tissue from foreign sources was being offered for sale in the United States with little or no documentation of the source. There was little, if any, information on the medical condition of the donor, the cause of the donor's death, or the results of donor screening and testing. This raised significant concerns about the safety and quality of that tissue. The agency quickly confirmed that the tissue was not adequately screened and tested for infectious diseases. The agency acted promptly by promulgating a regulation and exercising its enforcement powers.

In December 1993, FDA took action to minimize the risk of disease by issuing an interim rule for human tissue for transplantation, which required donor screening, infectious disease testing, and recordkeeping to prevent the transmission of infectious disease. Under this regulation, FDA could also conduct inspections, and when necessary, could order tissue to be detained, recalled, or destroyed. This interim rule was made final, with some modification, on July 29, 1997.

After careful consideration of the health issues and extensive public discussion, FDA published the proposed approach to the regulation of cellular and tissue-based products in 1997. This document described FDA's planned regulatory framework for human cellular and tissue-based product regulation. Subsequently, FDA has accomplished many of the regulatory goals described in the February 1997 document through publication of a series of proposed and final rules.

The 1997 proposed approach provided a framework for the regulation of both traditional and new products. This framework detailed the type of regulation necessary to protect the public health and provide a risk-based tiered approach to cell and tissue regulation. For human cells and tissue products where the risk is limited to disease transmission, FDA's proposed regulation is intended to prevent transmission of disease through the use of these products. For products that pose greater risk, the framework additionally provides for pre-market review and approval of product applications.

To accomplish the implementation of the proposed approach, the agency developed a tissue action plan that contained a description of the steps and time frames the agency would use. Many of these steps have already been accomplished, including a final registration and listing rule and the proposed rules on donor suitability and good tissue practices.

The registration and listing rule requires establishments to register and list with the agency their human cell tissues and cellular and tissue-based products. Under this final rule, establishments engaged in the recovery, screening, testing, processing, storage, or

distribution of tissues, with conventional tissues such as bones, skin, and corneas, are required to register and list their products. Other establishments that manufacture nonconventional or new cellular and tissue-based products, such as hematopoietic stem cells, are required to register and list by January 2003, although I might add that they can register voluntarily now.

In September 1999, FDA published a proposed rule regarding the donor suitability for cellular and tissue-based product. Disease agents, such as HIV, hepatitis B virus, hepatitis C virus, syphilis, and CJD have been detected in human tissue. The proposed rule, when final, will expand current screening and testing requirements to include donor screening for CJD and donor testing for syphilis and would apply broadly to cellular and tissue-based products. A donor who tested repeatedly reactive for a particular disease agent or who posed clinical evidence of or had risk factors for such a disease will be considered unsuitable and cells or tissues from that donor will not ordinarily be used. The agency is currently reviewing public comments on the proposed rule.

Tissue establishments perform various procedures that may affect the safety or quality of tissue products. Therefore, in January of this year, FDA published a proposed rule for good tissue practices for manufacturers of human cellular and tissue-based products. With this proposed rule, FDA completed the set of proposals that, when finalized, implement the new regulatory framework. The proposed rule will require manufacturers to follow good tissue practices, which include practices involving methods, facilities, and controls used in tissue manufacturing, tracking, process validation, and the establishment of a quality program. FDA is in the progress of carefully reviewing all comments received in response to this proposed rule.

In 2002, FDA estimates that the agency will dedicate $4.35 million to the regulation of human tissue. This is part of the President's Fiscal Year 2001 budget request for FDA, which represents a 10 percent increase for the agency over the Fiscal Year 2000 level. Estimates of the implementation of the tissue regulation will be developed as part of the 2003 budget process and may be revised as we garner additional information for future establishment registrations. Such additional information will help us determine with greater accuracy the amount of time and resources that will be needed to conduct inspections and other compliance-related activities.

FDA conducts on-site inspections of tissue establishments to determine compliance with FDA regulations. As a result of these inspections, FDA has taken the following actions: Fifteen orders for retention or recall, six warning letters, and nine opportunities for voluntary corrective action letters. Further, the number of voluntary recalls of banked human tissue have increased over the past 7 years, from approximately three in 1994 to 24 in the year 2000.

FDA is concerned about pooling of tissues from multiple donors during processing. In general, FDA believes that the risks associated with pooling tissues from multiple donors at this time appears to outweigh any identified medical benefits. Risks include possible exposure and cross-contamination from one tissue to another, such infectious disease agents as viruses, bacteria, fungi, and prions.

FDA currently can address these issues based on our communicable disease provisions of Section 361 of the Public Health Service Act.

In order to successfully implement agency plans for the regulation of human tissues, FDA has involved tissue establishments and medical professionals in many of our public discussions. In the future, FDA intends to provide opportunity for additional public discussions on issues related to cellular and tissue-based products.

FDA can assure the Subcommittee that we are committed to establishing a regulatory framework which will not only help ensure the safe use of human tissue for transplantation, but also allows the development of this technology and instills public confidence. While FDA has taken many steps towards this end, we realize that more remains to be done. We look forward to working with this Subcommittee regarding the regulation of tissues and I am happy to answer any questions you may have today.

Senator COLLINS. Thank you, Dr. Zoon.

I want to talk to you further about two issues that have arisen today. One is pooling, the other is repeat testing. You mentioned in your statement that you have just concluded that the FDA believes that the risks of pooling outweigh the benefits. Could you explain further why pooling could be problematic from a safety standpoint?

Ms. ZOON. Yes, I would be happy to. When you pool products, if there is just one component of a mixture of components, that component could have the ability to raise the infectious disease or communicable disease risk to the entire batch of product processed together, and that is why we are concerned about this. It is very important in those considerations to make sure that risks such as this are minimized.

Senator COLLINS. So it is a cross-contamination issue?

Ms. ZOON. That is correct.

Senator COLLINS. The FDA has recently proposed regulations that would require tissue banks to employ specific good tissue practices. As part of those good tissue practices, has the FDA banned pooling or prohibited pooling?

Ms. ZOON. The current proposed regulation states that the agency does not permit pooling, although it does give an opportunity for exemption or a waiver for this if one can validate that their procedure would inactivate certain infectious agents.

Senator COLLINS. With regard to repeat testing, we have heard very disturbing testimony today from the Office of the Inspector General that some tissue banks, when they do not like the first result that they get on a batch of tissues, they just keep testing it in the hopes of getting the all-clear result. That, to me, is just incredible and totally unacceptable. Has the FDA proposed anything that would deal with that issue?

Ms. ZOON. Yes. You cannot test a piece of tissue into compliance.

Senator COLLINS. That is a good way to put it. Is there any specific regulation, though, or part of the good tissue practices that speaks to that issue?

Ms. ZOON. Yes. Under our current regulation, which is the 1997 final rule on tissue, that addresses at least this issue with respect to HIV and hepatitis B and hepatitis C, and the same would be

true with respect to the donor suitability proposed regulation that would expand the infectious agent testing. But that provision is true. You cannot test a piece of tissue into compliance.

Senator COLLINS. Dr. Zoon, if you find that a tissue bank is engaged in these questionable practices, does the FDA have the authority to prohibit the tissue bank from operating?

Ms. ZOON. Well, we have the authority—under our current regulation, we can deal with the products. In the proposed regulation, it also allows the agency to deal with the establishment itself.

Senator COLLINS. We had testimony today from the private accreditation association AATB in which I asked the CEO whether or not there is any reporting from the AATB when they revoke an accreditation, whether that information is conveyed to the FDA, because, clearly, there is a serious problem with a tissue bank if it loses its accreditation. Now, I recognize that there is a difficult balance here because the accreditation is voluntary and we want, presumably, to encourage more tissue banks to become accredited. But it seems to me that once a tissue bank is accredited, if the AATB finds grounds that are serious enough that causes the Association to revoke its accreditation, that there should be some sort of report to the FDA. Would you agree, or what would your views be on that?

Ms. ZOON. Well, certainly, if the AATB wanted to provide that information to the agency, the agency would certainly look at that information and weigh that in on terms of prioritizing some of our inspectional proceedings.

Senator COLLINS. Would it be helpful for you to get that information? Would it be a red flag to you that perhaps you need to send an FDA inspector in? The problem here is AATB may discover a problem way before the FDA does, yet AATB's revocation of accreditation does not do anything to prevent that tissue bank from operating, whereas the FDA has the ability to stop the tissue bank from operating.

Ms. ZOON. Right. Well, we would welcome any information that could and would help facilitate our jobs.

Senator COLLINS. Let me talk to you a bit more about the FDA's inspection process. According to the HHS Inspector General, FDA performed 188 inspections which identified 98 problems and they resulted in 26 notices of official action. There were also 72 notices calling for voluntary corrective action. Could you explain to us what a notice of official action is and how serious that is on the scale of approaches or responses that the FDA could take?

Ms. ZOON. Right. Well, there are three levels of evaluation of an inspection. One is the one you would hope for, which is no action indicated, and that is called NAI.

And then you have a voluntary action indicated, which means that there were observations of concern that required the particular sponsor to take corrective action on their own in order to facilitate remedying these, and these would be checked as follow-up on the next inspection and they would address those issues to the agency in the interim.

OAI is the most serious classification of an inspection. It means official action indicated. And generally, this can result in a number of things. The most normal follow-up from something like this

might be a warning letter that the agency would then issue to the company in which this was observed. They would need to respond to this, as well.

Senator COLLINS. Could you give us some examples of the kinds of violations that would trigger a notice of official action?

Ms. ZOON. Yes. Improper infectious disease testing and issues related to quarantining tissues that might lead to increased risk of improperly using those tissues. Those are two examples. There could be many others, depending on the proper screening of a particular tissue. As you know, most of our regulations and issues are focused on communicable disease testing. So really those things that would increase the risk of infectious disease transmission would be the things that we would focus on.

Senator COLLINS. So these are pretty serious violations that could pose a significant threat to public health or to at least the recipient of the donated tissue, is that a fair assessment?

Ms. ZOON. Yes.

Senator COLLINS. You mentioned that FDA has included a 10 percent budget increase to assist with tissue inspections and your expanded regulatory process. Given the large number of tissue banks that have registered with FDA, which, based on our conversations with FDA and other experts, exceeded what was expected, do you believe that the FDA can conduct adequate inspections of these tissue banks?

Ms. ZOON. Well, as you know, there is not enough resources to inspect tissue banks biennially, which is where ultimately we would like to be, and we have diverted some of our blood and plasma inspectional resources to do some of the tissue inspections that we are currently doing today. So we are trying to balance many responsibilities to do the best job we possibly can. And in order to do this, we really have developed a risk-based strategy for doing tissue inspections, so those that we believe are the highest risk get the most attention and those with the lower risk are not.

So the risk strategy that we are currently using are those banks that have had a violative inspection have the highest priority. The next-highest priority are those which are tissue banks that have not been accredited and have not been inspected yet. Then the next level is the laboratories that actually do the infectious disease testing of these. And then it goes down to those tissue banks that have voluntary action indicated, and then tissue banks that are accredited and not inspected, and then finally the last tier is those banks that have not had problems.

Senator COLLINS. The problem is, it is difficult for you to set those priorities and say that the last tier are tissue banks that have not had problems when nobody even realized that there were so many tissue banks out there, and when scores and scores of tissue banks, perhaps 100 tissue banks, have never been inspected or regulated by anybody. So how can you tell that there are no problems? I mean, unless you have a plan to inspect every tissue bank once every 2 years or once every 3 years, how can you conclude that—how can you even rank them?

Ms. ZOON. Well, no. The ranking was based on—your point is well taken, that you would like to have the database of having biennial inspections for a while. But with the existing resources, we

wanted to use our resources most wisely to make sure that when we have a problem—and I forgot to mention, the second priority is actually for-cause inspections. I misspoke in the previous one. So the first is those with violative. The second is for cause, where that means we get a report from somebody who says that there is a problem in a particular bank so we can respond to that.

But your point is that with the registration and listing rule, we will now have the opportunity to have actually an inventory of what is out there, so now we will be in a position to finish the inspections of those banks that we have never inspected that are now registered. Our goal for this fiscal year is to do the remaining banks that were identified by the IG that had not been looked at by the FDA and any other banks we may find from the registration and listing provisions that have not yet been inspected by the FDA. So those are our two areas where we are really going to focus.

Senator COLLINS. The problem is that OIG identified 118 banks that have been inspected, if memory serves me correctly. OIG thought that the total universe was about 150. We now know it is about 350. It is over double what anyone expected. It seems to me until you have a plan to inspect every one of those 350 tissue banks, that it is just a shot in the dark. It is just throwing darts as far as trying to figure out what are the high-risk tissue banks.

Ms. ZOON. I might just make a comment that the 368 registered components actually includes each location of a tissue bank. So if a tissue bank has more than one location, it will register based on the number of locations. So I just want to make sure, some of those numbers—and there is also, if there are distributors or procurers, they will have to list separately and register separately. So when we use the term tissue banks, we need to be a little bit careful because there may be multiple locations in some of these, and I just thought I would point that out, so the numbers may not be as off as they might indicate.

Senator COLLINS. It still strikes me that is an enormous undertaking for FDA and yet an absolutely critical one in terms of protecting the public health and also in ensuring that the families of potential donors feel comfortable about donating tissue and do not experience some of the problems that we have heard today that are very disturbing.

Ms. ZOON. I think we would agree that we believe this is an important part of our program, and I think the inspectional programs have been extremely valuable in helping us deal with the scope of issues with respect to the tissue banks that are important to the Congress.

Senator COLLINS. I want to just ask you about one specific inspection that led to a warning letter, and it is going to be Exhibit 2[1] in your book, also the notebook that is right there should have it. I will give you a moment to find it.

[Pause.]

Senator COLLINS. It is a warning letter that the FDA sent to a particular tissue bank, Pacific Coast Tissue Bank, on April 21 of last year. The letter documents Pacific Coast's failure to develop and follow written operating procedures, its failure to ensure prop-

[1] See Exhibit No. 2 which appears in the Appendix on page 112.

er donor testing, its failure to maintain complete records. In this letter, the FDA also sets out its disagreements with Pacific Coast's response to a prior letter and requests that the tissue bank notify FDA of the corrective measures it will take to prevent a recurrence of similar violations.

What worries me about this case is it seems to me that this tissue bank has been found wanting on very serious grounds, such that this is the second letter that the FDA has had to send to this particular tissue bank. Could you tell me if the FDA has inspected Pacific Coast Tissue Bank for compliance since this letter was sent in April 2000?

Ms. ZOON. I am aware that the FDA will be inspecting Pacific Coast Tissue Bank this year, and it is inappropriate for me to tell you when in public.

Senator COLLINS. I can understand that. But what concerns me is it is over a year later and we do not have any guarantees that this tissue bank has corrected some very serious deficiencies that the FDA inspection identified. What process does the FDA use to make sure that serious problems are remedied?

Ms. ZOON. There are several. The company must respond to the warning letter, so that information comes back to the agency for review, and certainly the response of that will be evaluated and looked at, and any follow-up issues, such as the issues pointed out in this warning letter, will have direct follow-up with respect to the Pacific Coast Tissue Bank on their next inspection. So then there can be a series of other actions that the agency can take with respect to this particular company and we will be looking into our options, depending on the finding.

Senator COLLINS. One final question on behalf of Senator Durbin, who is unable to attend this part of the hearing. Senator Durbin sent a letter in January to Dr. Henney, who I realize is no longer Commissioner, but asking for a breakdown of costs for implementation of the new rules.[1] Are you familiar with that letter?

Ms. ZOON. Yes, I am.

Senator COLLINS. Has the FDA responded to that request?

Ms. ZOON. The FDA has prepared a response to that request. It has been cleared by the FDA and now it is being reviewed within the Department.

Senator COLLINS. I would ask that you share that request with the Subcommittee.[2]

In closing, I just want to encourage you, if you need more resources to make sure that our Nation's tissue supply is safe, you should ask for them. We know that this is a big task. We know that there are far more tissue banks than ever was anticipated, that the registration process would bring forth, and there is a certain frustration on the part of the Members of this Subcommittee that the FDA has been very slow in acting in this area.

If we want to increase the supply of tissue, and that is a goal that many of us share, of encouraging more donations for life-enhancing procedures, we need to make sure that we can both assure

[1] See Exhibit No. 2 which appears in the Appendix on page 112.

[2] As of July 2001, the Subcommittee staff was informed by the Food and Drug Administratoin that the response letter to Senator Durbin's January 2001 letter, has not yet been cleared for external release by the Department of Health and Human Services.

the public that the donated tissue will be treated with dignity and respect, and also that it is safe for the recipient. And until we have a vigorous regulatory structure in place, I do not think we can make those assurances, and that is troubling to me because I want to see this very positive trend of more tissue and organ donations increase.

So we look forward to working with you and making sure that you have the support that you need. I would also ask that you provide the Subcommittee in writing any suggestions for legislative changes that you might have. We have heard a number of suggestions this morning, of making the law more similar to that for organ donation, and we would welcome your suggestions.

Ms. ZOON. Thank you very much.

Senator COLLINS. Thank you. I want to thank all of our witnesses for coming today and sharing their perspectives on the tissue bank industry and the adequacy of Federal regulatory oversight. We entitled this hearing, "Tissue Banks: Is the Federal Government's Oversight Adequate?" and based on what I have heard today, I think the answer to that question is no, that it is improving, that the new regulations are going to make a big difference, but until we match the new regulations with an aggressive inspection process and until we in Congress work with the administration to provide the resources necessary, it appears to me that there are still going to be holes in the safety net of regulation.

I especially want to thank the Health and Human Services Office of Inspector General for its very comprehensive and helpful reports, which have shed some light on the state of the tissue bank industry and which formed the starting point for our discussions today. But the testimony of all of our witnesses has been extremely helpful.

I finally would like to thank the Members of my Subcommittee staff who have helped prepare for these hearings, especially Claire Barnard, Barbara Cohoon, Eileen Fisher, Chris Ford, and Mary Robertson. They have worked very hard on this area. Thank you.

The Subcommittee is adjourned.

[Whereupon, at 12:03 p.m., the Subcommittee was adjourned.]

APPENDIX

Testimony
Before the Permanent Subcommittee on Investigations
Committee on Governmental Affairs

United States Senate

"Examining Practices of the Tissue Bank Industry"

Testimony of George Grob
Deputy Inspector General for Evaluations and Inspections

May 24, 2001
9:30 a.m.
342 Dirksen Senate Office Building

Office of Inspector General
Department of Health and Human Services
Michael Mangano, Acting Inspector General

Testimony of
George F. Grob
Deputy Inspector General
for Evaluation and Inspections
U.S. Department of Health and Human Services

Good Morning, Madam Chairman. Human tissue is an important source of medical treatment, benefitting thousands of Americans every year. However, concerns have been raised about current practices and the future developments of this field.

Last year, more than 750,000 pieces of human skin, bone, and heart valves were distributed for transplantation. This does not include eyes and other types of human cells or tissue. It came from over 20,000 donors and their families who so generously made this important gift at the time of a loved one's death. These families and a relatively small number of tissue banks, who procure, process, store, and distribute tissue, have been the foundation of this medical service for many years. Recently, however, the tissue banking industry has expanded and become more complex. Tissue is being put to new uses, and processing has grown more sophisticated. Entrepreneurial firms have stepped in to develop and market new products and treatments from human tissue. Unfortunately, standards of practice have not kept pace with this growth and development.

Earlier this year, the Office of Inspector General issued two reports on tissue banking. We have provided copies of both reports to the members of this Subcommittee. Our reports address the adequacy of the quality assurance oversight mechanisms for this industry and the extent to which donor families can make informed decisions about consenting to donation. I will discuss both these facets of tissue banking and offer recommendations to improve them.

OVERSIGHT OF TISSUE BANKING

External oversight of the tissue banking industry is currently limited, although recent actions by the Food and Drug Administration have improved the situation. Regulations now under development will result in even stronger, and much needed, supervision of the industry. Portions of the industry have developed their own accreditation system, and two States license and inspect tissue banks. However, as of now, serious gaps remain.

The Food and Drug Administration

The Food and Drug Administration (FDA) focuses on preventing transmission of communicable disease by requiring donor screening and testing. No new cases of disease transmission through human tissue have been identified since the FDA's initial regulation of tissue in 1993. This absence of new cases points to significant strengths and accomplishments in the current system. Nevertheless, we identified situations that show the need for continued vigilance and monitoring. For example, FDA inspectors have found serious deficiencies in tissue banks' screening and testing practices where they have conducted inspections. It is reasonable to believe that similar problems exist where they have not conducted them.

Inspections. FDA has conducted 188 inspections of 118 tissue banks since 1993. However, at the time of our study some tissue banks had never been inspected by FDA. We found at least 36 tissue banks that have never been inspected, out of 154 tissue establishments that we identified. FDA has indicated that because regulation of tissue banks is an unfunded mandate, it has had to borrow resources from other programs to carry out these inspections.

FDA lacks a prescribed cycle for reinspection of tissue banks. At the time of our study, out of 118 tissue banks that FDA had inspected, 68 were inspected only once. Due to limited resources, the agency has established a priority list for follow-up inspections, focusing on banks with the most serious deficiencies.

Since we issued our report, FDA has begun inspecting all known tissue banks.

Registration. At the time of our study, the number and location of tissue banks were unknown. Information was unavailable about the number of tissue banks in operation and the products they produce and distribute. Subsequently, on January 19 of this year, FDA published a final rule requiring the registration and listing of all tissue banks.

Quality Control. FDA has also been developing two additional regulations that would provide stronger assurances regarding the handling and use of human tissues. The first, on good tissue manufacturing practices, was issued as a draft on January 8 of this year. The closing date for public comments was May 8. The second, on suitability of donors and tissue products, had been issued as a draft rule in September, 1999. The comment period was extended through July of last year, and comments are now being analyzed. The scope of FDA's current regulation is limited to donor screening and testing to prevent transmission of HIV and Hepatitis.

The American Association of Tissue Banks

The American Association of Tissue Banks (AATB) conducts a voluntary accreditation program. It currently accredits 58 tissue banks. Accreditation addresses not only donor screening and testing practices, but operational and organizational aspects, such as qualifications of tissue bank personnel and banks' safety practices, equipment testing, facilities, labeling, and quality assurance programs. Some banks have failed to meet basic standards of the AATB and have been denied accreditation.

Seeking accreditation is purely voluntary. We identified 90 tissue banks that are not accredited. These banks are under no obligation to meet the standards or policies set by the association, and for many banks there is no incentive to seek accreditation.

States

New York and Florida are the only two States to license and inspect tissue banks. In addition to screening and testing, these States require banks to report adverse incidents. They also address areas such as how tissue is recovered and tracked, emergency procedures, equipment standards, conflict of interest, community involvement, labeling standards, laboratory testing, and

disposition of unused tissue. A few States, including California, Georgia, and Maryland, require tissue banks to be licensed by the State.

Overall

Until FDA's proposed rule on good tissue practices is finalized, tissue banks have no external requirements for quality and handling of tissue if they are not accredited by AATB or licensed by New York or Florida. Of the 154 tissue banks we identified, 67 are neither accredited by AATB nor inspected by Florida or New York.

Recommendations Regarding FDA Oversight

In our reports, we called upon the Food and Drug Administration to take a number of steps to ensure the safety and quality of tissue transplanted in this country. Needless to say, FDA should move forward with pending oversight efforts. As noted earlier, we recommended that FDA set a realistic, yet aggressive, date by which it would complete an initial inspection of all tissue banks and determine an appropriate minimum cycle for tissue bank inspections.

We also believe FDA should examine whether there are areas in which oversight can be coordinated with other entities. We called on FDA to work with States and professional associations to determine in what areas, if any, oversight activities could be coordinated. If this approach were appropriate, it could help maximize agency resources and reduce redundant regulatory burden on tissue banks.

DONOR CONSENT

Expectations of Donor Families

Donor families have some basic expectations about their decision to donate a loved one's tissue. These relate to the way the donated tissue is used and to the respect of the donor, even after death.

Intended Use and Supply. Families expect that their loved one's tissue will be used to improve the lives of people with medical needs, either through transplantation or medical research. For many families, donation is seen as a way of creating something positive from the death of their loved one. However, concerns have been raised that some tissue may be used for purposes other than those intended by the donor. For example, donors may intend or believe that their skin will be used for the treatment of burn victims. However, in some cases it might be used for elective cosmetic surgery. Some believe that this might contribute to a shortage of skin for essential medical uses. However, there is no national system for tracking the availability and use of tissue and determining where there may be a shortage. It is not clear how much tissue goes for cosmetic uses or whether such use contributes to a shortage.

After we began our inspection, both the American Association of Tissue Banks and the American Burn Association published results of surveys which they took to determine the

adequacy of the supply of skin for burn surgery. Their reports indicate that supplies were tight, with surgeons having to delay or make do with alternative treatments in some cases. However, these surveys were not detailed enough to know if any burn victims were unable to get the treatment they needed, or if any supply shortages occurred as a result of diverting skin to lower priority usages.

Respect. Families we talked to emphasized their desire that the donor will be treated with respect during the surgical processes of tissue recovery, during funeral preparations, and while tissue is processed, distributed, and transplanted. Once it has been processed, however, tissue is treated more like a commodity than a donation. The packages in which human tissue is supplied—bottles, vials, containers shrink-wrapped in plastic—resemble many other medical supplies. The packaging does not indicate the special nature of the donation that underlies the enclosed materials. Nor do marketing materials indicate the nature of the donation. These product brochures look like typical medical supply catalogues, contributing to a perception that tissue is no different than any other supply. Neither of these practices reinforces the respect that donor families expect to be given for the donated gift of human tissue.

The Process of Obtaining Consent and Donations

Current practices in requesting consent raise concerns about what information is provided to families and how this is done.

Circumstances and Timing. Tissue banks must obtain consent for donation within hours following the death of a loved one. The recent, often sudden and unexpected, death of a loved one means that families may be upset at the time they are asked for consent to donation. In the face of sudden tragedy, they may simply be unable to understand detailed information about a topic as complex as tissue donation. Because of the circumstances, detailed discussion about multiple aspects of tissue donation and tissue banking—recovery, processing, distribution, commercial relationships—may go well beyond the capacity of families to comprehend what they are hearing.

At the same time, families may not wish to receive detailed information about tissue banking. Families may want to consent to donation, but do not want to hear specific details about the invasive surgical procedures associated with recovering tissues. As the mother of one tissue donor told us, "I really didn't need any more information than what was provided; frankly, I wouldn't have been able to deal with much more at that point." At the same time, however, much information needs to be communicated to the family at the time of consent; at a minimum, authorization for removal of specific tissues is required. Families also must agree whether the tissue may be used only for transplantation, or for other uses such as research and education.

Request by Telephone. Tissue banks often request consent over the telephone, rather than in person. In most cases, tissue banks make these requests after the family has left the hospital. Tissue bank staff told us that it is more productive to give the family time to return to the familiar surroundings of home, rather than the coldness of a hospital.

Staff Supervision. Many tissue banks rely on staff from other organizations to obtain consent. These external requestors could be staff from organ procurement organizations, telephone triage agencies, hospital staff, chaplains, or social workers.

Those banks that make the request directly are able to train and monitor the performance of their own staff. However, training and oversight are much more limited for external requestors. Those training programs tend to be shorter, and few tissue banks provide continuing education or follow-up training to these requestors. Tissue banks also do less direct monitoring of these requestors' performance, and we found that few tissue banks actively assess the performance of external requestors.

Written Materials. Tissue banks provide donor families with little written material at the time of donation. Few tissue banks routinely give families a copy of the form that they have signed, giving their consent to donation. The consent form is more than a receipt. It is the legal authorization governing the removal of tissue and specifying purposes for which the tissue may be used.

Following donation, it is general practice for tissue banks to send families a letter thanking them for the gift and expressing condolences. Aside from this letter, tissue banks provide little additional written information to families about tissue use, processing, or other entities with whom they have financial arrangements.

Because, as we noted above, families may not understand everything that is told to them at the time of donation, more information may be beneficial at a later date, so that the family could refer to it as desired.

Standards for Obtaining Consent

Until recently, standards governing how families are approached and what they are told about tissue donation have been sparse. Neither Federal law, such as the National Organ Transplant Act, nor the individual States' Anatomical Gift Acts address what information tissue banks should provide in obtaining consent. However, some initial progress toward development of standards has occurred.

Donor Family Advocates. Last Fall, the National Donor Family Council proposed key elements that should be included when tissue banks approach families for donation. These elements include:

- Explanation of how tissue is recovered, processed, stored and distributed;
- Explanation that the tissue may be used or modified for transplantation;
- Explanation that the family may limit or restrict the use of tissue; and
- Requirements that the consent form be reviewed with families and that a copy be offered to the family.

Tissue Industry. Also in the midst of our inquiry last Fall, The American Association of tissue Banks, the Association of Organ Procurement Organizations, and the Eye Bank Association of

America issued a joint statement that addresses elements of informed consent. This statement encourages the provision of information to families including:

- Identification of specific tissues that are being requested for donation;
- Explanation that retrieved tissues may be used for transplantation, therapy, research, or education; and
- A general description of the recovery process.

The statement also recognizes that families may seek additional information about donation. If so, additional explanations should be provided to address such issues as:

- The possibility that the gift may take a different form than originally recovered;
- Transplantation may include reconstructive and aesthetic surgery; and
- Multiple organizations (non profit and/or for profit) may be involved in facilitating the gift.

The full text of the statements from both of these groups is in our reports.

Recommendations Regarding Donor Consent

We have called upon the Department of Health and Human Services to provide assistance to efforts to develop standards. For example, we encourage the Health Resources and Services Administration (which houses the Division of Transplantation) to work with donor family groups representing the tissue banking industry. We believe that they could help these organizations develop guidelines for conveying information to families about tissue donation. We also have called upon the Health Care Financing Administration to address informed consent for tissue donation through its oversight of the organ procurement system.

Although the Department can provide guidance and assistance, the basic responsibility for ensuring that families are informed about all aspects of tissue donation must rest with the tissue banks themselves. The tissue banks and their staff and contractors are the ones who interact with the donor family at the time of requesting consent.

Because each case and each situation is unique, those who interact with families to request donation must have the flexibility to recognize the individual concerns present at that moment in time and to adapt their discussion to the unique needs and responses of each donor family. We do believe, however, that some essential precepts should govern the interaction that tissue banks have with families.

Written Materials. First, at the time of obtaining consent, tissue banks should provide families with written materials that provide fuller disclosure about the uses of tissue and the nature of the gift. Tissue banks should give written material to families at the time the banks ask for consent to donation, or in the days immediately following the request. The material would serve as one way to supplement the information that requestors give the family during their conversation about donation. At the same time, it would provide requestors with flexibility to adapt that conversation to the unique needs and responses of each donor family. At a minimum, this material should include:

- A copy of the signed consent form;
- Written material on how to follow up with the tissue bank if concerns arise;
- A full description of the uses to which donated tissue may be put; and
- A list and description of other companies and entities with which the bank has relationships for processing and distributing tissue.

Recognition of Donors. Second, tissue processors and distributors should ensure that information accompanying their product clearly indicates it is derived from donated human tissue. Such a step would require only minor changes in packaging and marketing materials. However, it would go a long way towards showing ongoing respect for the donor, the family, and the gift of donation. Tissue banks should:

- Indicate clearly on all tissue packaging that the contents are derived from donated human tissue; and
- Indicate clearly on all marketing and informational material that these products are derived from donated human tissue.

Conduct of Requestors. Third, tissue banks should foster greater accountability for the performance of those who request consent for donation. Responsibility for ensuring that requestors are providing accurate, sensitive, and appropriate information rests with tissue banks and the processors with whom they work. These organizations should:

- Ensure that requestors—both from their own organizations and elsewhere—are fully and appropriately trained;
- Provide continuing education for requestors; and
- Conduct an ongoing assessment of requestor performance to ensure they are providing full and accurate information to families approached for donation.

Public Disclosure. Fourth, the tissue banking industry should work with groups representing donor families to explore a process for periodic public disclosure about tissue banks' financing. Such disclosure would respond to family and general public concerns about knowing the sources of funding for tissue banks and other entities with which the bank has financial arrangements. The examination would consider whether financial information would be useful as part of a package of information provided to donor families. The examination would consider:

- What types and how much financial information would be useful for families and individuals making decisions about donation;
- The advantages and disadvantages of disclosure, including the potential impact of financial disclosure on donation;
- Whether the information should be provided in all cases, or only if requested by a family; and
- The content, style, and format of disclosure.

Supply and Usage. The tissue banking industry should refine and periodically repeat its surveys regarding the availability of tissue. The refinements should provide more precise information about the extent to which patients' needs are being met. Tissue banks should also try to obtain more information about the uses made of the tissue that passes through their operations. This will enable them to provide better information on this subject to donors. Finally, some

upgrading of inventory measurement and control systems should be adopted within the industry, probably through automated data systems, in order to allow for more effective sharing of tissues among tissue banks to meet situations where supplies are low and needs are critical.

CONCLUSION

Both FDA and the tissue banking industry have made progress toward improving the consent and donation processes and quality assurance oversight mechanisms for processing human tissue. But gaps remain. The recent gains need to be rounded out and solidified. Standards of operation still have to catch up with the growth and complexity of this health care sector. I hope the findings and recommendations in our reports will be helpful in this regard.

STATEMENT OF
THE AMERICAN ASSOCIATION OF TISSUE BANKS (AATB)
BEFORE A HEARING OF
THE PERMANENT SUBCOMMITTEE ON INVESTIGATIONS
COMMITTEE ON GOVERNMENTAL AFFAIRS
UNITED STATES SENATE
MAY 24, 2001

Senator Collins and Members of the Subcommittee,

My name is Bob Rigney. I am the Chief Executive Officer of the American Association of Tissue Banks, more commonly referred to as the "AATB." I am accompanied here today by our President, Dr. Richard Kagan. Dr. Kagan is the Medical Director of the Ohio Valley Tissue and Skin Center. He is also Assistant Chief of Staff at the Shriners Burns Hospital in Cincinnati and the Director of The University Hospital's Burn Special Care Unit.

On behalf of our members and the people we serve, I want to thank you for the invitation to appear here today. We welcome this opportunity to testify about this rapidly changing and critically important field of tissue banking and tissue transplantation.

As we begin our discussion, we need to recognize that tissue banking is only one element, indeed the first segment on the entire spectrum of tissue transplantation. Simply put, tissue banking involves the retrieval of life-enhancing, and sometimes life-saving, human tissues from living or cadaveric

donors; the processing and storage of those tissues; and their distribution for transplantation into patients who need them.

Today, human tissues are used in a host of medical procedures, and new clinical applications are being developed. Musculoskeletal tissues are utilized in spinal procedures, such as cervical fusions, to support the spinal column. Musculoskeletal grafts are also used in ligament and sports medicine procedures, in total joint replacement procedures, and in fracture management and general orthopaedics.

Cardiovascular tissue is employed to replace and repair heart valves and arteries. Soft and hard tissue grafts are used to correct periodontal defects and in craniofacial reconstruction. Soft tissue grafts are also used in reconstructive urological procedures, and human skin is utilized as a wound covering for burn and trauma victims.

In the past two decades, human cellular and tissue-based products have improved and/or saved the lives of millions of our fellow citizens. Not too long ago, only animal or synthetic valves were available to treat children with certain cardiovascular defects. Today, those children are transplanted with human heart valves. Those valves grow with the child, negating the need for any additional operations to replace the valves.

Not many years ago, men, women and children with bone tumors faced amputation of their limbs to remove those cancers. Today, surgeons can remove

the affected bone and replace it with a human bone. Many of these patients go on to resume normal lives.

There are a multitude of other examples that I could cite where human tissue transplants have helped change and even save the lives of our neighbors, friends and loved ones. We need to be certain, therefore, to first do no harm, to do nothing that discourages Americans from donating their organs and tissues.

Let me now turn to and address the items on which you asked us to comment.

1. The role of the American Association of Tissue Banks (AATB) in the tissue banking industry.

The AATB is a voluntary, professional, nonprofit, scientific and educational organization. The Association was founded in 1976 and is organized under Section 501(c)(3) of the Internal Revenue Code. We are not affiliated with, supported by, or chartered by the Government. We are not a trade association, and we do not employ a lobbying staff.

The AATB's mission is public health. We are dedicated to ensuring that human tissues intended for transplantation are safe and free of infectious disease, of uniform high quality, and available in quantities sufficient to meet national needs.

To further our mission, we publish the only private *Standards* for tissue banks, the AATB's *Standards for Tissue Banking*. This document is the recognized authoritative source for the industry. For more than 15 years, we

have also operated our own voluntary Accreditation Program to ensure that tissue banking activities are being performed in a professional manner in compliance with these *Standards*. All of our institutional members must be re-accredited every three years. Accreditation includes, among other requirements, an on-site inspection by independent inspectors, most of whom are former Food and Drug Administration (FDA) compliance officers, and none of whom are affiliated with any tissue facility. In addition, we offer a certification program for tissue bank personnel.

AATB members also adhere to the Association's *Ethical Principles* (adopted in 1994), our *Ethical Guidelines for Commercial Activities and Advertising* (adopted in 1996), and the *Guidelines on Tissue and Cell Resource Sharing* (adopted in 1996 and amended in 2000).

The Association's membership currently includes nearly 1,200 individual members and 74 accredited tissue banks engaged in the recovery, processing, storage and distribution of human tissue. Not every tissue bank is a member of the AATB, but most of the major tissue banks in the United States have obtained AATB accreditation. In fact, we believe that at least a majority of the tissue banks in the U.S. are AATB accredited.

With the exception of ocular tissue, we also believe that AATB members provide most of the commonly used structural tissues for clinical use in the United States. In 1999, for example, the year for which the most recent data is

available, the number of bone allografts distributed by AATB accredited tissue banks totaled 523,197, more than double what was distributed five years ago.

In addition, tissue donations are increasing significantly. AATB accredited banks recovered tissue from 17,010 donors in 1999. This represents about a 274% increase in donations in the past five years.

It is important to recognize that for nearly a decade following the publication of our first edition of *Standards* in 1984, the AATB was the only organization overseeing tissue banking in the United States. Today, 17 years later, our *Standards* are still the most comprehensive and authoritative source in tissue banking. Over those years, we have compiled a remarkable record of donor service and patient safety.

All of our programs and activities focus on respecting and honoring the tissue donor and his or her family and the safety of the recipient patients. That is why we are constantly reviewing and improving our *Standards*, programs and operations. AATB's response has always been to be open-minded and to adapt in response to changing circumstances.

2. *Instances in which AATB has denied accreditation to tissue banks.*

At the outset, it is important to recognize that the AATB's Accreditation Program is an educational program, not a regulatory enforcement program. Our goal is to bring tissue banks into compliance with the *Standards*, not to penalize them for being out of compliance. We process approximately 20-25 accreditation applications annually.

The accreditation process takes about one year for a tissue bank to complete. The applicant for accreditation or re-accreditation must complete and file a formal application along with a pre-inspection checklist, which is nearly 120 pages long. The tissue bank must also submit a complete copy of its Standard Operating Procedures (SOPs), which are reviewed by the Accreditation Program staff for compliance with the *Standards*.

If the documentation is determined to be in order, an on-site inspection by one of our independent inspectors is arranged. After the inspection, the inspector files a written report. That report is reviewed, blinded, and suggested recommendations, if any, are prepared and presented to the Accreditation Committee.

The committee can recommend that accreditation be approved or denied. If corrective action is necessary, the committee can also recommend that the bank be given a Level A (no re-inspection necessary), or a Level B (re-inspection necessary), and the bank has 60 days to take the necessary corrective action(s). The committee can also recommend that a tissue bank's accreditation be suspended for 90 days while the corrective action is being taken. The Board of Governors makes the final decision on every accreditation application.

Since the AATB's Accreditation Program began in 1986, a total of 116 tissue banks have been accredited. Of that number, 43 tissue banks are no longer accredited. Approximately 23 of the 43 banks no longer accredited have either closed, merged with other banks, or have not sought re-accreditation.

The remaining 20 tissue banks, failed to demonstrate compliance with AATB's *Standards*. Of these 20 tissue banks, 14 were denied accreditation following re-inspections. Inspections of four banks were aborted because of obvious non-compliance at the time of inspection, and these banks withdrew from the accreditation process. Two additional banks would have been recommended for denial, but because their current accreditation was about to expire, they withdrew from the process and let their accreditation lapse.

There has also been approximately 10 other tissue banks that applied for their initial accreditation, but were denied or dropped out of the process.

3. Views on the roles of for-profit and not-for-profit tissue banks.

AATB accreditation is open to any tissue bank that: (1) voluntarily agrees to abide by the policies and procedures of the Association; and (2) demonstrates adherence to the *Standards* by successfully completing AATB's Accreditation Program. To comply with our nation's antitrust laws, we do not now, nor have we ever differentiated between for-profit and not-for-profit tissue banks. Indeed, the current list of AATB accredited tissue banks includes both for-profit and not-for-profit entities.

In addition, the collection, processing or dissemination of financial information from our members has never been a goal or activity of the AATB. We have never collected detailed financial data from our accredited tissue banks, nor do we have any plans to do so. In fact, our attorneys have long cautioned us against soliciting or gathering this information since such activity may implicate

federal or state antitrust laws. Our mission is to establish and promulgate standards, to foster education and research, and to promote the quality, safety and availability of tissues and cells for transplantation. Our focus is the donor, the donor's family and the patients who receive the transplanted tissue.

4. Opinion regarding pooling tissue.

In 1984, the AATB published the first edition of its *Standards for Tissue Banking*. These *Standards* set rigorous performance requirements to prevent the transmission of communicable diseases. Our *Standards* are reviewed annually and amended as necessary. In January, 2001, we published the ninth edition of the *Standards for Tissue Banking*.

Over the years, the *Standards* have been revised to incorporate increasingly more stringent donor screening protocols. In addition, the *Standards* have been amended to require the use of additional FDA-licensed laboratory testing procedures for various markers of potentially transmissible diseases as they became available. Failure to comply with the standards designed to prevent infectious disease contamination and cross-contamination constitutes a material violation of AATB's *Standards*. Such a violation can result in the withdrawal of, or the refusal to renew a facility's accreditation. All tissue banks accredited by the Association are charged with knowledge of and compliance with all standards of the Association.

In all the public and private reporting about tissue banking and tissue transplantation, the greatest untold story is safety. During the past seven years,

for example, tissue banks accredited by the AATB have distributed more than two million allografts to surgeons without a single reported case of disease transmission from donor to recipient.

Safety is the basis for Section E1.200 of the *Standards,* which states that: "Cells and/or tissue from multiple donors shall not be pooled during retrieval, processing, preservation, or storage." The *Standards* (Section E1.210) also require that accredited tissue banks prepare, validate and follow written procedures to prevent "infectious disease contamination or cross-contamination by cells and/or tissue during processing."

For the past 12 years, AATB's *Standards* have prohibited the pooling or commingling of tissues to prevent infectious disease contamination and cross-contamination. This requirement was adopted after reports in the 1980's that linked the transmission of Creutzfeld-Jacob Disease (CJD) in Japan to human tissue that had been processed in batches in Germany. Since the prohibition on pooling was added to our *Standards*, there has never been a case of CJD transmission from tissue processed in the United States.

Advances in medical science and technology may soon unlock the answers that will allow for the pooling of tissues and prevent infectious disease contamination and cross-contamination. Until that time, the AATB will continue to work closely with the FDA to ensure that this exemplary record of safety is maintained.

5. Assessment of current regulatory oversight of the tissue banking industry.

Despite some media reports to the contrary, the FDA currently regulates human tissue intended for transplantation. In addition, the agency has exercised its considerable regulatory authority over tissue banks. Over the past several years, we understand that the FDA has regularly conducted more than 50 tissue bank inspections annually. In each of the past two years, the FDA has inspected approximately one-third to one-half of the AATB accredited facilities.

Tissue banks and tissue banking have been regulated by the FDA since the agency issued interim regulations that became effective immediately on December 14, 1993 (21 CFR 1270). This initial regulation required certain infectious disease testing, donor screening and record keeping to prevent the transmission of HIV and the hepatitis viruses from human tissue used in transplantation.

On July 29, 1997, the FDA issued its final regulations (21 CFR 1270) that were broader in scope. The final regulations cover all facilities that are engaged in the recovery, screening, testing, processing, storage or distribution of human tissues. They required that specified minimum medical screening and infectious disease testing be performed. Records documenting such screening and testing for each human tissue must be available for inspection by the FDA. The regulations also contain provisions for the inspection of tissue banking facilities

and for the retention, recall or destruction of human tissue for which appropriate documentation is not available.

The FDA's authority for this regulation is based on Section 361 of the Public Health Service (PHS) Act to control communicable diseases and, in particular, to "provide for such inspection...as in (the agency's) judgment may be necessary." A tissue bank that refuses to allow FDA inspection may be prosecuted under Section 368 of the PHS Act.

FDA has not extended its regulation to Organ Procurement Organizations (OPOs), nor has it covered hospitals or other clinical facilities that only receive and store human tissue for transplantation within the same facility. However, OPOs, hospitals or clinics that participate in recovery, screening, testing, processing, or distribution of human tissue in addition to storage for transplantation are covered by the regulations. FDA rules extend to all human tissue, imported and domestic.

The 1997 final rule requires tissue banks to permit inspection by authorized FDA inspectors of its facilities, equipment, processes, products and all records necessary to determine compliance with the regulation. These inspections can be made without notice; the frequency of the inspections is left to the agency's discretion. For human tissue that is imported, the importer must notify the director of the FDA district that has jurisdiction over the port of entry through which the tissue is imported or offered for import. All imported tissue must be quarantined until the FDA releases it.

Upon finding that human tissue may be in violation of the FDA's regulations, the agency may serve the tissue bank with an order for recall and/or destruction, or it may take possession of and/or destroy the tissue in question.

The 1997 regulation gives the FDA authority to inspect a tissue bank's facilities, equipment, processes, the screening and testing of donors, medical records, and products. The agency also possesses the police power to sanction tissue banks found in violation of the FDA regulations.

6. Opinion of the Food and Drug Administration's proposed rules to expand its oversight of the tissue bank industry.

The AATB has a long-standing history of support for the FDA's goal of developing an effective and reasoned program of tissue regulation. We have long advocated, and we continue to support balanced and reasonable FDA regulation of tissue banking. That support began with the FDA's first regulatory initiative, the 1993 promulgation of the Interim Rule for human tissue intended for transplantation (58 *Federal Register* 65514), whose content closely tracked our own *Standards*.

Over the years, we have provided useful information to assist the agency in addressing its public health challenges such as disease transmission. We have worked with the FDA to develop an appropriate regulatory scheme in this evolving field of medicine. We intend to continue that collegial and cooperative spirit. We also intend to continue to provide constructive criticism and recommendations for regulatory changes where we believe they are warranted.

We continue to support the FDA's concept for regulating human tissues that was published four years ago, shortly before the agency issued its final regulation. This 1997 publication was entitled, "A Proposed Approach to the Regulation of Cellular and Tissue-Based Products" (62 *Federal Register* 9721, March 4, 1997). The document outlined a regulatory framework to provide "a unified approach to the regulation of both traditional and new products."

The new FDA regulatory framework was based on "a tiered approach to cell and tissue regulation." The framework provided:

> "...only the degree of government oversight necessary to protect the public health. For products with limited public health concerns, the new framework allowed flexibility and innovation without an application review process."

The FDA's new approach to the regulation of human cellular and tissue-based products was designed to provide "more appropriate oversight," improve safety, "increase public confidence in these new technologies," and permit "significant innovation to go forward unfettered by unnecessary regulatory requirements." Cells and tissues that were extensively manipulated, combined with non-tissues, or intended to be used for other than their normal functions would be regulated as biologics or devices under Section 351 of the PHS Act (42 U.S.C. 262).

Tissue Action Plan. To implement this proposed approach and new regulatory framework, the FDA published its "Tissue Action Plan." The principal components of the FDA's Tissue Action Plan were the publication and

implementation of three separate regulations covering registration, donor suitability and good tissue practices.

A. Establishment Registration. The FDA published its first proposed rule entitled, "Establishment Registration and Listing for Manufacturers of Human Cellular and Tissue-Based Products," on May 14, 1998 (63 *Federal Register* 26744). The final rule was published on January 18, 2001 and became effective April 4, 2001. Tissue banks had 30 days to register with the FDA, so we should soon know the approximate size of the tissue banking community.

B. Donor Suitability. The second proposed rule entitled, "Suitability Determination for Donors of Human Cellular and Tissue-Based Products," was published on September 30, 1999 (64 *Federal Register* 52696). The initial comment period closed on December 29, 1999, but it was later re-opened for an additional 90 days. The FDA received more than 500 written and electronic comments on the donor suitability rule during the first comment period. A final rule has not yet been published.

C. Current Good Tissue Practices (CGTPs). The FDA's proposed rule on "Current Good Tissue Practices" was published on January 8, 2001 (66 *Federal Register* 1508). The comment period closed on May 8, 2001.

As we have noted previously, the AATB supports, in the main, the concepts presented by the FDA in the *Proposed Approach* documents. This document sets out a risk-based, tiered approach that applies regulation in direct

proportion to the perceived or likely risks to patients. Human tissues are not drugs, biologics or devices, and they should not be regulated as such.

In addition, since its first publication, the AATB has always supported the FDA's registration of tissue banks. We are pleased that registration and product listing are now a reality.

The AATB has also strongly supported mandatory donor screening and testing to prevent disease transmission as outlined in the FDA's proposed donor suitability rule. Since 1979, the AATB has had published guidelines on donor selection criteria, and donor suitability requirements have been included in every edition of our *Standards* since they were first published in 1984.

In addition, the AATB has generally endorsed the provisions of FDA's currently proposed CGTP rule that are specifically and directly designed to address the risk of disease transmission to patients. We do, however, have significant reservations about some of the provisions of the proposed rule. We have, therefore, filed extensive comments with the FDA that included recommendations for changes in this regulatory proposal.

The AATB believes that the FDA has adequate regulatory authority at this time. The agency has proposed a regulatory framework for human cellular and tissue-based products that is in keeping with the unique characteristics of human tissue. Once all three proposed rules are final, we believe that sound public policy dictates that the new regulations be given sufficient time to work before their effectiveness is evaluated.

In conclusion, let me simply reiterate that the principal focus of the AATB is the tissue donor, his or her family and the recipient patients. We respect and honor our donors and their families for helping to ensure that patients receive their life-enhancing and sometimes life-saving gifts. We are the stewards of their gifts, and we take that responsibility very seriously. We serve patients by helping to ensure the quality, safety and availability of tissues and cells for transplantation. This is our public health mission, and we are constantly reviewing and improving our *Standards*, programs and operations to address that mission.

I thank the Subcommittee for its time and attention. I will be happy to answer any questions that the Senators might have.

Testimony of William Minogue, M.D.
Chairman, Board of Directors, Washington Regional Transplant Consortium
to the Senate Subcommittee on Investigations

May 24, 2001

Good morning Chairman Collins, Senator Levin, and Members of the Subcommittee. I am Dr. William Minogue, Chairman of the Board of Directors for the Washington Regional Transplant Consortium (WRTC). I would like to thank you for this opportunity to testify before the Subcommittee today on what I consider to be a very important issue. My goal is to share with the Subcommittee WRTC's experience with the tissue banking industry.

The WRTC

The Washington Regional Transplant Consortium is the federally designated organ procurement organization (OPO) for the Washington, D.C. area. We perform organ recovery services for 48 hospitals in Maryland, Virginia, and the District of Columbia, a responsibility we have held since 1988. As you are aware, all organ procurement agencies are required by federal law to be non-profit organizations. We are a non-profit organization under section 501c(3) of the federal tax code. Each OPO has regulated functions, responsibilities, and reimbursement practices. Each OPO has a Board of Directors or an advisory board with federally mandated representation requirements. WRTC's Board of Directors includes transplant surgeons, a liver transplant recipient, a donor family member and a prominent biomedical ethicist. I am an internist.

Federal law makes one OPO responsible for organ recovery and distribution for a given geographical area. Further, federal law makes the OPO responsible for approaching the family regarding the option of organ donation. This arrangement avoids the confusion and damage that may result from having several agencies competing for the attention and cooperation of the same valuable resource -- people willing to donate organs. This same arrangement does not exist for tissue donation.

Although WRTC is not a tissue bank, in that it does not process or distribute tissue, we are a tissue recovery agency. As such, we evaluate potential tissue donors, approach potential donor families regarding their donation options, and recover donated tissue. We are designated by nearly all the hospitals in the Washington, D.C. metropolitan area to recover donated tissue for transplant, research and/or medical therapies.

WRTC has chosen to offer organ and tissue recovery services for one purpose, to protect the integrity of both the organ and tissue donation process. WRTC has made this decision for a simple reason: to the public, organ and tissue donation constitutes the same activity. People, and particularly families confronting the loss of a loved one, do not see any distinction between a person who recovers a loved one's heart, lungs, liver or kidneys and the person or organization that recovers skin, bone and eyes. A poor experience with tissue donation has a direct and adverse impact on the ability of the WRTC to carry out its responsibilities to recover life-saving organs for transplant. The reality is that each time a family decides not to donate because of confusion or suspicion, then we risk the lives of several people waiting for organ transplants.

To ensure that people remain willing to donate, they must trust the donation system. The organ and tissue recovery process affects people when they are most vulnerable. This circumstance can easily give rise to misunderstanding, causing suspicions that their loved one is being nudged toward premature death so that organs and tissues can be taken for the benefit of others. The public must have every confidence that no one will directly profit from the death of their loved ones and that the donation system will work to protect them and their loved ones from abuse or misuse.

WRTC seeks to protect the integrity of the donation process by offering a single, non-profit donation resource for hospitals and families. We have one high standard for family approach, donor screening and organ and tissue recovery. Additionally, we have, through practice and experience, developed an approach to working with donor families that respects their grief, while offering them the possibility of turning their loss into some greater good.

WRTC's Role in Tissue Recovery

Our goal is to ensure that all people who can donate are given that option and that both the donor and the donated gifts are treated with the respect that they deserve. We provide a valuable service to all members of our community: to the hospitals, to the recipients and most importantly, to the donors and their families. We are responsible for the integrity of the organs and tissues that are recovered. We are entrusted with protecting the recipient community from potentially unsafe organs and tissue. Moreover, we are accountable to the donors and their families to ensure that these gifts will be respected and utilized appropriately. This includes an open and honest discussion with the donor family about the viable options for donation.

For this reason, we endorse the recommendations brought forth in the "Model Elements of Informed Consent for Organ and Tissue Donation" developed jointly by the Association of Organ Procurement Organizations,

the American Association of Tissue Banks and the Eye Bank Association of America. We encourage its implementation industry-wide.

Organ versus Tissue Donation

Organ and tissue donation are different, both in the way they are regulated and in their clinical application. Organ donation is life-saving. However, donor organs are not readily available. There are over 75,000 people waiting nationwide for this life-saving gift. Tissue donation is life-enhancing and improves the quality of life. However, since there is no comparable shortage of tissue for donation, or urgency for tissue transplants, we impose stricter standards on tissue donor suitability. If tissue donor evaluation and recovery practices are unsafe, a recipient can be subjected to unnecessary risk. Tissue recipients must trust the recovery agency to ensure their safety. With non-profit organizations like WRTC, if a recovery places the potential recipient at risk, the recovery does not take place.

Organ donation procedures are comprehensively regulated while tissue donation is not. This absence of comprehensive regulation and oversight has caused significant difficulties, confusion, and standard variances for both organ and tissue donation because activities in tissue donation are integral with organ recovery activities and can directly impact organ donation. This, in part, is why we support the Food and Drug Administration's (FDA) proposed rules on donor suitability and good tissue practices.

An Example of Best Practices in Tissue Banking : LifeNet

WRTC has chosen LifeNet to process and distribute tissue recovered by WRTC. LifeNet is a federally designated OPO and a tissue bank fully accredited by the American Association of Tissue Banks. They are located in Virginia Beach, Virginia. We have chosen to work with LifeNet because of their high standards and because LifeNet also recognizes that tissue banking and organ donation are inextricably linked. LifeNet shares WRTC's view that, in order to protect the nation's organ donation program, tissue donation must work in concert with organ donation when dealing with hospitals and approaching donor families. We trust LifeNet as our partner because of their integrity, their quality products and services, and their commitment to donors and their families.

An Example of Inferior Tissue Banking

Regrettably, not all organizations involved in recovery, processing and distribution of tissue share our concern to maintain and respect the integrity of the donation process and the sanctity of the donated gift.

Consider the following scenario. This is an account of an actual event that occurred right here in the Washington, D.C. area.

An elderly patient died at a local hospital. In accordance with the federal regulations, the hospital referred this case to the local OPO for potential donation. The OPO determined that this patient was not a candidate for organ or tissue donation and communicated this to the hospital and the family. This decision was based on the generally accepted suitability criteria from tissue banks. Some time later, the OPO received an excited call from the local hospital. The hospital demanded to know why this patient was now being pursued for tissue donation when the family had already been told that their loved one was not a candidate for donation.

The OPO investigated this case and determined the following:

- *Another tissue recovery agency obtained confidential patient information without the hospital's knowledge.*
- *This second tissue recovery agency told the family that this tissue could be recovered for transplant purposes.*
- *The family specifically stated that they did not wish tissue to be recovered for use in medical research. However, research donation was the only realistic donation option for a patient with this profile.*
- *The second tissue recovery agency was pursuing the tissue for transplant even though the following medical conditions existed and had caused the OPO to decline the tissue:*
  - *The patient was outside the generally accepted age range for donation.*
  - *The patient had a history of cancer that had rendered the tissue medically unsuitable for donation by the OPO standards.*
  - *The patient had been dead for almost 24 hours when the second tissue recovery agency contacted the family. Twenty-four hours following cardiac arrest is the generally accepted time frame inside of which the safe recovery of tissue for transplant can occur. Tissue should not be recovered after twenty-four hours have expired.*
  - *There was evidence of a recent infection affecting this patient.*

The investigation points to the following conclusions:

A second tissue recovery agency inappropriately obtained the confidential patient information, without the hospital's knowledge or approval, and pursued the case for donation. The fact that the family had specifically stated that they did not wish to donate for research indicates that this agency was pursuing donation for transplant purposes or suggests that the agency was recovering tissue for research but not fully

disclosing that intent to the family. The second tissue recovery agency was recovering tissue in our area for a publicly traded, for-profit, tissue bank. Neither the for-profit tissue bank nor their local recovery agency had a written agreement with the hospital to recover tissue at this facility, nor were they authorized to talk to the family about tissue donation options. The local OPO was not aware of any disclosure by this second tissue recovery agency to the hospital that they were pursuing this case for tissue donation. Finally, the second tissue recovery agency did not notify the local OPO of their intent to recover tissue from this patient.

The hospital staff and the donor family were confused by the actions of this second tissue agency. The family was upset that they were subjected to conflicting and confusing information so soon after losing a loved one.

Situations like this occur when organizations that lack sufficient experience in tissue recovery and adequate regard for the donation process become involved in recovery. Furthermore, these organizations often operate from profit motives that supercede the public interest in donation. Our example illustrates, among other things, the importance of protecting donor families and patient confidentiality, as well as the necessity for clear industry standards with regards to the safety and soundness of the donated tissue. This disturbing donation event caused both the family and the donation process to suffer.

The Consequence of For-Profits in Tissue Donation

There are an increasing number of for-profit tissue processing and distribution agencies entering the donation arena. These entities need access to human tissue in order to generate revenue and are under shareholders' pressure to increase their market position to maximize profits. These organizations are not required to take the overall donation interests of the public into account and, unlike OPOs, their boards have no requirements to represent the public interest.

For-profit corporations influencing tissue donation practices hinder the overall organ and tissue donation process, and can bring about serious negative consequences. In our experience, the public interest is not being served by these developments.

- We have seen a for-profit tissue bank tell hospitals in our area that there are genuine transplantable tissue recovery options outside the criteria used by the local OPO. The WRTC standards in donor screening ensure the maximum potential for tissue donation, while maintaining the safety of the donated tissue. This practice by for-profit tissue banks has caused confusion among local hospitals regarding suitable donation options.

- We have seen a for-profit tissue bank engage in less than candid discussions with donor families regarding tissue donation options. We know that for-profit tissue banks working in our area have told donor families that tissue from loved ones over the age of 80 years old can be recovered for transplant. Tissue from these patients has a high likelihood of being unsuitable for transplantation. Given the high probability that this tissue would not be used for transplant, a family that donates tissue could justifiably feel misled and abused once they learn that the tissue was not transplanted. The consequence of these types of donation events is a wholesale public distrust of organ and tissue donation.

- We have seen a willingness by for-profit tissue banks to recover human tissues that are generally considered unsuitable for transplant. This raises concerns regarding recipient safety. As there is no shortage of human tissue for transplant, these types of recoveries constitute an unnecessary risk because they may produce sub-standard grafts and/or be at risk for infection or disease. A tissue bank's willingness to embrace this level of risk can be explained only by the tissue bank's need to increase corporate revenues and profits. Also, this need is not balanced by any countervailing obligation to serve and protect the public.

- We have observed a for-profit tissue bank create non-profit recovery agencies or use local, non-profit organizations as a conduit for human tissue into their processing and distribution facility. These non-profit groups usually have established relationships with hospitals outside of tissue donation, which gives them access to hospital facilities and patient information. Patients and their families, as well as members of the local non-profit organization themselves, are not aware that the donated gifts will go to a publicly traded corporation as raw material. Unlike OPOs, these non-profit groups will not serve the public interest in donation, nor will they work to protect the public trust in organ and tissue donation. Instead, they will serve their for-profit tissue bank. A for-profit tissue bank is under no obligation to take the integrity of organ donation into account in the activities it promotes or sponsors.

- A for-profit tissue bank increases its profits by the unrelenting pursuit of human tissue. In this case, this raw material is transplantable human tissue and those pursued are donor families. Under present conditions, we have seen donor families subjected to pressures from various third party agencies with different agendas and approach strategies at a time when these families are most vulnerable and suffering great sorrow. We are losing our ability to offer the single, sensitive, compassionate approach that OPOs have refined over the years. Families are confused by multiple donation approaches and one can imagine a family's disgust over multiple agencies competing for their loved one's body parts. This situation, if allowed to continue, will undoubtedly cause a groundswell of negative feeling against organ and tissue donation.

- We have experienced a third party tissue recovery agency responding to the tissue demands of its for-profit processor by recovering tissue from hospitals where it does not have a written agreement. This results in a third party entity gaining access to hospital facilities, patient information, and medical staff without the hospital's authorization or approval and then recovering tissue from a patient at that facility without the hospital's knowledge. These third party recovery agencies have also attempted to transfer bodies out of hospitals to locations such as funeral homes, where they are able to perform the recovery. This is all done without the knowledge of the local OPO. Hospitals hold the local OPO accountable for the quality of the donation activities. Yet, under the current system, the OPO is not always responsible for tissue donation actions. With several organizations recovering tissue from area hospitals, each using a different standard for family care and tissue recovery, both the donor and the recipient communities suffer.

In summary, WRTC has seen firsthand the adverse consequence of a for-profit sponsored tissue bank recently operating in our area. The testimony presented here today is a real account of our experiences over the past three years.

Recommendations

We strongly believe that both donors and recipients must be protected: the former by implementing an approach such as the "Model Elements of Informed Consent for Organ and Tissue Donation" and the latter by the swift adoption of the Food and Drug Administration's two proposed rules on expanded donor screening and testing and on standards for good tissue donation practices. We also endorse instituting an annual reporting mechanism for all entities, for-profit and non-profit, involved in the tissue donation process to ensure transparency. We are pleased that tissue banks have begun registering with the FDA in accordance with its newly implemented rule, and hope that comprehensive inspection of all tissue banks by the FDA will soon follow. Moreover, we agree with recent actions taken by the FDA in urging a large tissue processing and distribution organization to stop its practice of pooling tissue from multiple donors during processing. The experience with Creutzfeldt-Jacob Disease (CJD)-contaminated dura mater allograft is adequate evidence of the need to ban the practice of pooling tissue. WRTC would like to highlight two additional recommendations for your consideration.

- First, we recommend giving OPOs oversight authority over all donation activities, including family contact, donor evaluation, recovery, processing and distribution. We believe that this is essential to protecting the organ donor program and is critical for establishing mechanisms to uphold the public trust

in organ and tissue donation, especially as the organ transplant waiting list continues to grow. This would enable OPOs to ensure that all participants in the tissue donation process are adhering to the highest standards.

- Second, we recommend that all tissue recovery organizations be non-profit and that their relationships with for-profit corporations be strictly held at arm's length, free of monetary incentives and other forms of support. It is our hope that this will prevent for-profit organizations from pressuring non-profit companies to recover potentially unsafe tissues and to skirt the family approach protocols in an effort to increase recovery rates. It is neither wise, nor possible, to eliminate for-profit companies from all processing and distribution activities resulting from tissue donation. In fact, new patient care technologies, based on donated human tissue, may well be developed by for-profits or jointly between non-profit agencies and for-profit companies. However, for-profit organizations should not be involved, directly or indirectly, in the approach of donor families and the recovery of donated tissue. This is essential to ensuring that the public is able to trust the donation program. Regulating the recovery of donated tissue, and insisting that this service is carried out by a non-profit organization under the direct control of the OPO, will make certain that the integrity of and trust in the donation process is maintained.

Conclusion

The public does not distinguish between organ donation and tissue donation. Organ donation is well-regulated and closely controlled in the public interest. The task before us now is to ensure that the tissue banking industry is held to the same high standards. This is particularly necessary in order to protect organ donation. The actions of one unscrupulous tissue bank can adversely affect both organ and tissue donation. Any reduction in organ donation means the loss of life. We are already seeing instances of this reaction when, for example, in a hospital in Florida, the reported activities of a local tissue bank caused a family to decline their option of organ donation. This is the single greatest threat to the growing list of 75,000 individuals awaiting organ transplant in this country. Moreover, quality donated tissue transplants greatly improve the lives of countless numbers of people every day.

We must ensure that both the recipient and the donor communities are well served. We must work to advance the public perception of the organ and tissue recovery process, and bring this process to a point where it is understood and trusted. We look forward to the day when the general public completely accepts the benefits of organ and tissue donation as a common, dignified, and valuable contribution to the quality of life and of death.

Testimony of Valerie J. Rao, M.D.

Chief Medical Examiner, District Five, Leesburg, Florida

Before the Permanent Subcommittee on Investigations

May 24, 2001

Good morning Chairman Collins, Senator Levin, and Members of the Permanent Subcommittee on Investigations. My name is Dr. Valerie Rao, and I am the Chief Medical Examiner for District Five in the State of Florida. I would like to thank you for inviting me to appear today before the Subcommittee and I am pleased to discuss this most important issue. I believe that human donation is a selfless and invaluable gift, and as such, would like to see that all tissue recovery organizations are required to adhere to standards that promote safety and respect for donation. Unfortunately, my observations tell a different story and I would like to share my experience with the Subcommittee.

The role of the medical examiner in organ and tissue transplantation programs results from government mandated investigation into sudden and unexpected or traumatic deaths to determine the cause and manner (natural, accident, suicide, or homicide). A medical examiner death investigation includes documenting and evaluating the scene of death or injury as well as the body at the scene. Included is the determination of the terminal episode history and the decedent's medical history.

In Miami-Dade County, where I spent 18 years and nine months as an associate medical examiner, when a case arrives, it is initially screened by a tissue bank coordinator for consideration as a potential donor. If the quality appears suitable, next-of-kin authorization is received. In the meantime, the medical examiner performs a careful external examination. Next, the body is transported to a sterile autopsy suite where a tissue bank pathologist participates in the tissue excision process. During this procedure blood and lymph node tissue are retained for screening. The body returns to the medical examiner and the tissue bank pathologist. For the non-medical examiner case, the tissue bank pathologist performs the autopsy. At any time during this procedure, should testing raise doubt, the donor material is removed from the preparation and distribution pipeline.

Most medical examiner donor cases are people of prior good health who experience violence 24%, of sudden, unexpected, noninfectious cardiac dysrhythmia, or stroke, 76% (Statistics in Miami-Dade County, Florida 1995 through 1999). The very nature of such cases of previously healthy individuals with sudden death, creates a donor pool where infection and malignancy are minimize.

The protection against transmittal of infection and malignancies must be the primary principle in all transplantation programs; and the shortage of donor materials and business pressures should not work against this principle. Therefore, it is recommended that tissue bank physicians and

coordinators become aware of their own state medical examiner guidelines in order to understand the investigative process and its relationship to quality assurance.

As the medical examiner determines the cause of death, a complete autopsy and tissue for subsequent microscopic examination serve as a quality assurance step in the transplant process. Medical examiners are charged, in addition to forensic investigations of death also with public health issues particularly with regard to the possibility of transmission of infectious disease. Autopsies are required for donor acceptance, and medical examiners believe that autopsies should be routine for all donor cases. Autopsies are the only means by which diseases such as tuberculosis, histoplasmosis, degenerative disease of the brain, unsuspected malignancies, viral myocarditis, non-A, B, or C Hepatitis, diseases of unknown etiologies, and other potential transmissible diseases can be detected and those donors excluded from the donor pool.

The entire issue of medical examiner participation in the acquisition of tissues from cadaver donors must be also considered in light of recent developments. As I stated, medical examiners are guardians of the public health interest, and should be in a position to make a determination which tissue bank serves both the interests of the recipient-patient as well as satisfy the medical examiner statutory duties. Certainly a trust in the professional competence and reputation of the tissue bank personnel is an important factor in making such a determination.

Last April, I became concerned regarding several questionable practices by a tissue bank. My first concern, was when Regeneration Technologies, Inc., through its association with the University of Florida Tissue Bank, would accept donors with non-metastasizing malignant tumors of the breast, colon, cervix, and lung. They also accepted donors with septicemia, pneumonia, and intestinal obstruction. To the best of my knowledge, they do not perform routine blood or bone marrow aspiration cultures, which is done to detect for possible diseases. They do not require an autopsy, and hence do not know the cause of death in the donor. Tissue excisions are performed by technicians without physician supervision or participation; and the use of sterile precautions are not observed during the excision and retrieval processes. The technicians do not have sufficient training and knowledge to observe changes which would be noted by a pathologist, yet they performed an autopsy-removal of the brain which would obviously impair further medico legal investigation of the body of the deceased. Finally, the customary care and respect for the body of the deceased are not observed. I believe, the dead have rights, too! In contrast, the University of Miami Tissue Bank has demonstrated quite the opposite: all of their excisions are performed asceptically by trained physicians in an operating room environment; blood cultures and bone marrow cultures are also routinely performed.

As I said before, I believe that public trust in the professional competence and reputations of those involved in the donation process is vital to its continued success.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

STATEMENT BY

KATHRYN C. ZOON, Ph.D.

DIRECTOR

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

UNITED STATES SENATE

PERMANENT SUBCOMMITTEE ON INVESTIGATIONS

COMMITTEE ON GOVERNMENTAL AFFAIRS

May 24, 2001

RELEASE ONLY UPON DELIVERY

Introduction

Good morning, Madam Chairman and Members of the Committee. Thank you for inviting the Food and Drug Administration (FDA or the Agency) to participate in this hearing concerning human tissue banking. I am Dr. Kathryn C. Zoon, Director, Center for Biologics Evaluation and Research (CBER), FDA. CBER is the FDA Center responsible for regulation of many of the different types of human tissue and cells used in transplantation. I will provide background information on the regulation of human tissue for transplantation and FDA's current and future actions to help ensure the safety and availability of these products.

Transplanted human tissue products have the potential to treat or cure a wide variety of health conditions. Similar to any medical product or therapy, however, such transplants are not risk-free. FDA aims to help ensure that establishments take appropriate precautions to minimize the risks of transplanted human tissue.

The Agency's involvement in the regulation of human tissue is not new. FDA regulates tissue under the authority of the Public Health Service Act (PHS Act) and the Federal Food, Drug, and Cosmetic Act (FD&C Act). Several categories of

human tissue used for transplantation are being regulated as medical devices under the 1976 Medical Device Amendments. Many cellular and tissue products not categorized as medical devices are regulated by FDA as "biological products" under both the PHS Act and FD&C Act. Other cells, tissues, and cellular and tissue-based products are regulated solely under the communicable disease provisions of the PHS Act.

I am here today to talk about products primarily regulated by CBER and the many steps that FDA has taken in the past decade along with present and future actions to help ensure the safety of these products.

Background

FDA's goals with regard to human tissues are to prevent the spread of communicable disease; ensure that safety and efficacy is demonstrated for cellular and tissue-based drug, biological, and medical device products; enhance public confidence in these products; and, to accomplish these goals through implementing regulations in a manner that will not discourage the development of new products.

The term "tissue" covers products which have long been transplanted for widespread medical uses--such as skin

replacement after severe burns; tendons and ligaments to repair injuries; bone replacement; and, corneas to restore eyesight. Over the past decade, improved technology and techniques have expanded and enhanced the variety of potential therapeutic uses of tissue-based products. These new techniques hold the potential of providing therapies for cancer, AIDS, Parkinson's Disease, hemophilia, anemia, diabetes, and other serious conditions.

With the increased use of human tissue has come a heightened public awareness of the need for appropriate regulation to minimize the potential risks. Developments in the 1980s and 1990s prompted FDA to examine our approach to the regulation of tissue. Several incidents illustrated the risks of disease transmission when adequate precautions were not taken.

- In the 1980s, there have been multiple incidents of CJD transmission by dura mater (a brain covering) allograft due to pooling during manufacture.
- In 1991 it was discovered that seven people had been infected with Human Immunodeficiency Virus (HIV) through the transplantation of whole vascularized organs and tissue from a donor who tested negative for HIV. This led to intense discussions within the tissue bank community and the Public Health Service (PHS) on how to reduce the risk of infectious diseases from transplanted human tissues.

- There have been documented instances of distribution of tissue from donors who tested repeatedly reactive for hepatitis B (HBV).

- In October 1993, FDA learned that human tissue from foreign sources was being offered for sale in the United States with little or no documentation as to the source of the tissue. There was little, if any, information on the cause of the donor's death, the medical condition of the donor, or the results of donor screening and testing. This raised significant concerns about the safety and quality of the human tissue. The Agency quickly confirmed that the tissue had not been adequately screened and tested for infectious diseases.

- More recently, in 1999 a patient died from cardiac arrest during surgery to remove an infected corneal transplant. The probable source of the infection was contamination of the media that had been used to store the cornea.

- This year, significant bacterial contamination of patellar tendons resulted in two patients developing septic knees; one required removal of the graft. The establishment's procedures for irradiating the product to remove potential bacterial contamination were not followed.

Presently, heightened public awareness has resulted from various media articles including the Orange County Register series in April 2000 on the collection practices of local tissue banks.

FDA has prioritized the regulation of human cellular and tissue-based products, and the public should be confident that FDA is committed to regulating these products in a

manner where benefits to patients are maximized and risks to patients are minimized.

FDA's Approach to Tissue Regulation

After careful consideration of the myriad health issues and extensive public discussion, FDA published the "Proposed Approach to the Regulation of Cellular and Tissue-Based Products" on February 28, 1997. This document described FDA's planned regulatory framework for human cellular and tissue product regulation. Subsequently, FDA accomplished many of the regulatory goals described in the February 1997 document through publication of a series of proposed and final rules.

The 1997 Proposed Approach provided for a unified approach to the regulation of both traditional and new products. Additionally, the framework detailed the type of regulation necessary to protect the public health as applicable to different products. This framework provided a risk-based tiered approach to cell and tissue regulation. For human cells and tissue products with limited public health risk, FDA proposed regulation to prevent communicable disease transmission. For products that pose greater health risk,

the framework additionally provided for premarket review and approval of product applications.

FDA's Proposed Approach document focused on necessary actions needed to prevent the unwitting use of contaminated tissues with the potential for transmitting infectious diseases such as AIDS and hepatitis; preventing improper handling or processing that might contaminate or damage tissues; and, helping to ensure that clinical safety and effectiveness are demonstrated for tissues regulated as drugs, biological products and medical devices.

Tissue Action Plan

When FDA published the "Proposed Approach to the Regulation of Cellular and Tissue-based Products" in February 1997, we realized a blueprint was needed to implement the approach, including prescribed time frames for our planned actions. The Tissue Action Plan (TAP or action plan), implemented in March 1998, was the manifestation of this blueprint. The TAP contained a description of the steps FDA would take to create a tissue framework and respond to various recommendations by other organizations that are described below. TAP has been instrumental in implementing FDA's proposed framework for the regulation of human tissue.

In order to provide overall direction and coordination, a TAP Core Team was created with representation from various CBER Offices, the Center for Devices and Radiological Health (CDRH), and the Office of the Commissioner (Office of Policy, Office of Regulatory Affairs, and Office of Chief Counsel). The Core Team meets monthly to ensure progress in fulfilling TAP action steps; disseminate information externally; decide policy issues; and, finalize TAP documents.

FDA formed eleven task groups that meet on a routine basis, in accordance with set milestones. The task groups developed regulations and guidance in areas such as establishment registration, donor suitability, current good tissue practices (GTP), compliance and inspections.

As specified in the Proposed Approach document and action plan, FDA established the Tissue Reference Group (TRG), which provides a single reference point for product specific questions. The TRG considers the appropriate review criteria, responds to inquiries from the cellular and tissue product industry, identifies areas needing scientific or

policy development, and interacts with FDA's Ombudsman on product jurisdiction requests.

Rulemaking

After the tissue incidents of the 1990s, but prior to publication of the proposed approach document, FDA took actions to minimize the risk of disease transmission. On December 14, 1993, FDA issued an "Interim Rule for Human Tissue for Transplantation" (58 FR 65514) which required donor screening, infectious disease testing, and record keeping to prevent the transmission of infectious diseases through human tissue used in transplantation. The regulation applied to "conventional" human transplanted tissues (musculoskeletal, skin, ocular) but did not encompass tissue used in cellular therapies. Additionally, the regulation excluded semen and other reproductive tissue, human milk, bone marrow, and vascularized human organs, such as heart, kidney, liver, lung and pancreas. Under the regulation, FDA could conduct inspections and, when necessary, detain, recall, or destroy tissue. The Interim Rule was made final, with some modification, on July 29, 1997, now Title 21, Code of Federal Regulations (21 CFR) Part 1270.

As noted previously, FDA then created the proposed approach document. To implement the proposed approach, and in accordance with the action plan, FDA subsequently published three proposed rules that included requirements for establishment registration and product listing; donor suitability determination; and good tissue practice. Information on FDA's proposed and final rules that pertain to tissue are summarized in the chart below, and an explanation in greater detail follows:

Publication Date	Rule Type	Title of Rule	Effective Date	Numb. Of Comments
12/14/93	Interim	Human Tissue for Transplantation	12/14/93	73
07/29/97	Final	Human Tissue Intended for Transplantation	1/26/98	NA
05/14/98	Proposed	Establishment Registration and Listing for Manufacturers of Human Cellular and Tissue Based Product	N/A	28
09/30/99	Proposed	Suitability Determination for Donors of Human Cellular and Tissue-Based Products	N/A	481
04/18/00	Proposed	Reopening of Comment Period: Suitability Determination for Donors of Human Cellular and Tissue-Based Products (Reopen for 90 Days)	N/A	77
01/08/01	Proposed	Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products: Inspection and Enforcement	N/A	34 as of 5/15/01
01/19/01	Final	Human Cells, Tissues, and Cellular and Tissue Based Products; Establishment Registration and Listing	Staggered 75 days & 2 years	NA

As referenced in the chart above, FDA finalized the first of three rules on January 19, 2001 (66 FR 5447), entitled, "Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing." This rule requires establishments to register and list with the Agency their human cell, tissues, and cellular and tissue-based products. This rule is intended to identify establishments that engage in the recovery, screening, testing, processing, storage, or distribution of human tissue intended for transplantation. Under the registration final rule, establishments engaged in these activities with conventional tissues, such as bone, skin, and corneas, are required to register and list their products by May 4, 2001. New establishments involved in the manufacturing of conventional tissue must register and list within 5 days after beginning operations. Other establishments that manufacture non-conventional or new cellular or tissue-based products, such as hematopoietic stem cells, are required to register and list beginning January 19, 2003.

In order to prevent the spread of communicable diseases, it is necessary to screen and test donors of cells and tissues. FDA published a proposed rule "Suitability Determination for

Donors of Human Cellular and Tissue-Based Products" (64 FR 52696) on September 30, 1999. Disease agents such as HIV, HBV, hepatitis C virus (HCV), syphilis and the agent of Creutzfeldt Jakob desease (CJD) have been detected in human tissue, including bone, skin, corneas, and semen. The proposed rule would expand current screening and testing requirements to include donor screening for CJD and donor testing for syphilis. In addition, donors of leukocyte-rich cells or tissues would be tested for Human T-cell Lymphotropic Virus type I and type II (HTLV-I/II) and Cytomegalovirus (CMV). A donor who tested repeatedly reactive for a particular disease agent, or who possessed clinical evidence of or risk factors for such a disease, would be considered unsuitable, and cells and tissues from that donor would not ordinarily be used. The Agency is reviewing comments on the rule, which has not yet been finalized.

Because tissue establishments perform various functions that can affect the safety and quality of tissue products, FDA published a proposed rule for "Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement" (66 FR 1508) on January 8, 2001. With this proposed rule, FDA completed the

set of proposals that, when finalized, implement the new regulatory framework. The proposed rule would require manufacturers to follow current GTP, which is critical in ensuring the quality of tissue products. GTP include practices involving the methods, facilities, and controls used in tissue manufacture, and the establishment of a quality control program. FDA is in the process of carefully reviewing all comments received in response to this proposed rule.

Implementation Costs

In Fiscal Year (FY) 2002, FDA estimates that the Agency will dedicate $4.35 million to the regulation of human tissue. This is part of the President's FY 2002 budget request for FDA, which represents a ten percent increase for the Agency over the FY 2001 level. Estimates of the implementation of the tissue regulation will be developed as part of the FY 2003 budget process and may be revised as we garner additional information from future establishment registrations. Such additional information will help us determine with greater accuracy the amount of time and resources that will be needed to conduct inspections and other compliance related activities.

Tissue Inspections

FDA conducts on-site inspections of tissue establishments to determine compliance with FDA regulations. At the conclusion of the inspection, FDA's investigator may issue a notice of inspection observations (FDA Form 483) concerning potential deficiencies from regulatory requirements. The investigator will discuss the observations with the most responsible official at the establishment. Based on those observations, FDA classifies the establishment according to the corrective action steps indicated by the inspection. The three classifications are: Official Action Indicated (OAI), Voluntary Action Indicated (VAI), or No Action Indicated (NAI). A chart indicating the results of 380 FDA inspections of tissue establishments between October 1, 1993, and November 6, 2000, is provided below:

Fiscal	Inspection	District Decision		
Year	Count	NAI	VAI	OAI
94	41	25	6	9
95	30	9	7	12
96	4	1	3	0
97	36	16	13	3
98	111	54	47	7
99	65	26	33	4
00	93	54	29	8
Total	380	185	138	43

For various reasons, 14 of the inspections are not in the database. As a result of these 380 inspections, FDA has taken the following actions: Fifteen orders for retention or recall; six warning letters; and, nine opportunities for Voluntary Corrective Action Letters. Further, the number of voluntary recalls of banked human tissue has increased from three in FY 1994 to 24 in FY 2000. From the beginning of the current FY until April 30, 2001, there have been 12 recalls.

Pooling

FDA has concerns about the practice of pooling tissues from multiple donors during processing. In general, FDA believes that the risks associated with pooling tissues from multiple donors appear to outweigh any identified medical benefits.

Risks include exposure and possible cross-contamination from one tissue to another tissue of such infectious disease agents as viruses (enveloped and non-enveloped), bacteria, fungi, and prions, including known and emerging infectious agents.

FDA's January 8, 2001, proposed rule "Current Good Tissue Practice for Manufacturing of Human Cellular Tissue-Based Products; Inspection and Enforcement," (66 FR 1508) provides that human cells and tissue shall not be pooled, that is, placed in physical contact or mixed in a single receptacle, during manufacturing because of the risk of exposure to infectious agents. FDA is currently reviewing comments to this proposed rule.

Office of the Inspector General/General Accounting Office Recommendations

In January 2001, the Department of Health and Human Services' (DHHS) Office of the Inspector General (OIG) issued a report entitled, "Oversight of Tissue Banking." This report contained a number of observations and recommendations relevant to FDA's regulation of tissues (the report did not address eye banks), and several recommendations for other DHHS agencies. FDA is committed

to taking actions to address the findings. The OIG recommendations are listed below followed by FDA's actions:

- **FDA should expedite the publication of its regulatory agenda that requires registration of tissue banks, enhanced donor suitability screening and testing, and the use of good tissue practices.**

  All three of the proposed rules have been published; and the Establishment Registration and Listing Rule was finalized January 8, 2001.

- **FDA should set a realistic, yet aggressive, date by which it would complete an initial inspection of all tissue banks.**

  The OIG reported that 36 tissue banks had never been inspected by FDA. FDA intends to inspect these 36 and all other uninspected establishments in our inventory. Inspections of new firms identified as the result of the registration and listing rule will take priority for FY 2002 over inspections of firms previously covered by FDA and found non-violative.

- **FDA should determine an appropriate minimum cycle for tissue bank inspections.**

  The Agency established a prioritized scheme several years ago for the inspection of tissue establishments. Our priorities, from highest to lowest, include: firms previously violative, firms about which we have received complaints, firms never inspected and which are known to lack accreditation by a standard setting organization such as American Association of Tissue Banks (AATB) or Eye Bank Association of America (EBAA), firms never inspected and which are known to be accredited, and firms which were previously inspected and found not violative.

- **FDA should work with States and with professional associations that have inspection and accreditation programs to determine in what areas, if any, oversight activities could be coordinated.**

  FDA recognizes that States and professional associations have an important role in the quality of tissue

available. States and professional associations, however, may have different concerns and interests than FDA's. Accrediting organizations and State-regulated programs may cover fewer types of human cells, tissues, and cellular and tissue-based products and may set standards that would not cover the entire spectrum of products. Moreover, the goals of professional organizations differ in several critical ways from regulatory oversight programs. Such accrediting organizations often work with tissue establishments to attempt to bring them into compliance with their standards, but lack enforcement authorities. FDA's goals are to protect the public from unsafe tissue products and the Agency uses a variety of enforcement tools to help ensure public health and safety.

In other product areas, FDA has entered into mutually beneficial contracts with States to perform FDA inspections. This has been successful in areas where the State law parallels the Federal law and there has been sufficient experience with the regulatory program to standardize inspections. When these elements are present, FDA plans to seek ways to establish similar partnerships with such States.

The issue of how to best implement a comprehensive, resource efficient program of on-site inspections of tissue establishments is complex. We are aware of tissue recalls and market withdrawals conducted by firms, which are accredited, so accreditation can not be seen as an absolute guarantee of safety and suitability. FDA is carefully evaluating the recommendations of the OIG concerning the overall regulatory framework for tissues, including how to best assure adequate inspectional coverage.

For now, the Agency believes that FDA biennial surveillance inspections are necessary to determine whether establishments are complying with FDA regulations. FDA can not obtain this information through accrediting bodies or State inspections at this time. We will continue to explore ways to exchange information with accrediting bodies and States.

In December 1997, the General Accounting Office (GAO) published a report entitled, "Human Tissue Banks: FDA Taking Steps to Improve Safety, But Some Concerns Remain." Some of the GAO recommendations are listed below, followed by a summary of FDA progress to date:

- **FDA should move ahead with its plan to require:**

  Tissue facilities including reproductive and stem cell facilities to register with FDA;

  Reproductive and stem cell facilities to adhere to all requirements of the current regulation

  Facilities that collect and store cord blood to provide accurate oral and written communication to consumers with regard to the State of knowledge of collection, processing, and storage techniques, as well as the likelihood of requiring cord blood transplantation, and to portray the risks and benefits relative to other therapies.

FDA has published either proposed or final rules in all three of these areas.

- **FDA should also add to its oversight plans provisions that would require:**

  Tissue facilities to obtain informed consent before processing any tissues for transplantation from living donors.

GAO was specifically referring to cord blood. FDA did not agree with this recommendation. FDA believes that seeking informed consent for use of cord blood after collecting umbilical cord blood does not raise any additional safety concerns than would be raised by seeking informed consent before collecting cord blood.

The current cord blood banking protocols, operating under an FDA-accepted IND application, provide the opportunity through data collection to assess the safety and risks of

obtaining informed consent after cord blood has been collected. If FDA learns that the timing of informed consent affects the safety of the tissue, the Agency will modify its position.

Tissue facilities to report serious errors and accidents and adverse events to FDA

The proposed GTP rule (§1271.350(a)) would require establishments to report adverse reactions to CBER within 15 days, using FDA Form-3500-A. In addition, the proposed rule would require establishments that become aware of biological product deviations (formerly called "errors and accidents") involving distributed products to determine if they could reasonably be expected to lead to a reportable adverse reaction, and if so, to report the product deviation to CBER's Office of Compliance and Biologics Quality (OCBQ) as soon as possible.

Facilities that collect, store, process, distribute, transplant human tissues to establish validated systems to track tissues to consignees and recipients.

The proposed GTP rule (§1271.290) would require that facilities establish and maintain a method of product tracking that enables the tracking of all products from donor to recipient and vice versa.

Tissue facilities that collect, store, process, or distribute allogeneic peripheral stem cells and any cord blood stem cells to make premarket submissions if FDA determines that adequate safety and efficacy data are not available to such products.

The comment period for the January 20, 1998, Federal Register (FR) Notice entitled, "Request for Proposed Standards for Unrelated Allogeneic Peripheral and Placental/Umbilical Cord Blood Hematopoetic Stem/Progenitor Cell Products: Request for Comments," closed on July 17, 2000. FDA is currently reviewing the comments submitted to determine whether INDs would be required and/or whether standards could be developed for some of these products. FDA intends to publish a FR Notice when our review is complete and issue more specific guidance as appropriate.

Tissue facilities to inform FDA of the types of processing techniques used on tissues and supply information on the safety and efficacy of these techniques.

Under proposed GTP rule (§1271.220(a)), any establishment engaged in the processing of human cellular and tissue-based products would be required to develop, conduct, control, and monitor its manufacturing processes to ensure that each product: 1) conforms to its specifications, 2) is not contaminated, 3) maintains its function and integrity, and 4) is manufactured so as to prevent transmission of communicable disease by the product.

The proposed GTP rule (§1271.225) would require an establishment to develop and implement procedures for making changes to a process.

The proposed GTP rule (§1271.230(a)) would require establishments to validate their processes where verification is not feasible and validation activities must be documented and maintained at the establishment and made available for review on inspection.

For products that are regulated as drugs, biological products, and medical devices, in addition to regulation under the communicable disease provisions of the PHS Act, FDA reviews premarket applications for safety and efficacy.

Meetings/Outreach

In order to successfully implement Agency plans for the regulation of human tissues, FDA has involved tissue establishments and medical professionals in many public discussions. A list of our meetings and outreach is contained in Appendix I.

In the future, FDA intends to provide opportunity for public discussion on issues related to cellular and tissue-based products. FDA intends to use various venues to continue our dialogue with industry organizations such as the AATB, the EBAA, the American Association of Blood Banks(AABB),the American Society for Reproductive Medicine (ASRM)/Society or Assisted Reproductive Technology (SART), the Foundation for the Accreditation of Hematopoietic Cell Therapy (FAHCT) and the International Society for Hematotherapy and Graft Engineering (ISHAGE).

Conclusion

FDA can assure the Committee that we are committed to establishing a regulatory framework, which not only helps ensure the safe use of human tissue for transplantation, but also allows the development of this technology and instills public confidence. While FDA has taken many steps towards this end, we realize that more remains to be done.

We look forward to the Committee's continued interest in this area and would be happy to answer any questions.

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We look forward to the Committee's continued interest in this area and would be happy to answer any questions.

7/97	Federal Trade Commission - Discussion of Stem Cell Promotion

Specific Events with Industry:

5/01	Meeting with EBAA on GTP
4/16/01	FDA/ASRM meeting - Good Tissue Practice Proposed Regulation
3/28/01	Meeting between Health Canada and FDA to discuss the regulation of Human and Xeno Tissue Products.
8/14-15/00	Workshop: Unrelated Allogeneic Cord Blood Banking and Transplant Forum
8/2/00	Open Public Meeting - Human Bone Allograft: Manipulation and Homologous Use in Spine and Other Orthopedic Reconstruction and Repair
6/00	CDC Donor Suitability Workshop
2/10/00	FDA / ASRM Meeting Concerning the Donor Suitability Proposed Regulation
11/17-19/99	AATB QA Workshop, New Orleans, LA - FDA Review of Tissue Bank Inspections; Status of Required Serology Testing; Update Regarding Proposed Regulations
9/99	ASRM - Presentation - FDA Update on Regulation of Reproductive Cells and Tissue.
6/99	EBAA - Presentation on Registration Proposed Rule and Donor Suitability Proposed Rule
6/99	Institute of Science, Law and Technology (ISLAT) informational meeting with FDA to discuss ART issues
4/8/99	Human Tissue Industry Seminar hosted by ASQ and Los Angeles District, Los Angeles, CA

4/99	RESOLVE consumer association informational meeting with FDA to discuss ART issues
3/99	AATB - Presentation on Donor Suitability Proposed Rule
2/9-11/99	FDA Central Region Human Tissue Course for FDA Investigators
12/98	FDA Science Forum on Proposed Approach
11/98	EBAA - Compliance with Final Rule
10/98	ASRM - FDA update on Regulation of Reproductive Cells and Tissue
9/10/98	Workshop: Hematopoietic Stem/Progenitor Cell Products: Discussion of Unrelated Allogeneic/Umbilical Cord Blood and Peripheral Blood Cell Banking and Transplantation
8/98	AATB Annual Meeting - FDA Update and Implications of FDA Regulation of Reproductive Tissue
7/98	AATB Informational meeting with FDA concerning establishment certification and standard development
6/98	EBAA Annual Meeting - Establishment Registration and Listing - proposed rule
5/98	AATB mid-year meeting - FDA - What's Ahead/ CJD and Dura Mater
4/20/98	FDA/AATB Meeting Concerning Summary of Records
4/9/98	Video Conference arranged by FDA Southwest Region and Dallas District on the Regulation of Human Tissue Intended for Transplantation presented to EBAA members located in the Southwestern U.S.
3/98	Training and Review - Regulatory Issues in Tissue Banking

2/98	FDA presentation at CDC and RESOLVE (a federation of infertility patient associations) sponsored meeting "Approaches to A.R.T. Oversight: what's Best in the U.S.".
12/23/97	Workshop: Ethical Issues in Cord Blood Banking
11/97	Meeting with Society of *InVitro* Biology - Proposed Approach
7/11/97	FDA/AATB - Discussion of Regulation of Demineralized Bone Matrix
6/97	Discussion of Regulation of Eye Tissue with EBAA
3/17/97	FDA Open Public Meeting for comments on the "Proposed Approach"
3/12/97	Training provided to Baltimore District Biologics Cadre, regarding Inspection of Human Tissue Establishments.
12/96	FDA invited to discuss Good Tissue Practices with AATB, EBAA and ASRM
10/96	Heart valve industry - Discussion of regulation of heart valve allografts
12/13/95	Workshop: Cord Blood Stem Cells - Procedures for Collection and Storage
10/95 and 3/96	FDA invited to discuss reproductive tissue donor testing, screening and establishment registration with ASRM and AATB
6/20-21/95	Tissue Workshop: Tissue for Transplantation and Reproductive Tissue: Scientific and Regulatory Issues and Perspectives
3/95	Workshop on Human Tissue Intended for Transplantation and Human Reproductive Tissue: Donor Screening and Infectious Disease Testing
2/1-3/95	FDA Mid-Atlantic Region Tissue Bank Training for FDA Investigators, Baltimore, MD
6/94	Workshop on Human Tissue Intended for Transplantation

Senate Permanent Subcommittee
On Investigations
EXHIBIT # 1

HFI-35

DEPARTMENT OF HEALTH AND HUMAN SERVICE

Public Health Service

Refer to: CFN 1125034 / FEI 3001236466

Food and Drug Administration
Baltimore District Office
900 Madison Avenue
Baltimore, MD 21201-2199
Telephone: (410) 962-3396
FAX: (410) 962-2219

August 25, 2000

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Dr. Frederick G. Caudle
Chief Executive Officer
Lions of District 22-C
Eye and Tissue Bank and Research Foundation, Inc.
9470 Annapolis Road, Suite 415
Seabrook, Maryland 20706

Dear Dr. Caudle:

During a Food and Drug Administration (FDA) inspection of your tissue bank located in Seabrook, Maryland, conducted June 27 through July 21, 2000, our investigator documented violations of Section 361 of the Public Health Service Act and Title 21, Code of Federal Regulations (21 CFR), Part 1270, as follows:

> Failure to accurately document quarantine of corneas coded as being suitable for surgical transplantation prior to and during distribution, as required by 1270.35 (c). For example, corneas coded as being for surgical implant were shipped to [redacted] prior to the receipt of serological testing showing they were repeat reactive HIV-I/II. There was no documentation to show that they had been identified as being quarantined or that the corneas had not yet been determined to be suitable for implant, as required by 1270.33 (c).
>
> Failure to maintain accurate, indelible, and legible records of each significant step in the identification, testing, and disposition of tissue for human transplantation, as required by 1270.33(a), in that records had been altered with no explanation, whiteout was used in the records obscuring the original information, records conflicted with one another and lacked dates and signatures to show review by responsible individuals.
>
> Failure to follow written procedures as required by 1270.31. For example, corneas identified as being distributed for research purposes were not documented in the "Research Tissue Requests" or Practice Logs as required by your procedures.

The above violations are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure that your establishment is in compliance with all requirements of the federal regulations.

We acknowledge receipt of your FDA-483 response letter, received August 24, 2000. Your response, however, does not provide sufficient detail of exactly what corrections are being made or how they are to be accomplished. Without this information, we can not adequately assess your corrections.

You should take prompt measures to correct these deviations. Failure to do so may result in regulatory action without further notice. Such actions include seizure and/or injunction.

You should notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations and to prevent their recurrence. If corrective action can not be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your reply should be sent to the Food and Drug Administration, Northern Virginia Resident Post, 101 West Broad Street, Suite 400, Falls Church, Virginia 22046, to the attention of Gerald W. Miller, Compliance Officer. Mr. Miller can be reached at (703) 235-8440, extension 504.

Sincerely,

Lee Bowers
Director, Baltimore District

Senate Permanent Subcommittee
On Investigations
EXHIBIT #__2__

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administratic
FOI m36760n

19900 MacArthur Blvd., Ste :
Irvine, California 92612-244!
Telephone (949) 798-7600

APR 2 1 2000

WARNING LETTER

CERTIFIED MAIL – RETURN RECEIPT REQUESTED

Eli Gendler, M. D., Ph. D.
Medical Director
Pacific Coast Tissue Bank
2500-19 South Flower Street
Los Angeles, CA 90007

W/L 50-00

Dear Dr. Gendler:

During an inspection of Pacific Coast Tissue Bank conducted January 24th through February 2nd, 2000, our investigators documented violations of Section 361 of the Public Health Service Act and Title 21, Code of Federal Regulations, Part 1270 as follows:

Failure to develop adequate written procedures for all significant steps used in determining the suitability of banked human tissue intended for transplantation as required by 21 CFR §1270.31(a) in that the firm's SOPs allow for confirmatory testing of repeatedly reactive Hepatitis B Surface Antigen donors and supplemental testing of repeatedly reactive Hepatitis B Core Antibody donors as a means of potentially qualifying those donors as suitable for transplantation in violation of 1270.21(h)(1).

Failure to ensure that donor specimens are tested using FDA licensed donor-screening tests in accordance with manufacturer's instructions as required by 21 CFR 1270.21(a) in that you have no assurance that your contract testing facilities are meeting the above requirements.

Failure to follow written procedures for all significant steps used in determining the suitability of banked human tissue intended for transplantation as required by 21 CFR §1270.31(b) in that the firm uses both intake and output volumes when calculating plasma dilutions of a donor; the use of output volumes is not referenced in the firm's SOPs.

Failure to maintain records concurrent with the performance of each significant step required in §1270 in the performance of infectious disease screening as required by 21 CFR §1270.33(a) and 21 CFR §1270.35(b) in that the firm does not completely document the oral interview with the coroner's office regarding autopsy results. The records do not include the date, time, contact person or detailed autopsy results.

Failure to maintain records concurrent with the performance of each significant step required in §1270 in the performance of infectious disease screening as required by 21 CFR §1270.33(a) and 21 CFR §1270.35(d).

The firm does not maintain disposition records of tissues unsuitable for transplantation but that are retained by the firm.

Failure to prepare and follow written procedures for designating and identifying quarantined tissue as required by 21 CFR §1270.31(c) and failure to quarantine tissue until it is disposed of as required by 21 CFR §1270.33(e) in that tissue that has been found unsuitable for transplant but that is retained by the firm is not quarantined or identified as unsuitable for use.

Failure to validate written procedures for prevention of infectious disease contamination or cross-contamination by tissue during processing as required by 21 CFR §1270.31(d) in that you have not validated the cleaning procedure outlined in [redacted].

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure that your establishment is in compliance with all requirements of the federal regulations.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in further regulatory action without further notice, which may include Order for Retention, Recall and/or Destruction, and/or Injunction.

We acknowledge receipt of your response to the FDA-483, Inspectional Observations dated February 20th, 2000, in which you commit to specific corrective actions. We disagree with your arguments regarding confirmatory and supplementary testing of repeatedly reactive tissues and your interpretation of the preamble to the final rule 21 CFR Parts 16 and 1270, Human Tissues Intended for Transplantation published July 29th, 1997 in the Federal Register. In addition, we are concerned that your apparent disagreement with the need for several provisions of the regulations may influence your ability to achieve and maintain compliance. Please contact this office to arrange a meeting with us to discuss this matter. You may contact the District Director's Office at 949-798-7714 to schedule this meeting.

You should notify this office in writing within fifteen (15) working days of receipt of this letter of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which corrections will be completed.

Your written response should be directed to the Food and Drug Administration, Attention:

Thomas L. Sawyer
Director, Compliance Branch
Food and Drug Administration
19900 MacArthur Blvd., Suite 300
Irvine, CA 92612

Sincerely,

Acting District Director

05/09/2001 11:22 3523656438 DISTRICT V M.

Senate Permanent Subcommitte
On Investigations
EXHIBIT # 3a

DR. VALERIE RAO
LAKE COUNTY MEDICAL EXAMINER
LAKE COUNTY
LADY LAKE, FLORIDA

3/26/2001

DEAR DR. RAO,

I JUST FINISHED READING YOUR EXCELLENT ARTICLE IN THE "NEW HONDON DAY CONNECTICUT NEWSPAPER.

YOU HAVE ENLIGHTED ME ABOUT BODY PARTS DISPOSITION AND CAN'T THANK ENOUGH FOR THE KNOWLEGDE YOU IMPARTED TO MY INCOMPLETE INFORMATION I HAD ON THE SUBJECT.

I HAVE FOR MANY YEARS (I AM 84 YEAR OLD-MALE- 85 ON 11/19/2001) AND AM VERY DESIRIOUS OF DONATED ALL OF MY BODY PARTS-ALL THAT CAN BE USED.

I AM IN REASONABLE GOOD HEALTH RN WOULD LIKE-MOSTLY CHILDRE OR A YOUNG MOTHER OR FATHER TO HAVE WHAT IS USEABLE AND NEEDED.

BUT YOUR ARTICE MAKES ME A LITTLE GUN SHY. I DON'T WANT CHILDREN OR FATHER OR MOTHER OR A YOUNG CHILD WHO COULD NOT AFORD TO PAY TO BE CHARGED

IN FACT I DON'T WANT ANY BODY TO SELL MY PARTS

PLEASE TELL HOW I CAN WRITE OUT MY WISHES AND WHAT MEDICAL TERMS TO USE.

THAT'S AGAIN FOR YOU WONDERFUL ARTICLE;

SINCERELY,

[redacted]

[redacted]

05/09/2001 11:22 3523656438 DISTRICT V M.

Senate Permanent Subcommittee
On Investigations
EXHIBIT #3b

VALERIE J. RAO, M.D.
CHIEF MEDICAL EXAMINER
DISTRICT FIVE MEDICAL EXAMINER'S OFFICE
809 PINE STREET
LEESBURG, FLORIDA 34748
(352) 326-5961
FAX: (352) 365-6438

May 2, 2001

[redacted]

COPY

Dear [redacted].

I was very pleased to receive your extremely touching letter. It is so refreshing to know that there are people as selfless and generous as yourself. The gift that you are addressing is invaluable and that is how it should be viewed. If I were in your situation, wanting to give this gift, I would write the sentiments that you have expressed to me, in so eloquent a fashion, in my last will and testament. I would also tell a loved one about your intent and ask that they see that it is fulfilled in the way you want it to. If you are in good health and strong, I do not think age will be a deterrent. Contact your local bone and tissue bank after doing some research into their reputation and track record. See what suggestions they may have to offer. You do not really need to use any medical terms, just tell it like it is.

I am going to keep your letter and show it to others who may want to do the same thing.

May God bless you and continue to give you good health.

Sincerely yours,

Valerie J. Rao, M.D.
Chief Medical Examiner

VJR/cm

Senate Permanent Subcommittee
On Investigations
EXHIBIT # 4

WRTC Donor Referral/ Tissue Donor Worksheet

WRTC Tissue Donor #_____ Tissue Bank Donor #_____ UNOS# _____

REFERRAL INFORMATION

WRTC Staff: Dave D Date: 10/26/92 Time: 3:03 pm Referral Type: ☐ Organ ☑ Tissue ☐ Eye

Passed From: _____ Date/Time: _____ Passed to: _____ Date/Time: _____

HOSPITAL INFORMATION

Donor Site (Hospital): DC [redacted] Hospital documented call in chart: YES NO

Referring Person: Dr. [redacted] Unit: ICU Site Phone: 202-782-7085

PATIENT INFORMATION

Pt.Name: [redacted] Age/Sex/Race: 82 / M / Medical Record#_____

Address: _____ Height: _____ Weight: _____

DOB: ___/___/___ Admit (D/T): ___/___

Diagnosis: Hx Prostate CA; Time of Death/Asystole / last seen alive (D/T): 10/25/92 / 16

Cause of Death: CPR Refrigeration (D/T): ___/___

Pronounced by: _____ Chart Location: _____ Body location: _____

Next of Kin: [redacted] Relationship: [redacted] Phone: [redacted]

EYE BANK REFERRAL RESULTS

[redacted] called Eye Bank

Eye bank called? ☐ YES Bank Name: _____ Spoke to: _____ Time(s): _____

☐ NO Reason: _____ Cornea donor? ☐ YES ☐ NO ☐ UNK

If yes, is Eye Bank performing serologies? ☐ YES ☐ NO ☐ UNK Spoke to: _____ Time(s): _____

TISSUE BANK REFERRAL RESULTS

Tissue bank called? ☐ YES ☐ NO Bank Name: _____ Spoke to: _____ Time(s): _____

Hosp. person & dept. spoken to about NOT releasing body: _____ Time(s): _____

Hospital contact for tissue team: _____ Phone: _____

Time O.R. available: _____ O.R.# _____ Time Tissue Teams must exit O.R.? _____

If valves recovered, return heart? ☐ YES ☐ NO Return to: _____

Tissue Bank heart pathology review? ☐ YES ☐ NO

MEDICAL EXAMINER (M.E.) AND FUNERAL HOME (F.H.)

M.E. Case? ☐ YES ☐ NO M.E. Name: : _____ Contacted (D/T): ___/___

Autopsy? ☐ YES ☐ NO Autopsied by: : _____ Completed(D/T): ___/___

M.E. Restrictions: _____ M.E. Requests: _____

F.H. known? ☐ YES ☐ NO Name: _____ Contact: _____ Phone: _____

Estimated donation completion time (D/T): ___/___

Notified of estimated donation time end? M.E: ☐ YES ☐ NO F.H: ☐ YES ☐ NO

Notified of case completion? M.E: ☐ YES ☐ NO F.H: ☐ YES ☐ NO

Patient Name: _____ OPO ID # _____

CLINICAL INFORMATION

YES	NO		YES	NO	
☐	☐	Extended downtime. If yes, how long? _____	☐	☐	Active Sepsis. Recent temperature: _____
☐	☐	History of cancer? _____			Recen: WBC with Differential:
☐	☐	Hx high dose steroid use>1mo. Dose: _____			WBC: _____ > (4.8 – 10.8) Segs: _____ > (45 – 73%)
☐	☐	On respirator. If yes, how long? _____			Bands: _____ > (3 – 5%) Lymphs: _____ < (20 – 40%)
☐	☐	Positive HIV or Hepatitis	☐	☐	Antibiotic therapy. If yes, length? _____
			☐	☐	Positive cultures. If yes, organism: _____

Events surrounding death/Current Clinical course: Include manner of death, Attending physician's impression and progress notes indications. Document last hour of crystalloid infusions and last 48 hrs blood/colloid transfused. Attach extra paperwork if necessary.

FSN to Eyes => ; Consent
3:12 pm => Spoke to Dr. [redacted] from [redacted] the
Stated that LER [illegible] calling and asking @ time
Donation => FSN to ~~time~~ Consent / Eyes but yes since time
3:14 pm => Spoke to Person – he stated that [illegible]

→ Joe ?
Sex => [redacted] ; "No Research"

REFERRAL AND CONSENT DATA

Patient referred to WRTC? ☐ Yes ☐ No ☐ Unk	Was donation discussed prior to death? ☐ Yes ☐ No ☐ Unk
Did the family initiate discussion? ☐ Yes ☐ No ☐ Unk	Was there a donor card? ☐ Yes ☐ No ☐ Unk
Approachers:	Requesters:
Name: _____	Name: _____
Title: _____	Title: _____
A/S/R:	A/S/R:

	Medically Suitable (Answer Yes or No) (If no give reason)	Consent (Answer Yes or No) (If no give reason)	Recovered (Answer Yes or No) (If no give reason)
Skin	☐ Yes ☒ No Age : Hx CA	☐ Yes ☐ No _____	☐ Yes ☐ No _____
Bone	☐ Yes ☒ No _____	☐ Yes ☐ No _____	☐ Yes ☐ No _____
Valves	☐ Yes ☒ No _____	☐ Yes ☐ No _____	☐ Yes ☐ No _____
Eye	☐ Yes ☒ No _____	☐ Yes ☐ No _____	☐ Yes ☐ No _____

Senate Permanent Subcommittee
On Investigations
EXHIBIT # 5

LIONS EYE BANK
LIONS EYE BANK

CONFIDENTIAL

LIONS EYE & TISSUE BANK OF DISTRICT 22-C DONOR MEDICAL & SOCIAL HISTORY QUESTIONNAIRE SSN OR MEDICAL RECORD #	LTB #: LEB# Donor Name: [redacted]

Date: [redacted]-00

Name of Person Interviewed: [redacted]

Relationship: SON

Name of Person Conducting Interview: [redacted] J. Paparo
Print Name

Technical Director
Title

Joseph J Paparo
Signature

Do you feel that you knew the deceased well enough to answer questions regarding his/her medical and social history? ☑Yes ☐No
If no, is there some other individual that may provide the information regarding these medical and social history questions? ☐Yes ☐No N/A

Name: Phone #:

Please answer the following questions to the best of your knowledge. Give explanation when indicated in the left column.

1. Has the deceased ever had cancer, tumors, leukemia or lymphoma? Received radiation therapy or drugs for cancer?	☑Yes ☐No Prostate w/ Prostatectomy All Removed
2. Has the deceased been seen by a physician, or hospitalized in the past two years? If yes, name of physician, hospital, psychiatric, or long term care facility:	☑Yes ☐No Weakness / Fell Had to go to Hospital
3. Please name surgical procedures that you know the deceased has ever had? Please name if any eye surgeries that you know the deceased has ever had?	☐None ☑Procedures: Prostatectomy Colostomy in Early 90's ☑None ☐Procedures:
4. What medications, if any that you are aware of did the deceased take on a regular basis?	☐None ☑Medications: Cumidin

 PZ0004-R001 8/6/99

Senate Permanent Subcommittee
On Investigations
EXHIBIT #____6____

Date: Wednesday, May 16, 2001 9:22 AM
From: JLegalMedicine@aol.com

DEAR SIRS:

I AM CURRENTLY DEVELOPING A COMPANY IN CENTRAL FLORIDA THE PURPOSE OF WHICH
IS TO ACQUIRE DONORS AND HARVEST THE VARIOUS TISSUES. I HAVE DEVELOPED A PROGRAM THAT IS DIFFERENT FROM ANY OTHER IN THE COUNTRY. TEST MARKETING RESULTS WERE STAGGERING IN SO FAR AS THE NUMBERS OF DONORS ACQUIRED. CURRENTLY WE ARE IN THE PROCESS OF ACQUIRING AGREEMENTS WITH COMPANIES SUCH
AS YOUR TO PROVIDE UNPROCESSED TISSUE FOR YOUR RESPECTIVE USES. WE ANTICIPATE APPROXIMATELY 300 DONORS OUR FIRST YEAR. IF YOU WOULD BE INTERESTED IN A RELATIONSHIP PLEASE CONTACT JOHN M. GASTON AT 383-738-2091 OR 383-801-2661

THANK YOU

JOHN GASTON

Senate Permanent Subcommittee
On Investigations
EXHIBIT # 7

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville MD 20852-1448

MAY - 3 2001

James Grooms, President/CEO
Regeneration Technologies, Inc.
1 Innovation Drive
Alachua, Florida 32615

Dear Mr. Grooms:

An inspection of your human tissue processing facility was conducted by the Food and Drug Administration (FDA) from July 25 – 28, 2000. During the inspection, it was confirmed that Regeneration Technologies, Inc. (RTI) has begun using the BioCleanse™ Tissue Processing System (BioCleanse System). Use of this system includes the pooling of tissue from multiple donors during processing.

Your firm provided data to the investigator during the inspection which, together with information previously provided to the agency by RTI, have been reviewed by FDA's Center for Biologics Evaluation and Research (CBER). Based on the data reviewed, we have concerns regarding the ability of the BioCleanse System to prevent infectious disease contamination or cross-contamination.

CBER does not agree with RTI's risk/benefit assessment of pooling tissues from multiple donors. The risks of pooling musculoskeletal tissues from multiple donors far outweigh the benefits. These risks include exposure and possible cross-contamination from one tissue to another tissue of such infectious disease agents as viruses (enveloped and non-enveloped), bacteria, fungi, prions, and other emerging infectious agents. RTI has attempted to validate the BioCleanse system for certain viruses, bacteria and fungi. As explained below, these validation studies do not appear to be adequate. To our knowledge, RTI has not attempted to validate the BioCleanse system for prions. Currently, there is no accepted method for validating a system for prevention of cross-contamination by prions. If prion contamination were to occur, the risk to recipients would be significantly magnified and multiplied using a system that involved pooling.

Prion diseases, such as Creutzfeldt-Jakob Disease (CJD) and variant CJD, are neurological degenerative diseases, known generally as Transmissible Spongiform Encephalopathies (TSEs), that are ultimately fatal and as yet, untreatable. There is evidence of transmission of CJD through the transplantation of dura mater and cornea. Of particular relevance here is the evidence that transmission of CJD, across several continents, resulted from the transplantation of dura mater that had been pooled during processing. Following discussion at FDA's TSE Advisory Committee, FDA's CDRH published guidance on dura mater, currently regulated as a medical device, that prohibits pooling. In addition, the American Association of Tissue Banks (AATB) has stated in its 2001 Standards for Tissue Banking that, "cells and/or tissue from multiple donors shall not be pooled during retrieval, processing, preservation, or storage."

Moreover, in FDA's proposed rule entitled, "Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement," which published in the Federal Register (66 FR 1508), on January 8, 2001, the agency provides in section 1271.220(c) that human cells and tissue from two or more donors shall not be pooled (placed in physical contact or mixed in a single receptacle) during manufacturing.

While there has been no known transmission of CJD through the transplantation of musculoskeletal tissue, the transmission of CJD through dura mater and cornea suggests the possibility of transmissibility through other tissues, as occurs with other infectious disease agents. Only limited data exist about the tissue distribution and infectivity of transmissible spongiform encephalopathies, particularly variant CJD, in the asymptomatic and clinical phases of the disease. Our knowledge based on animal studies is limited by small numbers, sample size, species barriers, and level of prion detection, and extrapolation to human disease may not be valid. We do know that routine materials and processes known to destroy traditional human and animal pathogens do not appear to destroy prions. Currently, there are no validated methods of decontaminating or sterilizing tissues contaminated with prions.

Under current Title 21 Code of Federal Regulations, section 1270.31(d), you are required to have validated written procedures for the prevention of infectious disease contamination or cross-contamination by tissue during processing. CJD has been transmitted from pooled tissue to human tissue recipients with fatal consequences. To date, while there are methods to detect prions, no validated method to detect prions in tissues has been provided to FDA for review. Without a validated method, pooling procedures for the prevention of CJD contamination or cross-contamination cannot be validated. At this time, therefore, the use of pooling procedures for human tissue intended for transplantation is not only contrary to AATB's standards, but is inconsistent with FDA regulations.

When pooling can be validated for the prevention of CJD transmission, RTI's process may once again be considered. At that time, you must ensure that validation for the prevention of other infectious diseases has been completed. After reviewing the data from the four validation studies that were performed (Cross-Contamination, Viral Clearance, Antimicrobial Capacity, and Sterilization of the Reaction Chamber), we have concluded that the validation is not adequate. Among the deficiencies, we found that the studies lacked: validation data to show that the scaled-down laboratory models accurately simulate the full-scale process; a sufficient degree of log reduction for HIV, HAV, and PPV; convincing evidence from the cross-contamination study using Bacillus stearothermophilus to conclude that enveloped viruses and vegetative bacteria would be unlikely to transfer from one tissue to another; information about penetration and removal of germicides; validation data indicating the absorbency of the model viruses onto the tissues tested; and evidence that pressure variation was tested as a validation parameter.

Lastly, we note that you claim benefits of increased graft consistency from pooling. This claimed benefit has not been demonstrated using validated methods. Unlike plasma derivatives which, by necessity, are manufactured from pools of plasma in order to obtain a therapeutic dose and provide lot-to-lot consistency, musculoskeletal tissue does not require pooling to be used

effectively. Your end product consists of a random mixing of tissues from multiple donors, without any apparent increase in graft consistency.

Therefore, in the absence of an acceptable level of evidence documenting the ability of the BioCleanse™ System to prevent the contamination or cross-contamination of tissue, we believe it prudent to discontinue immediately its use for processing of tissue in your facility. Failure to do so, pending a response to the issues raised in this letter deemed acceptable to the FDA, may expose individuals to unwarranted risks.

Please notify this office in writing, within fifteen (15) working days of your receipt of this letter of the specific action(s) you have taken or intend to take with regard to the BioCleanse™ System. If your action(s) cannot be completed within 15 working days, please state the reason for the delay and the time within which the action(s) will be completed. Your response may be directed to Ms. Kathleen M. Lewis, Chief, Blood and Tissue Compliance Branch, Division of Case Management, Office of Compliance and Biologics Quality, CBER, at the address above.

Sincerely,

Steven A. Masiello
Director,
Office of Compliance and Biologics Quality
Center for Biologics Evaluation
and Research

Jay S. Epstein, M.D.
Director,
Office of Blood Research and Review
Center for Biologics Evaluation
and Research

Senate Permanent Subcommittee
On Investigations
EXHIBIT #___8___

PERMANENT SUBCOMMITTEE ON INVESTIGATIONS

Staff Background Memorandum

"Tissue Banks: is the Federal Government's Oversight Adequate?"

Senate Dirksen Office Building
Room 342
9:30 a.m.
Thursday, 24th May 2001

☆ ☆ ☆

This memorandum collects and summarizes some important background information that may help you and your Members prepare for our hearing on Thursday into the practices of the tissue bank industry.

Introduction

Human tissue is an important resource for medical treatment. Physicians and dentists use cadaveric human tissue for a variety of medical purposes. Donated skin can meet critical needs in healing burn victims and in reconstructive surgery. Bone can be used in knee and hip replacements, and in spinal surgery; it can also be used to replace cancerous bone, and can be processed into powder for use in dental surgery. Donated heart valves can replace defective valves in young children, thus saving their lives. Although the exact number of tissue donors is not known, they are clearly on the rise. In 1999, more than 20,000 donors provided cadaveric tissue, an increase from approximately 6,000 donors in 1994.[1] The National Donor Family Council has recently estimated that there are nearly 500,000 tissue transplants performed in the United States each year.

Tissue banks procure, process, store, and distribute human tissue. Because human tissue can transmit disease, and since tissue from a single donor may be implanted into many different recipients, federal regulation requires that testing be performed to screen and prevent the transmission of HIV-1 and -2, and hepatitis B and C.[2] The Food and Drug Administration (FDA)

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1 Department of Health and Human Services, Office of Inspector General Report, "*Oversight of Tissue Banking,*" January 2001, OEI-00-0044.

2 Those requirements relate exclusively to the Food and Drug Administration requirements. New York and Florida have additional screening requirements, which are addressed hereinbelow.

has proposed expanding the screening and testing requirements of human tissue, which are explained later in this memorandum.

There are three issues that currently dominate discussions of the U.S. tissue industry: (1) oversight of tissue banks; (2) informed consent from donor family members; and (3) the recent increase in the number of "for-profit" tissue-recovery and -processing organizations (insofar as tissue banks have traditionally been operated by *non*-profit organizations, which are now expressing concern that profit incentives may encourage the use of unethical and potentially unsafe tactics to acquire tissue).

I. *Oversight of Tissue Banks*

There are currently three types of tissue bank oversight: (a) the FDA concentrates on preventing transmission of communicable diseases by requiring donor screening and testing; (b) the American Association of Tissue Banks (AATB) conducts a voluntary accreditation program; and (c) the states of New York and Florida both inspect and license tissue banks (though they are the only U.S. states to do so).[3]

A. *Food and Drug Administration*

FDA first began regulating tissue in December 1993, under the auspices of its public health authority. In response to evidence about transmission of HIV to recipients of organs and unprocessed tissues from an infected donor, the agency issued an interim regulation that required tissue banks to perform donor screening for HIV.[4] In 1997, this regulation was modified when FDA inspectors found imported foreign tissue that had tested positive for hepatitis B. The final rule, which became effective on January 26, 1998, requires that tissue banks screen for HIV-1 and -2, and for hepatitis B and C.

The banks are required to maintain and make available to FDA inspectors' records documenting screening and testing for each donor of human tissue. FDA has the authority to order the retention, recall, and destruction of tissue that does not comply with those requirements. Since 1993, the FDA has conducted 188 inspections of 118 tissue banks. In more than half of those inspections, the FDA found deficiencies that needed correction. In 26 instances, the agency issued a "notice of official action" – indicating the most serious level of deficiency – which requires the bank to take some remedial action. (In 72 other inspections, FDA recommended that the bank take voluntary action to meet the agency's requirements.)

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3 Although New York and Florida are the only states that inspect tissue banks prior to issuing them licenses, a few other states, including California, Georgia, and Maryland, require tissue banks to be licensed by the state. .

4 *See* C.F.R. Pts. 16, 1270 (Dec. 14, 1993).

Prior to this year, there was not a central repository which could identify all of the tissue banks currently operating. However, on May 4, 2001, FDA completed the first stage of its newly imposed requirement for tissue banks to register with the agency.[5] Nevertheless, FDA still lacks a prescribed cycle for inspection and subsequent re-inspections of tissue banks. (For example, of the 118 banks that FDA has inspected since 1993, 68 have been inspected only once.) Despite receiving a letter from Senator Durbin in January 2001 requesting a cost estimate for establishing the registration and listing rules inspection protocol, the FDA has not been responsive. Even if it were, additional funds might need to be appropriated to FDA so that one oversight function is not simply defunded in order to pay for another. We have spoken with FDA representatives about their agency's failure to respond to the Durbin letter; they have indicated that FDA hopes to have an approved cost figure by the time our hearing takes place.

B. *Private Accreditation by the American Association of Tissue Banks*

The AATB is a private body that currently accredits 58 cadaveric tissue banks in the United States.[6] Of those 58, five are for-profit organizations, and the remainder are non-profit. Two of the largest processors – Regeneration Technologies, Inc. (RTI), based in Florida, and Cryo-Life, headquartered in Georgia – are not members of AATB. We were told by AATB's executive director that RTI is not a member because it engages in a practice known as "pooling" – that is, combining tissue from multiple donors.

Pooling is very controversial within the tissue industry, and is actually prohibited by the AATB. Though New York regulators disagree,[7] the general feeling elsewhere appears to be that pooling is risky because it is *not* possible either to test for emerging pathogens or to use sterilization to eliminate all the potential dangers of commingling tissue from many different bodies. Nonetheless, RTI wishes to join AATB, and is likely to seek an exemption from FDA regulations for its pooling practices. However, such an exemption is highly unlikely because on May 3, 2001, the FDA sent RTI a letter informing them that

> "[without] an acceptable level of evidence documenting the ability of the BioCleanse System to prevent the contamination or cross-contamination of tissue, we believe it prudent to discontinue

---

5 Tissue banks that manufacturer bone, skin, corneas, and fasica are required to have registered by May 4, 2001. Establishments that manufacture reproductive cells and tissue, and hematopoietic stem cells must register by January 21, 2003.

6 There are actually 71 AATB-accredited banks. However, 11 are reproductive banks, and two are located in Canada.

7 RTI has created a sanitizing process called BioCleanse which it says sterilizes tissue and eliminates bacteria and viruses. New York state granted RTI an exemption from its pooling prohibition because its chief virologist was satisfied that BioCleanse is effective.

> immediately its use for processing of tissue in your facility. Failure to do so, pending a response to the issues raised in this letter deemed acceptable to the FDA, may expose individuals to unwarranted risk."

Cryo-Life, the largest processor of heart values in the United States, is also not a member of AATB, but for different reasons. Cryo-Life was involved in a patent dispute with a competitor and considered AATB to be the ally of that competitor. Consequently, it did not seek to join. (It appears not to have suffered on account of this decision.)

The AATB's accreditation standards are consistent with, and in some cases even exceed, FDA standards. In addition to screening and testing for HIV and hepatitis, for example, the AATB requires that tissue banks test for human T-lymphotropic viruses (HTVL) and screen for Creutzfeld-Jakob Disease (CJD), which is closely related to the disease – bovine spongiform encephalopathy (BSE) – commonly known as "mad cow disease."[8] The AATB standards also address operational and organizational issues such as the qualifications of tissue bank personnel, safety practices, equipment testing, and quality assurance.

Accreditation involves review of a bank's written procedures and on-site inspection. The accreditation is given for a three-year period, at the end of which the bank is subject to another review, including an on-site inspection. Since 1986, AATB has accredited a total of 98 tissue banks. It has denied accreditation to 19 banks.

C. *State Regulation*

New York and Florida are the only two states that require tissue banks to be both licensed and inspected. New York law stipulates that all tissue banks conducting business within the state are subject to its regulations, regardless of where the bank is actually located. (In other words, tissue banks that are located out of state and are not licensed by New York regulators may not sell tissue to New York health care providers.) The state currently licenses 13 banks located in New York, and 36 located out-of-state. New York inspects all tissue banks prior to initial licensing, and every two years thereafter. Licensure requires an initial application – in which banks must disclose the identity of their owner and key staff – as well as an on-site survey. The banks must update their information annually, and report statistics on tissue procurement, processing, and distribution. In addition to testing and screening for HIV and hepatitis, New York also requires testing for HTVL and syphilis.

Like New York, Florida also licenses both in-state and out-of-state tissue banks. Currently, the state has issued licenses to nine Florida-based banks and 11 located in other states. Like New York, Florida inspects both in-state and out-of-state banks prior to initial licensure, and every two years thereafter. Applicant banks must disclose their ownership as well as information on equipment, donor selection, and testing criteria. The banks must comply with current FDA

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[8] BSE occurs only in animals, but a variant has been known to afflict humans as well.

regulations and must report to state officials, within 24 hours, all adverse events that could affect tissue recipients' medical conditions.

D. *FDA Initiatives*

In 1997, the FDA proposed a new approach to its regulation of human cellular and tissue-based products. Although tissues had long been used in transplantations, new scientific techniques had by then been developed that allowed for expanded and enhanced use of human cells and tissues as therapeutic products. The existing FDA regulatory framework of human cells and tissues was highly fragmented, and the agency did not clearly identify criteria for product characterization, which often resulted in confusion for both industry and FDA reviewers. Thus, the agency sought to implement a new regulatory framework that would provide a more unified approach to regulation of traditional and new products, with only the minimum amount of government oversight necessary to protect public health.

Accordingly, the FDA's proposal consisted of a tiered approach to cell and tissue regulation and focused upon: (1) preventing unwitting use of contaminated tissues with the potential for transmitting infectious diseases; (2) preventing improper handling or processing that damage or contaminate tissues; and (3) ensuring that clinical safety and effectiveness is demonstrated for tissues that are highly processed, are used for other than their normal function, are combined with non-tissue components, or are used for metabolic purposes.

To achieve the above identified goals, the FDA proposed the following three rules:

(1) *Registration of all tissue banks.* All tissue banks would be required to register with FDA and list their products. The proposed regulation would apply to organizations engaged in "recovery, screening, testing, processing, storage, labeling, packaging, or distribution of human cellular or tissue-based products." As mentioned above, the first phase of this regulation has been implemented; the second phase will be completed in January 2003.

(2) *Expanded screening and testing for communicable diseases.* In addition to the current requirement of screening and testing for HIV and hepatitis, screening and testing for the diseases HTLV and CJD would become mandatory under this rule. This "donor suitability" regulation would also address the prevention of cross-contamination through pooling.

(3) *Standards for "good tissue practices."* These standards – akin to the "good manufacturing practices" required of medical device pharmaceutical manufacturers – would cover areas such as proper handling, processing, and tracking of tissue. Each bank would be required to maintain standard operating procedures reflecting the regulatory requirements.

The response to the proposed rules has generally been favorable. The rules are patterned after the AATB standards, so AATB participated extensively in the drafting. (RTI supports all of the proposed FDA rules – with the exception of the pooling prohibition.)

The Association of Organ Procurement Organizations (AOPO) issues accreditation for facilities that deal with solid organs rather than tissue. Last fall, however, responses to a survey AOPO conducted made clear to the organization that over 90 percent of its members were also involved in tissue recovery. (As a result of this finding, AOPO established an "Ad Hoc Task Force on Tissue Donation" to address OPO-wide standards for entering into arrangements with tissue organizations and to review informed-consent policies.) AOPO has had little interaction with the FDA, but agrees with the rules.

II. *Informed Consent in Tissue Donation*

As part of its examination of the tissue industry, HHS-OIG concluded that the expectations and altruistic motives of donor families are the foundation of tissue banking. In agreeing to make donations, families make certain assumptions about the process, which generally include the beliefs that: (a) the tissue will be used for important medical needs; (b) the donor's body and the donor family's emotional needs during tissue recovery will be respected; and (c) organizations involved in procuring and using the donation will act as stewards of the gift, treating it with the dignity families feel it deserves.

The reality of tissue banking, however, is often at odds with such assumptions. Families are generally not aware of the commercialization of tissue banking, the incorporation of donated skin into products that are used for cosmetic purposes, and the marketing and selling of processed tissue products such as medical supplies.

A. *Requests and Consent for Donation*

The process for obtaining consent for tissue donations presents a marked contrast with that used in the case of organ donations. Solicitation of organ donations by organ procurement organizations (OPOs) occurs while the donor is on a life support system.[9] During this time, family members have an opportunity to contemplate and discuss the request. By contrast, tissue banks commonly obtain consent after the death of a loved one.[10] Acknowledging and discussing the profits

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[9] Under current regulations, organs may only be donated if the body has not yet reached "full" death – *i.e.*, if the donor is brain dead but is still being kept physically "alive" by artificial means. This, of course, necessitates that solicitation occur prior to taking the donor off life support.

[10] Tissue donations are permitted within a short period of time after death, so procurement organizations can afford to be much more reactive – often undertaking solicitation only after being notified of a death.

generated by donated tissue, and its potential cosmetic uses, may well exceed the emotional capacity of surviving families at a such a grievous time. Adding to the impersonal nature of such discussions is the fact that requests for tissue donations are usually made by telephone, since it would be logistically difficult for tissue bank staff to travel to every hospital where a person has died to request a donation.

The widely-divergent training of persons who solicit tissue donations on behalf of banks raises some concern. HHS-OIG found that when tissue banks rely on in-house personnel to obtain donor family consent, the banks conduct training and monitoring themselves. These fairly extensive training programs typically include lectures, presentations, role playing exercises, and mentors for less experienced personnel. These programs are generally provided by organizations with longstanding experience in this field. Personnel employed by external sources of solicitation services, however, generally received more minimal training, which was completed in an average of approximately four hours. (Following their initial training, solicitation personnel operate with very little oversight or accountability.)

HHS-OIG found that few tissue banks routinely give families a copy of their signed consent form, even though this document constitutes the legal authorization governing the removal of tissue. The banks also generally fail to provide families with an itemization of the specified purposes for which donated tissue may be used. A common alternative practice is for the banks simply to send families a letter expressing condolences and thanking them for the gift. This letter typically includes only a very general description of how tissue can be used to improve lives. Aside from such a letter, however, the banks often provide little additional information about tissue use, processing, or other entities with which the banks have financial arrangements.

B. *Industry Initiatives*

In September 2000, the National Donor Family Council (NDFC) approved its Informed Consent Policy for Tissue Donation. NDFC believes that a crucial element of the tissue donation process is that the informed consent of the donor family must include a voluntary decision based on full disclosure of the facts. Donor families should be: given a general explanation of the tissue donation process; told what tissue can be recovered based on medical suitability; informed that tissue can be used or modified in various ways in transplantation and/or medical research or education; and told that they have the right to limit or restrict the use of the tissue. In addition, NDFC believes that the completed consent form must be reviewed with the donor family before final consent and that a copy of the completed form should be offered to the family.

In November 2000, the AATB, AOPO, and the Eye Bank Association of America, adopted what they called "Model Elements of Informed Consent for Organ and Tissue Donation." These Elements recognize that families may seek additional information about donation. If a family makes such an inquiry, the Elements indicate, the bank seeking donation should provide sufficient information to address the family's questions. (Common disclosures that banks should anticipate include: the possibility that donated tissues may be manufactured into different products, such as

bone screws and joints; that transplantation may include reconstructive and aesthetic surgery; that multiple organizations, both non-profit and for-profit, may be involved in the process; and a reference to the possibility that tissue and/or organs may be transplanted abroad.)

C. *Laws and Regulations*

Currently, federal laws and regulations do not prescribe the manner in which tissue banks obtain consent for donation. The National Organ Transplant Act (NOTA), the principal regulation that governs organ donations and transplantations, requires that OPOs assist hospitals in establishing and implementing protocols for making routine inquiries about organ donations. No similar requirement exists for solicitation of tissue donations. Existing FDA regulations do require tissue banks to conduct an interview to obtain information regarding the donor's medical history and social behavior, but they stop short of addressing the method of obtaining consent.[11] While some state laws include stipulations on obtaining consent of anatomical gifts, none address the content of informed consent.

III. *Profit versus Non-Profit Tissue Banks*

In recent years, there has been a proliferation of for-profit tissue organizations entering the industry. The principal reasons cited for the increase have been both the development of new surgical procedures – cosmetic and otherwise – and advances in technology that enable technicians to reshape tissues and bones for uses that were previously unimaginable. According to an article in the *Orange County Register*, a single donor can yield more than $220,000 in revenue to tissue banks.[12] Moreover, the demand for tissue has become so intense that a board member of a California tissue bank described it as "[not] just competitive – it's predatory."[13] While it is illegal to sell tissue, the law does allow for "reasonable" fees to be charged to cover processing costs without defining reasonable.

One apparent effect of this competition for tissue is a discordant and antagonistic relationship between the for-profit and non-profit tissue banks. Both sides have charged the other with making misrepresentations and concealing information from potential donor families. For example, we heard from the Washington Regional Transplant Consortium (WRTC) that a local Lions Club received a $40,000 donation from a major for-profit processor, RTI, ostensibly to purchase a van that was equipped to travel throughout the community and conduct eye examinations. In exchange for this donation, however, the Lions Club reportedly agreed to establish a tissue bank. As a result of this

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[11] The FDA issued these regulations under the legal authority of section 361 of the Public Health Service Act, which authorizes the Secretary to make and enforce regulations judged necessary to prevent the introduction, transmission, or spread of communicable diseases.

[12] *Orange County Register* (May 4, 2000).

[13] *Id.*

transaction, the Lions Club is now essentially acting as an innocuous front for the somewhat controversial RTI.

The for-profits respond that they are better equipped to build superior tissue banks. Through the profits they derive, they say they can afford to purchase the best technological tools available to assist with the sterilization, storage, and transportation processes. Furthermore, they note that they can also fund research projects to help develop advances in medicine that will ultimately benefit the general population, and help people live a better quality of life. (Whether or not this is the case, their profits are certainly considerable. Last year, for example, RTI posted net revenues of $57.9 million, which was a 75 percent increase over 1999.)[14]

According to representatives of Osteotech, a for-profit tissue processor located in New Jersey, the for-profit and non-profit designation is largely meaningless – being reflective of nothing more significant than merely whether or not an organization pays taxes. Non-profit status, they emphasize, should not be confused with altruism. It is their opinion that non-profit tissue processors generally use the same business structure as the for-profits, and the competition is just as fierce among the non-profits. "Good" and "bad" actors in the tissue business, Osteotech argues, are distinguished not by their tax status by rather simply by the business and tissue practices in which they engage. (It was a *non*-profit tissue recoverer and processor that inadvertently spread AIDS to a number of tissue recipients in 1985.[15]) Osteotech also suggests that the non-profit tissue procurers should be required to disclose to donor families that they engage in business relationships with for-profit processors.

It is important to note that the AATB or FDA do not distinguish between for-profit and non-profit tissue organizations during the course of their inspections. Neither did the HHS-OIG during its examination. Instead, all tissue banks are evaluated based on the same criteria, regardless of their commercial status. We believe there may be much to be said for requiring *all* tissue banks to produce annual reports that disclose their financial situation; this would produce much greater transparency in their operations.

The HHS-OIG has suggested that the industry should work with donor family groups to develop a process for periodic public disclosure about all tissue banks' financing. Non-profit entities are already required to disclose information about the sources and uses of funds they receive; publicly-owned entities submit annual public reports to the Securities and Exchange Commission. These disclosures contribute to public accountability and could serve as a basis for building greater trust among donors, families, and tissue banks. The OIG has recommended that the industry

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14 *Orlando Sentinel* (March 26, 2001).

15 In 1991, it was determined that in 1985, LifeNet Tissue Bank had unwittingly harvested 54 tissue grants from an HIV-positive donor. The infected tissue, which reportedly tested negative for HIV twice before being delivered, was subsequently transplanted into 56 separate recipients. At least three of the patients who received tissue grants contracted HIV.

consider whether financial information would be useful as part of a package of information provided to donor families. Such consideration should include: (1) what types of – and how much – financial information would be useful for families and individuals in making decisions about donation; (2) the advantages and disadvantages of financial disclosure, including its potential impact upon donation decisions; and (3) the most appropriate content, style, and format of disclosure.

IV. *Hearing Plan*

Thursdays' hearing is structured so as to help us identify the strengths and weaknesses of current tissue industry and regulatory practices, with a particular focus upon issues at the forefront of current debates about the industry such as informed consent, the safety and soundness of tissue, and the role of nonprofit and for-profit tissue banks.

Panel One

The first panel will consist of a single witness, **Mr. George Grobb**, who is the Deputy Inspector General for Evaluations and Inspections at HHS-OIG. Grobb will discuss the findings detailed in HHS-OIG's two reports on the tissue industry: *Oversight of Tissue Banking* and *Informed Consent in Tissue Donation*. His testimony will focus on FDA's tissue bank inspection record, the safety and soundness of tissue, HHS-OIG's views on the informed consent process, and on the oversight structure governing the tissue bank industry.

Panel Two

The second panel comprises three witnesses. The first is from the AATB; the second is from the Washington Regional Transplant Consortium (WRTC); the third is a medical examiner from Florida.

(a) **Mr. P. Robert Rigney**, Esq. is the Chief Executive Officer of AATB. He will testify about the role the AATB plays in the tissue banking industry. He will also discuss the accreditation process and instances in which AATB has denied or revoked accreditation to tissue banks. He will testify about AATB's views on the controversial "pooling" method of tissue processing, and about AATB's opinions on the current regulatory framework and FDA's proposed rules.

(b) **Dr. William Minogue** serves as Chairman of the Board of the WRTC. The WRTC is the federally designated OPO for the metropolitan Washington, D.C. area, and is involved in both organ and tissue recovery. In accordance with federal law, the WRTC works with the staffs of local hospitals to offer the option of organ

and tissue donation to potential donor families. Minogue has been involved with the WRTC since its inception, approximately 14 years ago. Minogue is also Vice President for Medical Affairs at Suburban Hospital in Bethesda, Maryland. He will testify about the WRTC's experiences with tissue banks – good and bad – and about the WRTC's opinion of the current regulatory oversight of the tissue industry.

(c) **Dr. Valerie Rao** is the Lake County, Florida, Chief Medical Examiner, a position she has held for approximately one year, although her experience in this field dates approximately twenty years. Rao is the President-elect of the Florida Association of Medical Examiners, and serves as a member of the Medical Examiners Commission for the State of Florida.

Rao will testify that she became so concerned about the practices of the University of Florida (UF) tissue bank and RTI that she terminated her office's relationship with UF.[16] Until recently, UF and RTI had a very close relationship. (Indeed, RTI was a for-profit company spun off from UF in 1998, and the two organizations shared executives.) Rao says she was highly offended by what she saw of the treatment of donor bodies by these organizations. She will recount her experiences at the hearing, offer her opinion of the medical screening process that was being performed on donors, and convey her views of the regulatory oversight of tissue banks.

Panel Three

The third panel will consist of a single witness, **Dr. Kathryn Zoon**, who is the Director of the FDA's Center for Biologic Evaluations and Research (CBER). CBER's mission is to protect and enhance the public health through regulation of biological products including blood, vaccines, therapeutics and related drugs and devices according to statutory authorities. CBER currently regulates human tissue intended for transplantation that is recovered, processed, stored, or distributed by methods that do not change tissue function or characteristics and that is not currently regulated as a human drug, biological product, or medical device.

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16 Until recently, UF and RTI had a very close relationship due to the fact that RTI was a for-profit company spun off from UF in 1998. The organizations shared executives and administrative staff. The reason for the recent split is unknown.

Zoon will testify about FDA's role in tissue bank oversight, and may have a cost estimate for the costs involved in tissue bank inspection. She will also discuss FDA's recently proposed rules, and the comments FDA has received on them. She will also testify about problems FDA inspectors have found at tissue banks. Zoon will discuss FDA's opinion of tissue pooling, particularly at RTI, and the exemption granted to RTI by New York state regulators.

If you have any questions about this information or about our hearing, please contact Subcommittee Investigators Claire Barnard or Eileen Fisher, at 4-3721.

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Senate Permanent Subcommittee
On Investigations
EXHIBIT #9

Department of Health and Human Services

OFFICE OF INSPECTOR GENERAL

Informed Consent in Tissue Donation

Expectations and Realities

JANUARY 2001
OEI-01-00-00440

EXECUTIVE SUMMARY

PURPOSE

To assess expectations for and limitations of informed consent for tissue donation.

BACKGROUND

Human tissue is an important source of medical treatment. The specific number of tissue donors in this country is unknown. It is clear, though, that the numbers are growing. In 1999, more than 20,000 donors provided cadaveric tissue, up from perhaps 6,000 donors in 1994. Tissue banks distributed over 750,000 allografts for transplantation in 1999.

A first step in tissue donation is obtaining consent from a deceased individual's family. Even if the individual had indicated willingness to donate organs (*e.g.*, on the driver's license), it is practice in this country to obtain consent from the next-of-kin.

Tissue banking is subject to more limited regulation than is the nation's organ procurement system, even though both organ procurement organizations (OPOs) and tissue banks are involved in approaching families to request consent for donation. For example, the National Organ Transplant Act requires OPOs to meet certain organizational and staffing requirements; the Act also requires OPOs to assist hospitals in establishing and implementing protocols for making routine inquiries about organ donation by potential donors. No similar requirements exist for tissue banks.

This report responds to a request from the Secretary of Health and Human Services, asking the Office of Inspector General to examine issues related to informed consent for tissue donation. We base our report on interviews with 30 organizations involved in tissue recovery and processing; responses from more than 50 donor families to questions posted on an Internet web site; interviews with officials of associations representing sectors of the tissue banking industry; and a review of laws, regulations, and association standards for tissue banking.

In this report, we use the term "tissue banks" to refer to entities involved in procuring, processing, storing, and distributing tissue. We use the term "tissue" to refer to skin, heart valves, and musculoskeletal tissue such as bone, cartilage, ligaments, and tendons.

FINDINGS

The expectations and altruistic motives of donor families are the foundation of tissue banking. Donor families and tissue bank staff told us that in agreeing to donation, families make some basic assumptions:

- **Enhancing the lives of others.** Tissue will be used to meet important medical needs.
- **Respect for the donor and the family.** The donor's body will be respected during tissue recovery, the gift will be recognized as coming from donated human tissue, and

the donor family's emotional needs will be respected.

- **Trust in the tissue banking community.** Organizations involved in procuring and using the donation will act as stewards of the gift.

However, the reality of tissue banking raises some underlying tension with families' assumptions.

- **Commercialization of tissue banking.** Large scale financial operations may overshadow the underlying altruistic nature of tissue donation.
- **Tissue viewed as a commodity.** After processing, tissue and products containing tissue often are marketed and sold as a medical supply, rather than as a donation.
- **Cosmetic uses of tissue.** Some tissue, particularly skin, may be processed into products that are used for cosmetic purposes that may not be medically indicated.

Fundamental factors limit the amount of information that is given to families.

- Families are asked to give their consent at a point in time when they are extremely vulnerable.
- Families may not wish to receive detailed information about tissue banking.
- Obtaining consent and documenting a donor's medical suitability require time-consuming and invasive questioning about a recently deceased loved one.

Current practices in requesting consent raise concerns about how and what information is provided to families.

- Tissue banks often request consent over the telephone, rather than in person.
- Many tissue banks rely on staff from other organizations to obtain consent. There may be little training and accountability of external tissue requestors.
- Tissue banks provide donor families with little written material at the time of donation.

Until recently, standards governing how families are approached and what they are told about tissue donation have been nonexistent. However, some advice and guidance have emerged.

- Federal laws and regulations do not address the manner in which tissue banks obtain consent.
- States' Uniform Anatomical Gift Acts do not address what information tissue banks should provide in obtaining consent.
- The National Donor Family Council has proposed key elements of an informed consent policy for tissue donation.
- Organizations representing the tissue banking industry have issued a statement that addresses elements of informed consent. These organizations include the American Association of Tissue Banks (AATB), the Association of Organ Procurement Organizations, and the Eye Bank Association of America. The AATB is incorporating this statement into its accreditation standards for tissue banks.

CONCLUSION

Tissue banking and processing practices have gradually diverged from donor families' expectations in recent years. The tissue banking industry has expanded and become more complex and costly. New ways of using tissue for medical treatment have been developed. Processed tissue often is marketed and sold like any other medical product. For some people, these practices call into question the non-profit basis of the tissue banking community. Despite these changes, the industry's foundation remains that of human tissue altruistically donated by individuals and their families at an extraordinarily sensitive time. The special nature of this product, and the circumstances under which it is made available, call for steps to be taken above and beyond those that would apply to most other business or philanthropic enterprises.

RECOMMENDATIONS

Importance of increasing donation. The Office of Inspector General has examined issues related to organ, tissue, and bone marrow donation, allocation, and transplantation for more than a decade. The principles underlying our work have focused consistently on enhancing equity for patients, improving access to transplantation, and encouraging donation.

Encouraging donation was of paramount importance to us as we developed our recommendations. It is our hope that these recommendations will encourage donation. Our recommendations encourage joint action among groups representing the tissue banking industry, donor families, and the government.

RECOMMENDATIONS TO THE DEPARTMENT

The Health Resources and Services Administration should work with groups representing donor families and the tissue banking industry to develop guidelines for conveying information to families about tissue donation.

HRSA's Division of Transplantation supports the development of programs to increase donation. In that role, HRSA has gained considerable expertise about effective practices in requesting consent. The agency could act as a resource to tissue banks and families.

HRSA's efforts could focus on such areas as:

- Identifying principles and guidelines that should underpin consent requests, such as those outlined recently by the National Donor Family Council and by industry groups;
- Making suggestions as to the type, format, and content of written information about donation that tissue banks could share with families.
- Making recommendations on information that would be useful for training tissue bank staff and external requestors; and
- Making recommendations on assessment tools that would be useful in evaluating the effectiveness of requestors.

The Health Care Financing Administration should address informed consent for tissue donation through the Medicare conditions of participation.

HCFA requires hospitals to assure that the family of each potential donor is aware of its options to donate tissues, organs, and eyes. Elsewhere in this report, we call upon donor family groups, the tissue banking industry, and HRSA to develop guidelines for conveying information to families about tissue donation. HCFA could use these guidelines as it provides information about the conditions of participation for organ, tissue, and eye donation. The agency could publicize these principles through the HCFA Internet site.

In the longer term, the agency may wish to examine the Medicare conditions of coverage governing organ procurement organizations. In that examination, the agency could consider additional requirements to strengthen working relationships between OPOs and tissue banks. Such requirements might include:

- Holding OPOs responsible for informed consent for tissue donor families when they request consent on behalf of tissue banks; and
- Requiring OPOs to include tissue banks in the training that they conduct for designated requestors.

RECOMMENDATIONS TO THE INDUSTRY

At the time of obtaining consent, tissue banks should provide families with written materials that provide fuller disclosure about the uses of tissue and the nature of the gift.

Tissue banks should give written material to families at the time the banks ask for consent to donation, or in the days immediately following the request. The material should be appropriately thorough. It would serve as one way to supplement the information that requestors provide to the family during their conversation about donation, while providing requestors with flexibility to adapt that conversation to the unique needs and responses of each donor family. At a minimum, this material should include:

- A copy of the signed consent form;
- Written material on how to follow up with the tissue bank if concerns arise;
- A full description of the uses to which donated tissue may be put; and
- A list and description of other companies and entities with which the bank has relationships for processing and distributing tissue.

Tissue processors and distributors should ensure that information accompanying their product clearly indicates it is derived from *donated* human tissue.

Such a step would require only minor changes in packaging and marketing materials. But it would go a long way towards showing ongoing respect for the donor, the family, and the gift of donation. Tissue banks should:

- Indicate clearly on all tissue packaging that the contents derive from donated human tissue; and

- Indicate clearly on all marketing and informational material that these products derive from donated human tissue.

Tissue banks should foster greater accountability for the performance of those who request consent for donation.

Responsibility for ensuring that requestors are providing accurate, sensitive, and appropriate information rests with tissue banks and the processors with which they work. These organizations should:

- Ensure that requestors — both from their own organizations and from hospitals — are fully and appropriately trained;
- Provide continuing education for requestors; and
- Conduct an ongoing assessment of requestor performance as a means of ensuring that they are providing full and accurate information to families approached for donation.

The tissue banking industry should work with groups representing donor families to explore a process for periodic public disclosure about tissue banks' financing.

The purpose of the examination we recommend here is to respond to family and general public concerns about knowing the sources of funding for tissue banks and other entities with which the bank has financial arrangements. The examination would consider whether financial information would be useful as part of a package of information provided to donor families. The examination would consider:

- What types and how much financial information would be useful for families and individuals in making decisions about donation;
- The advantages and disadvantages of disclosure, including the potential impact of financial disclosure on donation;
- Whether the information should be provided in all cases, or only if requested by a family; and
- The content, style, and format of disclosure.

COMMENTS ON THE REPORT

We received comments on a draft of this report from the Department of Health and Human Services. They are supportive of our findings and recommendations. The full text is included in Appendix C.

Our work in tissue banking continues. We will maintain an active watch on how the tissue banking community responds to the concerns we have raised.

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INTRODUCTION

PURPOSE

To assess expectations for and limitations of informed consent for tissue donation.

BACKGROUND

Transplantation of Human Tissue

Human tissue is an important resource used in medical treatment. Physicians and dentists use cadaveric human tissue for a variety of medical purposes. Donated skin can meet critical needs in healing burn victims and in reconstructive surgery. Donated bone can be implanted to replace cancerous bone, for knee and hip replacements, and for spinal surgery; it can be processed into powder for use in dental surgery. Donated heart valves can replace defective valves in young children, saving their lives.

The exact number of tissue donors in this country is unknown. It is clear, though, that the numbers are increasing. In 1999, more than 20,000 donors provided cadaveric tissue, up from perhaps 6,000 donors in 1994. Tissue banks distributed over 750,000 allografts for transplantation in 1999.

Consent for Donation

A first step in tissue donation is obtaining the consent of a deceased individual's family. Even if the individual had indicated willingness to donate organs and tissues (*e.g.*, on the driver's license), it is practice in this country to obtain consent from the next-of-kin. A family may refuse to give consent, or it may give consent for donation of all or only some tissues.

Tissue banking is subject to more limited regulation than the nation's organ procurement system, even though both organ procurement organizations (OPOs) and tissue banks are involved in approaching families for consent. For example, the National Organ Transplant Act requires OPOs to meet certain organizational and staffing requirements; the Act also requires OPOs to assist hospitals in establishing and implementing protocols for making routine inquiries about organ donation by potential donors. No similar requirements exist for tissue banks.[1]

Concerns about Tissue Banking

Several press reports in the Spring of 2000, appearing in the *Orange County Register* and the *Chicago Tribune,* raised a number of concerns about tissue banking. A particular focus of these articles related to financial aspects of the tissue banking industry. Several members of Congress asked the Secretary of Health and Human Services to examine the

tissue banking industry, including the extent to which families were informed about financial arrangements or uses to which tissue might be put.

This Inquiry

The Secretary asked the Office of Inspector General to review two aspects of tissue banking: consent for donation and the overall regulatory structure governing the industry. This report responds to the first of those requests, focusing on informed consent. Our companion report, *Tissue Banking Oversight* (OEI-01-00-00441), provides a profile of the oversight system for tissue banking and addresses limitations in that system.

We use the term "tissue" to refer to skin, heart valves, and musculoskeletal tissue such as bone, cartilage, ligaments, and tendons. Our report does not address eyes and reproductive tissue.

METHODOLOGY

We conducted interviews with senior staff from 30 organizations involved in obtaining, processing, and distributing human tissue; 25 of these organizations were involved in obtaining consent and recovering human tissue.[2] Our interviews focused on their policies, practices, and experiences relative to consent.

With assistance from the National Kidney Foundation, we posted a series of questions on the web site of the National Donor Family Council. These questions sought to provide us with a donor family perspective of experiences with the donation process. We received 50 responses from donor families through this web site. We recognize that the findings from this posting do not constitute a random sample from which projections can be made. Nevertheless, we believe that the responses provide important information and a valuable perspective on the process of obtaining consent.

We interviewed officials and staff, and reviewed documents, from associations involved with tissue banking, including the American Association of Tissue Banks (AATB), National Donor Family Council, Eye Bank Association of America, Association of Organ Procurement Organizations, and North American Transplant Coordinators Organization.

We reviewed State and Federal laws and regulations related to tissue banking, and standards from the AATB.

We conducted this inspection in accordance with the *Quality Standards for Inspections* issued by the President's Council on Integrity and Efficiency.

FINDINGS

The expectations and altruistic motives of donor families are the foundation of tissue donation. Donor families and tissue bank staff told us that in agreeing to donation, families carry some basic assumptions:

Expectation that the donation will enhance the lives of others.

Families expect that their loved one's tissue will be used in meeting important medical needs. The primary expectation is that the tissue will be used for transplantation, as a way of improving the lives of people with medical needs. Many families also provide consent to use tissue for medical research and medical education.

Families may view donation as a way of creating something positive from the death of their loved one. The mother of one tissue donor captured this view when she told us, "If my son helped just one person live a better life, then his donation was worth it." This expectation is reflected in the comments we received from a number of donor families. These families hoped for some type of follow-up with people who had benefitted from their loved one's gift of tissues, as a way of confirming the usefulness of and appreciation for the gift.

Respect for the donor and the family.

Respect has two broad components. First, families anticipate that the donor will be respected. This respect should last through the entire donation process. It includes, for example, respect for the donor's body during tissue recovery. Tissue recovery requires invasive surgery. For families, respect entails that no more harm is done to the body than absolutely necessary.

During processing, distribution, and transplantation, respect entails that the gift be recognized as coming from a donation of human tissue. Musculoskeletal tissue often is processed into many forms. These forms include bone screws, dowels, and bone chips, which have many different medical uses. These final products often bear little resemblance to human tissue; in fact, they look more like tools, hardware, supplies, and devices than what most people would call human tissue. The mother of a donor exemplified the concern that respect be maintained for the donor when she told us, "That 'screw' is not a screw to me — it came from somebody's loved one or child."

Second, donor families expect that their own needs will be respected by the tissue banks. Respect for the family includes discussing the option of donation in a sensitive manner, answering all questions, and ensuring that the timing of and plans for funeral arrangements are not disrupted by tissue recovery.

The AATB's Statement of Principles reflects the importance that the association and its members accord to the importance of respect. Member banks pledge "to honor and treat with respect the gifts that have been donated and to reflect this in all activities related to cell and tissue procurement."[3]

Trust in the organizations involved in procuring and using the donation.

At the time of their loss, families are asked to place enormous trust in tissue banks. Prior to requesting donation, it is unlikely that any relationship existed between the donor family and the tissue bank. Quite possibly, the family may never have heard of tissue donation. Tissue banks request a donation of their loved one's body at the time the family is grieving. As a member of one donor family noted, "It is an extremely emotional display of trust, to allow someone to take parts of a loved one."

Tissue banks we spoke with echoed the sentiments of donor families. One tissue bank director viewed tissue procurement as a public service and said that the bank has the responsibility for ensuring that tissue is "used for the right purposes." Another tissue bank director shared her view of this responsibility: "We are stewards of the gift the family is giving, and it is up to us to handle it in an appropriate manner."

However, the reality of tissue banking raises some underlying tension with families' assumptions.

Commercialization of tissue banking

Families view tissue donation as an altruistic act. This perspective is buttressed by the National Organ Transplant Act, which states that it is "unlawful to acquire, receive or otherwise transfer any human organ [including several defined types of tissue] for valuable consideration for use in human transplantation."[4] Although the act permits recovery of reasonable costs associated with activities such as retrieval and processing, concerns have been raised about whether individuals and firms may be receiving unreasonable financial enrichment from procuring, processing, or distributing the altruistic donation.[5]

No one denies that there are costs associated with processing tissue, conducting research, developing new products and uses, and advancing science. However, the large-scale financial aspects of tissue banking create tensions with an altruistic act.

These tensions have particular relevance to the operation of for-profit firms in what is, at least nominally, an altruistic enterprise based on donation. Publicly-traded companies have raised capital and brought entrepreneurial energy to tissue processing, leading to the development of new processes and products. Yet, it is precisely at this point that tension arises. The concern may be best characterized as unease about a focus on the "bottom line," as portrayed in the following question: If a company's primary interest is financial benefit to its stockholders, is it making choices to put tissue to more lucrative uses over

medical needs?[6]

A second facet of tension with commercialization relates to the level of salaries and costs incurred by both non-profit and for-profit firms. Although reasonable costs are permitted, there is no definition of, and undoubtedly no consensus about, what constitutes "unreasonable costs." In fact, no guidelines are in place regarding disclosure of costs, and no comparative data are available publicly on the range of costs that would permit such a determination.

Finally, the industry is intensely competitive, with firms establishing proprietary patents on a number of products and processes. Some observers view this as primarily an effort to gain competitive advantage and market share in the distribution of tissues.

In a vacuum, these issues do not raise concerns. Yet in an industry that is premised on donation of parts of a loved one's body, it should not be surprising that donor families could feel misled as they question why "everyone is making money off of this altruistic gift except the donor and the donor's family."

The importance of concerns about commercialization for informed consent relates to whether families may wish to know about commercial relationships that exist between the agency to which it makes an altruistic donation, and an entity — be it non-profit or for-profit — that realizes revenue from the gift. If they are not made aware of these relationships, it may be difficult to say that their consent truly is informed.

Tissue viewed as a commodity

Maintaining respect for the donor and the donor's family is an underpinning of the tissue system. As we discuss above, tissue is processed extensively for many different uses. The marketing of human tissue as a commodity bears particular relevance to donor families' assumption that their loved one's tissue will be treated with respect and honor, and that it will be respected by the users and the recipients of tissue.

The packages in which human tissue is supplied — bottles, vials, containers shrink-wrapped in plastic — resemble many other medical supplies. The labeling does state that the contents are human tissue, but this is related to concerns about safety and disease transmission rather than respect for the donor. The packaging does not indicate that the enclosed materials derive from *donated* human tissue.

We reviewed marketing materials from both for-profit and non-profit companies. These product brochures look like typical medical supply catalogues, contributing to a perception that tissue is no different from other supplies. As with the packaging, the marketing materials rarely indicate that the materials derive from *donated* human tissue.

Cosmetic uses of tissue

A number of products used in reconstructive surgery utilize donated tissue, particularly

skin. These products are used in procedures that most people would, no doubt, consider medically appropriate and necessary. Examples of such procedures include alleviating serious scarring or constructing a bladder sling for treatment of urinary incontinence.

On the other hand, there clearly are some uses of these products that many people would consider to be non-essential cosmetic uses.[7] It is not clear how much tissue goes for such cosmetic uses; because the actual use of these products is determined by physicians and patients, tissue banks that manufacture them do not have that information. However, a family may be reluctant to give its consent for donation if it is aware that the gift would be used for purposes that are not medically indicated.

The American Medical Association's policy provides a useful framework for considering the differences between cosmetic and reconstructive surgery. That policy states that "*cosmetic* surgery is performed to reshape normal structures of the body in order to improve the patient's appearance and self-esteem. *Reconstructive* surgery is performed on abnormal structures of the body, caused by congenital defects, developmental abnormalities, trauma, infection, tumors or disease. It is generally performed to improve function, but may also be done to approximate a normal appearance."[8]

Fundamental factors limit the amount of information that is given to families.

Families are asked to give their consent at a point in time when they are extremely vulnerable.

The recent, often sudden and unexpected, death of a loved one means that families are likely to be distraught when they are asked for consent to donate. In the face of sudden tragedy, they may simply be unable to understand detailed information about tissue donation.

Tissue donation is a complex topic. Tissue banks must obtain consent for donation within hours following the death of a loved one. Because the family may be in shock, discussing multiple aspects of tissue donation and tissue banking — recovery, processing, distribution, commercial relationships — may go well beyond the capacity of families to comprehend what they are hearing. The father of a tissue donor echoed this sentiment when he commented to us, "I doubt donor families can process much information; they hear very little at a time when they are immersed in profound shock and grief."

At the same time, families may not wish to receive detailed information about tissue banking.

Often, families know they want to consent to donation, but do not want to hear specific details about the process. As one tissue donor mother told us, "I really didn't need any more information than what was provided; frankly, I wouldn't have been able to deal with much more at that point." Her thoughts were echoed by a tissue bank director who told

us that it is crucial to be able to give families as much or as little information as they want, depending on where they are in the grief process.

Tissue bank staff with whom we spoke cited the balance they must strike when speaking with families. Much information needs to be communicated to the family at the time of consent; at a minimum, authorization for removal of specific tissues is required. Families also must agree to whether the tissue may be used only for transplantation, or for other uses such as research and education.

Tissue bank staff told us that families generally have two primary concerns: whether the family will incur any costs for donating tissue and whether the body will be suitable for an open-casket viewing. They noted that it is rare for families to ask about other concerns. On the other hand, some families may wish to have more information to help them reach a decision, or they may wish to receive more information that they could reflect upon at a later date. The challenge for those seeking consent is to gauge how much detail a particular family wishes to receive.

Obtaining consent and documenting a donor's medical suitability require time-consuming and invasive questioning about a recently deceased loved one.

Because tissue can transmit disease, FDA requires tissue banks to screen donors for evidence of behaviors that place them at high risk for HIV and hepatitis.[9] This screening requires completion of a lengthy medical and social history questionnaire as part of determining donor suitability. Tissue bank personnel who administer the medical and social history questionnaire to families note that the process may take as long as an hour or more to complete. The tissue bank staff must administer this questionnaire shortly after the family consents to donation.

Donor families must answer questions about the deceased's medical history and personal behaviors, including uncomfortable questions about drug and alcohol use, and about sexual behavior. Under any circumstances, questions such as these are intrusive. After the death of a loved one, this effect undoubtedly is amplified.

Current practices in requesting consent raise concerns about how and what information is provided to families.

Many tissue banks rely on staff from other organizations to obtain consent.

We interviewed staff from 25 banks that recover tissue; 14 of these banks rely primarily on their own staff to request consent from families, and 11 banks rely on others to make the requests. The American Association of Tissue Banks conducted an informal survey of its members. AATB found that 42 percent of accredited tissue banks use their own staff to request consent for tissue donation, while the other 58 percent of banks use individuals not employed by the bank for requesting.

About half of the external requestors are staff from organ procurement organizations

(OPOs). OPOs play an important role in tissue donation, even if they do not operate a tissue bank. Recent changes to the Medicare conditions of participation for hospitals gave OPOs an important gatekeeping function by requiring a hospital to notify its OPO of all deaths. Thus, even for persons who do not meet the stringent criteria for organ donation, OPOs play a role in referring the call to the appropriate tissue bank and, in some cases, seek consent from the family for tissue donation.[10]

External requestors include staff from telephone triage agencies with which the tissue bank contracts for the specific purposes of requesting consent. Tissue banks also rely on hospital staff, primarily nurses, chaplains, and social workers, to obtain consent from families. Tissue banks may wish to keep hospital staff involved in and committed to donation. These staff may well have been in close contact with the family, and families may be more trusting and receptive to donation when it is discussed by these caregivers.

Other tissue banks prefer to handle the consent process themselves. The director of one OPO that also operates a tissue bank told us she "simply feels more comfortable knowing that trained coordinators are doing the requesting." This approach also benefits hospitals; it is a way of relieving a hospital of liability for its own staff should problems arise.

Tissue banks often request consent over the telephone, rather than in person.

Consent requests for tissues contrast sharply with requests for organ donation. In requesting organ donation, OPO staff seek consent from the family while they are still at the hospital. OPO staff often have spent long hours with the family prior to disconnecting the ventilator, and they likely have established a rapport with that family.

In our interviews, 16 of 25 tissue banks that recover tissue said that they primarily request consent over the telephone, rather than in person. In most cases, tissue banks make these requests after the family has left the hospital. Tissue bank staff told us that it is more productive to give the family time to return to the familiar surroundings of home, rather than the coldness of a hospital. At a practical level, it also would be quite difficult for the tissue bank staff to travel to every hospital when someone has died in order to request donation.

There may be little training and accountability of external requestors.

Tissue banks train and monitor their own staff who request consent. Training programs typically include classroom lectures, written materials, presentations, observing other requestors, role playing, and mentoring by seasoned requestors. Many banks send requestors to training courses offered by organizations with longstanding expertise in the field. Most tissue banks we spoke with also provide their staff with continuing education.

Training programs for tissue requestors not employed by the bank tend to be briefer. Training programs for external requestors at tissue banks we spoke with ran about 4 hours on average. Training generally comprises presentations by tissue bank staff and covers topics including how to interact with families, the use of tissues, and how tissues are recovered. A few tissue banks offer longer programs that include role-playing exercises.

After the initial training, only a small number of tissue banks we spoke with offer continuing education or follow-up training to external tissue requestors.

Training for tissue donation also may take place through an OPO's designated requestor training program. Yet, as we have shown elsewhere, few OPOs conduct this training.[11] Tissue bank staff we interviewed also indicated that OPOs give only limited attention to training about requesting tissue donation, because organ donation is often seen as a higher priority than tissue donation. This difference in emphasis is likely to be more pronounced in areas where there is competition between the tissue bank and the OPO.

Providing in-depth training of external requestors faces some major constraints. Tissue bank directors we interviewed noted that it is difficult for hospital staff to take time from their duties for intensive training as a tissue requestor. Additionally, tissue banks that rely on hospital staff to request consent may be unable to select the hospital staff to be trained. Thus, staff who may not want to be tissue requestors may be trained for the process and, subsequently, may do a poor job of it.

Even among those tissue banks that train external requestors, we found that few actively assess their performance. The primary vehicle we found for assuring accountability was that some tissue banks use their own staff to contact the donor family at home to complete the medical-social history questionnaire. These banks told us that having their own staff speak with the donor family provides a checkpoint for the consent process, because staff can answer questions, provide more information, and reaffirm the consent.

Tissue banks provide donor families with little written material at the time of donation.

Few tissue banks routinely give families a copy of the signed consent form. The consent form, however, is the legal authorization governing the removal of tissue and specifying purposes for which the tissue may be used. One tissue bank told us that it asks family members if they want to receive more information. Other tissue banks indicated that they would give the family the form if someone requested it. However, requiring a family to make such a request places it in a deferential position, when the bank could proactively make the consent form available.

Following donation, it is general practice for tissue banks to send families a letter thanking them for the gift and expressing condolences. We reviewed copies of these letters from 11 tissue banks; about half gave a general description of which tissues were recovered, and the other half conveyed information in broad, generic terms about how tissue can be used to improve people's lives. Many of the tissue banks we spoke with provide additional materials about grieving and about support groups.

Aside from this letter, tissue banks provide little additional written information to families about tissue use, processing, or other entities with which they have financial arrangements. Tissue bank staff we spoke with told us they are hesitant to provide more information to families, either at the time of consent or afterwards, because the family is

grieving and may not want to think about the donation.

Many donor families told us that consenting to donation was a positive outcome that came from their loved one's death. Because families may not comprehend everything that is told to them at the time of donation, more information may be beneficial at a later date. One donor mother captured this sentiment when she told us, "I know there are many families who would like to have some reading material to refer to when or if they are ready, since there is so much information that is not heard within this horrific moment."

Until recently, standards governing how families are approached and what they are told about tissue donation have been nonexistent. However, some advice and guidance have emerged.

Federal laws and regulations do not address the manner in which tissue banks obtain consent.

The Health Care Financing Administration has no statutory or regulatory authority over tissue banks. However, the 1998 Medicare conditions of participation for hospitals relating to organ, tissue, and eye donation require hospitals and tissue banks to work together to establish donor suitability criteria. The regulations also require hospitals to ensure that all families of potential donors are informed of their options to donate organs, tissues, and eyes, and that programs for training hospital-based requestors are designed in conjunction with the local tissue banking community.[12] However, the regulation does not provide specific guidelines on the content, circumstances, or manner of approaching donor families.

The Health Resources and Services Administration (HRSA) provides resources and support to the transplantation community. HRSA recently published a resource guide that provides information and approaches on training hospital staff and procurement agencies in working and communicating with grieving families as part of the donation process.[13]

The Food and Drug Administration's (FDA) authority over tissue banks derives from Public Health Service Act provisions authorizing regulations to prevent the spread of communicable diseases. The agency requires that donor screening and testing for HIV-1 and -2 and for Hepatitis B and C. FDA regulations do not address the issue of obtaining consent for donation; however, the regulations do require tissue banks to interview someone such as a close relative about the donor's medical history and social behavior.[14]

States' Uniform Anatomical Gift Acts do not address what information tissue banks should provide in obtaining consent.

All States and the District of Columbia have enacted versions of the Uniform Anatomical Gift Act.[15] These laws establish procedures for competent adults to make anatomical gifts by completing and signing a legal document. These gifts are irrevocable at the donor's death. The laws also include some stipulations on obtaining consent, such as the

order in which next-of-kin may make decisions, documentation required, or the number of persons who must provide legal witness. However, these laws do not address the content of informed consent.

The gift acts in some States specify the informed consent document that must be signed. The consent form itself, however, is a legal document, not a mechanism for sharing pertinent information about donation with the family.

The National Donor Family Council has proposed key elements of an informed consent policy for tissue donation.

The National Donor Family Council (NDFC) represents about 8,000 donor families. The NDFC recently approved a position statement on tissue donation that addresses important considerations for discussing donation with donor families. The full position statement appears in Appendix A. Key elements include:

- Explanations on how tissue is recovered, processed, stored and distributed;
- Explanations that the tissue may be used or modified for transplantation;
- Explanation that the family may limit or restrict the use of tissue; and
- Requirements that the consent form be reviewed with families and that a copy be offered to the family.

Organizations representing the tissue banking industry have issued a statement that addresses elements of informed consent to be included in discussions with families.

The American Association of Tissue Banks (AATB), the Association of Organ Procurement Organizations, and the Eye Bank Association of America, issued a joint statement in December, 2000. The full position statement appears in Appendix B. AATB, which accredits 58 cadaveric tissue banks, is incorporating the elements contained in this statement into its accreditation standards. The updated standards are scheduled for publication in January, 2001.

The statement addresses basic elements of informed consent which should be provided to all families. These basic elements include:

- Identification of specific tissues that are being requested for donation;
- Explanation that retrieved tissues may be used for transplantation, therapy, research, or education; and
- A general description of the recovery process.

The statement also recognizes that families may seek additional information about donation. If so, additional explanations should be provided to address such issues as:

- The possibility that the gift may take a different form than originally recovered;
- Transplantation may include reconstructive and aesthetic surgery; and
- Multiple organizations (non profit and/or for profit) may be involved in facilitating the gift.

CONCLUSION

Tissue banking and processing practices have gradually diverged from donor families' expectations in recent years. For donor families, the altruistic donation of tissue from a loved one is a charitable act. Donation is made with few expectations other than that it will be used to enhance the lives of others, that the donor will be treated with respect, and that the organizations with whom tissue banks work will take special care to ensure that the gift is used for these purposes.

Today's tissue banking industry and the beneficial uses of human tissues and related products have become more complex and costly. New ways of using tissue for medical treatment have been developed. Tissue banking has been infused with capital and entrepreneurial practices. Processed tissue often is marketed and sold like any other medical product. For some, these practices call into question the non-profit basis of the tissue banking community.

Despite these changes, the foundation of the industry remains that of human tissue freely donated by individuals and their families at a most difficult and extraordinarily sensitive time.

The special nature of human tissue, and the circumstances under which it is made available, call for certain steps to be taken above and beyond those that would apply to most other business or philanthropic enterprises. In the following section, we share our recommendations that take these into account.

RECOMMENDATIONS

Importance of Increasing Donation

The Office of Inspector General has examined issues related to organ, tissue, and bone marrow donation, allocation, and transplantation for more than a decade. The principles underlying our work have consistently focused on enhancing equity for patients, improving access to transplantation, and encouraging donation.

Encouraging donation was of paramount importance to us as we developed these recommendations. It is our hope that these recommendations will encourage donation. Our recommendations encourage joint action among groups representing the tissue banking industry, donor families, and the government.

The Department of Health and Human Services

The Health Resources and Services Administration should work with groups representing donor families and the tissue banking industry to develop guidelines for conveying information to families about tissue donation.

HRSA's Division of Transplantation supports the development of programs to increase donation. In that role, HRSA has gained considerable expertise about effective practices in requesting consent. The agency could act as a resource to convey information about donation to tissue banks and families.

HRSA's efforts could focus on such areas as:

- Identifying principles and guidelines that should underpin consent requests, such as those outlined recently by the National Donor Family Council and jointly by the American Association of Tissue Banks, Association of Organ Procurement Organizations, and the Eye Bank Association of America;
- Making suggestions as to the type, format, and content of written information about donation that tissue banks could share with families;
- Making recommendations on information that would be useful for training tissue bank staff and external requestors; and
- Making recommendations on assessment tools that would be useful in evaluating the effectiveness of requestors.

The Health Care Financing Administration should address informed consent for tissue donation through the conditions of participation for hospitals and for organ procurement organizations.

As we note above, HCFA requires hospitals to assure that the family of each potential donor is aware of its options to donate. This requirement applies to tissue donation, as

well as to donation of organs and eyes.

Elsewhere in this report, we recommend that HRSA work with donor family groups and the tissue banking industry to develop guidelines for conveying information to families about tissue donation. HCFA could use these guidelines as it provides information about the hospital conditions of participation for organ, tissue, and eye donation. The agency could publicize these principles through the "Questions and Answers" document posted on the HCFA Internet site. For example, the agency may wish to encourage hospitals to include a protocol for informed consent in their agreements with tissue banks, using the recommended guidelines in those protocols.

In the longer term, the agency may wish to examine the Medicare conditions of coverage governing organ procurement organizations. In that examination, the agency could consider whether it would be beneficial to include additional requirements to strengthen working relationships between OPOs and tissue banks. Such requirements might include:

- Holding OPOs responsible for informed consent for tissue donor families when requesting consent on behalf of tissue banks; and
- Requiring OPOs to include tissue banks in the training that they conduct for designated requestors.

The Tissue Banking Industry

At the time of obtaining consent, tissue banks should provide families with written materials that provide fuller disclosure about the uses of tissue and the nature of the gift.

Tissue banks could do a better job of providing basic information to families, either at the time they ask them to consent to donation, or in the days immediately following that decision. At a minimum, this material should include:

- A copy of the signed consent form. We believe that this is a basic legal protection for the family, as well as a recognition of the nature of the gift to which they have consented;
- Written information to the family on how it can follow up with the tissue bank in the case concerns arise;
- A full description of the uses to which donated tissue may be put; and
- A list and description of other entities with which the bank has relationships for processing and distributing tissue.

Written materials should be appropriately thorough. Such materials would serve as a way to supplement the information that requestors provide to the family during their conversation about donation, while providing requestors with the flexibility to adapt that discussion to the unique needs and responses of each donor family.

Tissue processors and distributors should ensure that information accompanying their product clearly indicates it is derived from *donated* human tissue.

The FDA does not currently have labeling requirements for packaged tissue, and the AATB's standards (which apply only to banks accredited by the association) address labeling within the context of ensuring that users know it is a biologically-based product, capable of transmitting disease. Neither set of standards addresses donor families' concerns that recognition be given to the fact that the products are the result of a freely made donation of human tissues.

The following steps could help to address perceived concerns that donated human tissue is no different from any other medical product. Tissue banks should:

- Indicate clearly on all tissue packaging that the contents derive from donated human tissue; and
- Indicate clearly on all marketing and informational brochures that these products derive from donated human tissue.

This recommendation responds to concerns that tissue is viewed as a commodity, rather than an altruistic donation. Implementing it would require only minor changes in packaging and marketing materials. But it would go a long way towards showing ongoing respect for the donor and the gift of donation.

Tissue banks should foster greater accountability for the performance of those who request consent for donation.

We found wide variation in practices among tissue banks with respect to how consent for donation is requested, who requests consent, and how these individuals are trained and monitored. There is no doubt that the responsibility for ensuring that requestors are providing accurate, sensitive, and appropriate information rests directly with the tissue bank. To ensure greater accountability of requestors, tissue banks should:

- Ensure that their requestors are fully and appropriately trained. This applies both to requestors from their own organizations as well as other entities, such as hospitals;
- Provide continuing education for requestors; and
- Conduct ongoing assessments of requestor performance to ensure that they are providing full and accurate information to families approached for donation.

The tissue banking industry should work with representatives of groups representing donor families to explore a process for periodic public disclosure about tissue banks' financing.

Non-profit entities are already required to disclose information about the sources and uses of funds received; publicly-owned businesses submit annual public reports to the Securities and Exchange Commission. These disclosures contribute to public

accountability and can serve as a basis for building greater trust among donors, families, and tissue banks.

The purpose of the examination we recommend here is to respond to family and general public concerns about knowing the type and extent of financial arrangements which the tissue bank has with other entities, both nonprofit and for profit. The examination would consider whether financial information would be useful as part of a package of information provided to donor families. The examination would consider:

- What types and how much financial information would be useful for families and individuals in making decisions about donation;
- The advantages and disadvantages of financial disclosure, including its potential impact on donation; and
- The content, style, and format of disclosure.

COMMENTS ON THE REPORT

We received comments on a draft of this report from the Department of Health and Human Services. They are supportive of our findings and recommendations. The full text is included in Appendix C.

Our work in tissue banking continues. We will maintain an active watch on how the tissue banking community responds to the concerns that we have raised.

APPENDIX A

National Kidney Foundation®
Making Lives Better

NATIONAL DONOR FAMILY COUNCIL
EXECUTIVE COMMITTEE

POSITION STATEMENT ON TISSUE DONATION

The National Donor Family Council (NDFC) of the National Kidney Foundation recognizes and supports tissue donation as an end-of-life option for donor families and recognizes its life-enhancing capacity to help thousands who are awaiting tissue transplantation.

The NDFC strives to enhance the sensitivity and effectiveness of the organ and tissue procurement process. To further this mission, the NDFC believes that tissue donation should always be treated as a gift of life. We believe that the tissue community as a whole must promote sensitivity to and support for organ and tissue donor families.

While the NDFC recognizes that financial resources are an important factor in maintaining the highest quality of tissue services, it is our position that tissues must be collected, processed, stored and distributed in an efficient manner that minimizes costs and maximizes the benefit to patients. The NDFC believes that donated tissue must be used in a way that promotes healing for people with the greatest need.

The tissue community should resist the tendency to make the generous gift of donated tissue a commodity. Professionals should refrain from referring to donated tissue as a "product." All packaging for donated tissue should include a statement indicating that the package contains donated tissue and is a gift of life. The tissue community should educate health care professionals, including physicians who use donated tissue, about the donor family perspective and the nature of the gift. The tissue community should also work to raise awareness among funeral services professionals and strengthen their commitment to follow the wishes of donor families. The tissue community must pay all expenses incurred by the donor family that are directly associated with tissue donation, including any increased funeral charges.

As approved by the NKF National Donor Family Council Executive Committee and the NKF Board of Directors, September 25, 2000

NOTE: This Policy Statement is subject to further revision based on a survey of donor families currently in progress

APPENDIX A

National Kidney Foundation®

Making Lives Better

NATIONAL DONOR FAMILY COUNCIL
EXECUTIVE COMMITTEE

INFORMED CONSENT POLICY FOR TISSUE DONATION

As with organ donation, the National Donor Family Council (NDFC) of the National Kidney Foundation believes that a crucial element of the tissue donation process is the informed consent of the donor family. With respect to tissue donation, the informed consent of the donor family must, at an absolute minimum, include a voluntary decision based on full disclosure of the facts.

Full disclosure includes the following elements:

1. Donor families should be given a general explanation of the tissue process, including:
   - medical and social history
   - communicable disease testing
   - laboratory testing
   - medical suitability
   - how tissue is recovered, processed, stored and distributed
2. Donor families must be told what tissue can be recovered from their loved ones based on medical suitability. If heart valves will be recovered, families must be informed that the heart will be removed from the donor's chest and sent to a facility where the valves will be removed. If the entire eye will be removed for corneal donation, families should be informed.
3. Donor families must be informed that tissue can be used or modified in various ways for transplantation in a life-saving capacity, transplantation in a life-enhancing capacity, and medical research or education.
4. Donor families must be told that they have the right to limit or restrict the use of the tissue.
5. Donor families must be told about the likelihood that the donated tissue will be stored, how it will be stored, the duration of storage, and the possibility that the tissue may not be utilized.
6. The completed consent form must be reviewed with the donor family before final consent, and a copy should be offered to the family. Other written material explaining tissue donation should be offered to the family.
7. Donor families must be given the option of receiving acknowledgment of their gifts. This acknowledgment should include both disposition and any recipient information available at that time, while protecting the anonymity of both donor and recipients. To obtain additional information about the gift, the donor family should be provided with contact information (including phone number and address) for the recovery agency.

As approved by the NKF National Donor Family Council Executive Committee and the NKF Board of Directors, September 25, 2000
NOTE: This Policy Statement is subject to further revision based on a survey of donor families currently in progress

APPENDIX B

Model Elements of Informed Consent for Organ and Tissue Donation

American Association of Tissue Banks
Association of Organ Procurement Organizations
Eye Bank Association of America

Human organ and tissue transplantation has become an important and growing part of modern medical practice. Advances in medical science have made it possible for millions of Americans to receive these life-saving and life-enhancing gifts. None of this would be possible, however, were it not for the tens of thousands of donors and donor families who give their organs and tissues to help their fellow men and women.

The decision to donate must, therefore, be an informed consent, and it must be conducted under circumstances that are sensitive to the consenting person's situation. Information concerning the donation should be presented in language and in terms that are easily understood by the consenting person. The consent should be obtained under circumstances that provide an opportunity to ask questions and receive informative responses. An offer should be made regarding the availability of a copy of the signed consent form, and information should be provided regarding ways to reach the recovery organization following donation. Consent should be obtained in accordance with federal, state and/or local laws and/or regulations. The person seeking the consent should be trained to appropriately answer any questions that the consenting person may have. In addition, coercion should not be exerted in any manner, nor monetary inducement offered to obtain consent for donation. The identification of who may be the appropriate person to consent to donation, and whether the consent of any person in addition to the donor needs be obtained, should be evaluated in accordance with the applicable laws and organizational policy and is not addressed in this statement.

The following list of "Basic Elements of Informed Consent" is intended to highlight the information that may be considered critical to informed decision making by a family member or other legally authorized person, who is being approached for consent to organ and/or tissue donation. This listing, whether communicated verbally or included on consent forms, is not intended to preempt any applicable federal, state, or local laws or regulations that may require more or less information to be disclosed for informed consent to be legally effective.

Basic Elements of Informed Consent

In seeking informed consent, the following information should be provided to the person(s) being approached for consent:

- A confirmation/validation of the donor's identity and his or her clinical terminal condition.
- A general description of the purposes (benefits) of donation.

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- Identification of specific organs and/or tissues (including cells) that are being requested for donation (with subsequent information provided on specific gifts recovered).
- An explanation that the retrieved organs/tissues may be used for transplantation, therapy, medical research, or educational purposes.
- A general description of the recovery process (including timing, relocation of donor if applicable, contact information, etc.).
- An explanation that laboratory tests and a medical/social history will be completed to determine the medical suitability of the donor, including an explanation that blood samples from the donor will be tested for certain transmissible diseases.
- An explanation that the spleen, lymph nodes, and blood may be removed, and cultures may be performed, for the purpose of determining donor suitability and/or used to determine compatibility of donor and recipient.
- A statement granting access to the donor's medical records, and that the medical records may be released to other appropriate parties.
- An explanation that costs directly related to the evaluation, recovery, preservation, and placement of the organs and tissues will not be charged to the family.
- An explanation regarding the impact the donation process may have on burial arrangements and on appearance of the body.
- Any additional information required by federal, state and/or local laws and/or regulations.

Additional Elements of Informed Consent

In some situations, there may be additional information that should be known by the consenting person(s), or that might be helpful for family decision making. At a minimum, if the donor family inquires about any of these or additional matters, explanations should be provided.

The guiding principle for the use of these "Additional Elements of Informed Consent" is to advance simplicity and reasonableness in seeking informed consent, i.e. include these elements or additional comments if they are appropriate and might clarify any

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exigencies. For example, if there is the likelihood that the patient will become a Medical Examiner's case, then it should be appropriate to so inform the family. If it is unlikely that donated tissue is going to be used for aesthetic surgery, then it would not be reasonable to address this issue in the family approach.

One or more of the following elements of information may also be appropriate for communication to the person(s) being approached for consent, depending upon the circumstances surrounding the donation and the potential gift(s):

- A description of any involvement by the Medical Examiner and/or Coroner, including an explanation that an autopsy may be performed.
- An explanation that transplantation may include reconstructive and aesthetic surgery.
- A reference to the possibility that the final gift may take a different form than originally recovered.
- An explanation that multiple organizations (nonprofit and /or for profit) may be involved in facilitating the gift(s).
- Reference to the possibility that tissue and/or organs may be transplanted abroad.

American Association of Tissue Banks

Association of Organ Procurement Organizations

Eye Bank Association of America

November 30, 2000

Comments from the Department of Health and Human Services

APPENDIX C

THE DEPUTY SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

DEC 26 2000

TO: Inspector General, HHS

SUBJECT: Department Comments on OIG Report on Informed Consent in Tissue Donation

I commend the Office of the Inspector General (OIG) for its quick response to my request to review the status of informed consent for tissue donors.

The Department finds considerable merit in the OIG's recommendations toward making more -- and more meaningful -- information available to tissue donors and tissue donor families. Working with the industry and donor families to facilitate better understanding of this process is likely to produce positive results.

The Department notes that important activities relevant to the OIG's recommendations are underway:

> The Health Resources and Services Administration (HRSA) already works closely with donor and recipient families and other representative groups to develop educational information about organ and tissue donation. To include tissue banks in such activities would be a logical extension.
>
> The Health Care Financing Administration (HCFA) currently is engaged in several activities with hospitals, organ procurement organizations, and tissue banks to increase organ and tissue donation. The OIG recommendations for additional efforts toward ensuring that donors and donor families receive information adequate for informed consent is consonant with the current activities and should be readily accommodated. While tissue banks are not directly under HCFA's jurisdiction, they have worked closely with HCFA and organ procurement organizations with a view to having appropriate donors referred to them.

If the OIG's recommendations that are directed toward the tissue industry were to be implemented in full and promptly, such action could go far toward easing the concerns that have been raised about the uses to which donated tissues are put. Tissue donors and tissue donor families undoubtedly would welcome increased efforts toward ensuring informed consent, giving explicit recognition for the donation on the packaging associated with tissues or products prepared from them, and providing more insight about the fiscal aspects of tissue handling and processing. Although the Department has no way to compel action in these areas by the tissue industry, the pertinent agencies of the Department are prepared to support the industry in taking such steps.

Kevin Thurm

APPENDIX D

Endnotes

1. The National Organ Transplant Act specifies that organ procurement organizations must be nonprofit entities, establishes requirements for their service area, and imposes certain organizational and staffing requirements. (42 U.S.C., Section 273(b))

2. Of the tissue bank officials we interviewed, five banks only process and distribute tissue; they do not recover tissue and would not be directly involved in obtaining consent. In addition, eight banks that recover tissue also do some processing and distribution.

3. "AATB Statement of Ethical Principles," adopted November 1994.

4. 42 U.S.C., Section 274e. This is the one provision of the National Organ Transplant Act that specifically addresses human tissue. The act defines organ to include "bone marrow, cornea, eye, bone, and skin or any subpart thereof," as well as vascular organs such as kidney, liver, heart, lung, and pancreas.

5. The Act specifies that the term "'valuable consideration' does not include the reasonable payments associated with the removal, transportation, implantation, processing, preservation, quality control, and storage of a human organ."

6. The web sites of the major processing firm contain information and press releases on new products and uses. Web sites of all the for-profit firms that we examined have a prominently displayed category addressing investor relations, as well.

7. Often cited examples include enhancements of lips or other body parts among Hollywood starlets. During our visit to one tissue processing firm, we were struck by framed blowups of covers from various fashion magazines that were displayed prominently on the walls of the reception area.

8. American Medical Association Policy H-475.992

9. 21 C.F.R. 1270.21, added at 62 *Fed.Reg.* 40,445, July 29, 1997.

10. Organ donation generally requires that the donor be declared brain dead (*i.e.*, death through cessation of neurologic function), rather than suffering cardiac death. A small number of total deaths — perhaps 12,000 - 15,000 at the most — meet this criteria in any given year.

11. U.S. Department of Health and Human Services, Office of Inspector General, "Medicare Conditions of Participation for Organ Donation: An Early Assessment of the New Donation Rule," (OEI-01-99-00020), August 2000.

12. 42 C.F.R., section 283.45, added at 63 *Fed.Reg* 33,875, June 22, 1998.

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13. U.S. Department of Health and Human Services, "Roles and Training in the Donation Process: A Resource Guide," September 2000, available at http://www.organdonor.gov.

14. 21 C.F.R., Parts 16 and 1270, added at 62 *Fed. Reg.* 40,429, July 29, 1997. The FDA issued these regulations under the legal authority of section 361 of the Public Health Service Act. This section authorizes the Secretary to make and enforce regulations judged necessary to prevent the introduction, transmission, or spread of communicable diseases.

15. The original Uniform Anatomical Gift Act was first developed in 1968 by the National Conference of Commissioners on Uniform State Laws. Many States have incorporated the features of a revised version developed in 1987.

Senate Permanent Subcommittee
On Investigations
EXHIBIT # 10

Department of Health and Human Services

OFFICE OF INSPECTOR GENERAL

Oversight of Tissue Banking

JANUARY 2001
OEI-01-00-00441

EXECUTIVE SUMMARY

PURPOSE

To provide a profile of the current external oversight system for tissue banking, and to identify limitations in that system.

BACKGROUND

Human tissue is an important resource for medical treatment. For example, it is used in burn treatment, reconstructive surgery, cancer care, and heart valve replacement.

Tissue from one donor can be processed into many forms and used to treat many people. The exact number of donors is not known, but it is growing. In 1999, more than 20,000 donors provided cadaveric tissue, up from perhaps 6,000 donors in 1994. It is estimated that tissue banks distributed more than 750,000 allografts for transplantation in 1999.

Human tissue can transmit disease. In the early 1990's two events raised major concerns. First, HIV was transmitted from one infected donor to several recipients of organs and unprocessed tissues. Second, investigators from the Food and Drug Administration (FDA) found instances of domestic suppliers accepting foreign tissue that had not been tested or screened; in one case the FDA found tissue that tested positive for Hepatitis B.

These concerns led FDA to issue an interim final rule in December 1993. FDA modified this regulation and reissued it as a new rule, effective in January 1998. It requires that tissue banks screen and test donors and that they maintain the appropriate records. The rule also provides for FDA inspections of tissue banks and retention, recall, and destruction of tissue that doesn't comply with these requirements.

This report responds to a request from the Secretary of Health and Human Services, asking the Office of Inspector General to examine the oversight system for tissue banking. We analyzed available data related to tissue banking, and we reviewed regulations, laws, and standards. We interviewed staff from FDA, from 30 tissue banks, and from associations representing various sectors of the tissue banking industry.

In this report, we use the term "tissue banks" to refer to entities involved in procuring, processing, storing, and distributing tissue. We use the term "tissue" to refer to skin, heart valves, and musculoskeletal tissue such as bone, cartilage, ligaments, and tendons. Our report does not address eyes and reproductive tissue.

PROFILE OF TISSUE BANKING OVERSIGHT

Oversight of tissue banking takes place at three levels:

- **The Food and Drug Administration** focuses on preventing transmission of

communicable disease by requiring donor screening and testing. FDA has conducted 188 inspections of 118 tissue banks since 1993. The agency has proposed two regulations and is developing a third that would expand its oversight of tissue banking. These regulations would require registration of all tissue banks, expanded screening and testing, and use of good tissue practices, akin to good manufacturing practices.

- **The American Association of Tissue Banks** (AATB) conducts a voluntary accreditation program. While AATB currently accredits 58 tissue banks, we identified another 90 that are not accredited. Accreditation addresses not only donor screening and testing practices, but operational and organizational aspects, such as qualifications of tissue bank personnel and banks' safety practices, equipment testing, facilities, labeling, and quality assurance programs.

- **New York and Florida** are the only two States to license and inspect tissue banks. In addition to screening and testing, these States require banks to report adverse incidents. They also address areas such as tissue procurement processes, tracking practices, emergency procedures, equipment standards, conflict of interest, community involvement, labeling standards, laboratory testing, and disposition of unused tissue. A few States, including California, Georgia, and Maryland, require tissue banks to be licensed by the State.

LIMITATIONS IN TISSUE BANKING OVERSIGHT

No new cases of disease transmission through human tissue have been identified since the FDA's 1993 regulation. This absence of new cases points to significant strengths and accomplishments in the current system which has focused on preventing the spread of communicable disease. Nevertheless, in the course of this limited inquiry, we identified situations that show the need for continued vigilance and monitoring. For example, FDA inspectors have found serious deficiencies in tissue banks' screening and testing practices. Banks have failed to meet basic standards of the AATB and been denied accreditation. States have received notification of adverse incidents involving tissue.

The rapid development of the tissue banking field means that traditional oversight methods may not keep pace with growth and changes in the industry. Consequently, thoughtful consideration needs to be given to the nature of any oversight approach.

Below, we outline limitations and vulnerabilities in current approaches, and we offer a combination of options that, taken singularly or in combination, could provide a way of enhancing oversight of the tissue banking field.

FDA oversight

Some tissue banks have never been inspected by FDA. We found at least 36 tissue banks that have never been inspected, out of 154 tissue establishments that we were able to identify. FDA has indicated that regulation of tissue banks is an unfunded mandate, and that in order to carry out these inspections, the agency has had to borrow resources

from other programs, such as blood and plasma.

FDA lacks a prescribed cycle for reinspection of tissue banks. Of 118 tissue banks that FDA has inspected, 68 have been inspected only once. Due to limited resources, the agency has had to establish a priority list for followup inspections. The first priority is reinspection of firms whose previous inspection was classified as Official Action Indicated, the most serious level of deficiency.

The number and location of tissue banks are unknown. Information is lacking about the number of tissue banks in operation and the products they produce and distribute. FDA has proposed a regulation to require tissue banks to register and list their products. The regulation would address directly this limitation in knowledge about tissue banking.

The scope of FDA's current regulation is limited. Because the agency's current regulation focuses on donor screening and testing to prevent transmission of HIV-1 and -2 and Hepatitis B and C, other important aspects of tissue bank quality are not monitored. Until FDA's good tissue practices rule is finalized, tissue banks have no external requirements for quality and handling of tissue if they are not accredited by AATB or licensed by New York or Florida. Of the 154 tissue banks we identified, 67 are neither accredited by AATB nor inspected by Florida or New York.

Private accreditation

Many banks do not seek AATB accreditation. AATB accredits 58 tissue banks. However, we identified 90 tissue banks that are not accredited. These banks are under no obligation to meet the standards or policies set by the association. For many tissue banks there is no real incentive to seek accreditation. There are a number of ways to encourage private accreditation of tissue banks. For example, FDA could provide technical advice and information that could be used in developing standards. FDA also could consider in what areas, if any, the agency could accept accreditation as showing compliance with FDA regulations. In such a case, legislation would be needed.

State oversight

Only two States inspect tissue banks. In many ways, these inspections go beyond FDA requirements; yet the inspections are limited to banks that conduct business in Florida and New York. Other States could give consideration as to whether they wish to regulate tissue banking and, if so, how they would coordinate with other entities to limit redundancy and regulatory burden.

Information on supply and availability of tissue

Concerns about shortages. There is no national system for tracking the availability of tissue. Two recent surveys by industry representatives raised concerns that skin may not be available when needed for treating burn victims. However, some shortcomings in these studies suggest that additional research is warranted to examine the extent and implications of shortages of tissues.

RECOMMENDATIONS

The Food and Drug Administration should expedite the publication of its regulatory agenda that requires registration of tissue banks, enhanced donor suitability screening and testing, and the use of good tissue practices.

At present, FDA is able to inspect only those banks that it knows about. Requiring registration of all tissue banks would ensure that the agency has a comprehensive list of tissue banks as a first step in assuring their compliance with standards.

In addition, many tissue banks are neither accredited by the AATB nor licensed and inspected by New York or Florida. Those banks that are not accredited or inspected do not have to meet any standards beyond the current FDA minimum requirements that they screen and test tissue donors for HIV and hepatitis.

FDA should set a realistic, yet aggressive, date by which it would complete an initial inspection of all tissue banks.

This could be accomplished under FDA's existing regulatory authority. Establishing a baseline of information will provide a minimum level of assurance that tissue banks are meeting basic public health and safety standards to prevent transmission of communicable diseases.

FDA should determine an appropriate minimum cycle for tissue bank inspections.

This, too, could be accomplished under FDA's existing regulatory authority. A minimum cycle for inspections would help ensure that tissue banks are meeting standards on an ongoing basis.

FDA should work with States and with professional associations that have inspection and accreditation programs to determine in what areas, if any, oversight activities could be coordinated.

FDA, the industry, and the States with regulatory programs could benefit from examining where standards are in agreement, as well as areas in which standards might conflict. Following such an examination, determination could be made of whether formal partnership or other arrangements would be appropriate to maximize the effectiveness of the oversight process. Such arrangements could require enactment of legislation.

COMMENTS ON THE REPORT

We received comments on a draft of this report from the Department of Health and Human Services. They are supportive of our findings and recommendations. The full text is included in Appendix B.

Our work in tissue banking continues. We will maintain an active watch on how the tissue banking community responds to the concerns that we have raised.

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INTRODUCTION

PURPOSE

To provide a profile of the current external oversight system for tissue banking, and to identify limitations in that system.

BACKGROUND

Transplantation of Human Tissue

Human tissue is an important resource for medical treatment. Physicians and dentists use cadaveric human tissue for a variety of medical purposes. Donated skin can meet critical needs in healing burn victims and in reconstructive surgery. Donated bone can be implanted to replace cancerous bone; it can be used in knee and hip replacements and for spinal surgery; and it can be processed into powder for use in dental surgery. Donated heart valves can replace defective valves in young children, saving their lives.

The exact number of tissue donors in this country is not known. It is clear, though, that the numbers are increasing. In 1999, more than 20,000 donors provided cadaveric tissue, up from perhaps 6,000 donors in 1994.

Initial Concerns about Disease Transmission

Human tissue is capable of transmitting disease. Tissue from one donor can be implanted into many different people. Thus, if a donor has a communicable disease, using that tissue places multiple recipients at risk. It is estimated that tissue banks distributed more than 750,000 allografts for transplantation in 1999.

In the early 1990's two events occurred that raised concerns about disease transmission through tissue donation. First, HIV was transmitted to a number of recipients of organs and unprocessed tissues from an infected donor. Second, investigators from the Food and Drug Administration (FDA) found instances in which domestic suppliers were accepting foreign tissue that had not been adequately tested or screened; in one of these cases the FDA found tissue that tested positive for Hepatitis B.

Since these initial two cases, no other cases have been identified. However, without proper screening and testing, these problems could reemerge. As we discuss below, FDA continues to uncover deficiencies in the course of its inspections of tissue banks.

Limited Federal Oversight of Tissue Banking

Tissue banks procure, process, store, and distribute human tissue. Federal regulation of tissue banking focuses on donor screening and testing to prevent the introduction, transmission, and spread of HIV-1 and -2, and Hepatitis B and C.[1] By way of contrast, organ procurement organizations (OPOs) must meet statutory requirements about their organization and operation; they are regulated and certified by the Health Care Financing

Administration. Furthermore, the procurement and allocation of human organs are governed by Federal statute and are administered through a contract with the Health Resources and Services Administration (HRSA). Likewise, legislation authorizes the operation of a national bone marrow donor registry, also administered under contract with HRSA.

Recent Concerns about Tissue Banking

Several press reports in the Spring of 2000, appearing in the *Orange County Register* and the *Chicago Tribune,* raised concerns about tissue banking, including the extent to which the performance of the industry was monitored. Several members of Congress expressed their concerns to the Secretary of Health and Human Services. The Secretary asked the Office of Inspector General to examine two aspects of the tissue banking industry: consent for donation and the external oversight structure. This report responds to the second of those requests. Our companion report, *Informed Consent in Tissue Donation: Expectations and Reality* (OEI-01-00-00440), addresses consent for donation.

This Inquiry

This report provides a profile of the oversight structure for tissue banks. We also identify limitations of current oversight efforts and steps that could be taken to address those limitations.

Throughout this report, we use the term "tissue banks" to refer to entities involved in procuring, processing, storing, and distributing tissue. We use the term "tissue" to refer to skin, heart valves, and musculoskeletal tissue such as bone, cartilage, ligaments, and tendons. Our report does not address eyes and reproductive tissue.

METHODOLOGY

Our inquiry is based on data analysis, document reviews, an observational visit, and interviews. We analyzed data from FDA's Program Operations Data System which tracks information about FDA inspection activity across the nation. Our analysis examines this data from December 15, 1993 (following the issuance of the interim rule on tissue banking) through the end of Fiscal Year 2000.[2] Our analysis includes only tissue banks involved in procuring, processing, storing, and distributing tissues such as skin, heart valves, and musculoskeletal tissue. We do not include establishments that are involved in eye banking, or hospitals and laboratories inspected under the FDA tissue compliance program.[3]

We also reviewed pertinent FDA documents and inspection reports from the central office and from 3 of the 20 FDA district offices. We conducted interviews with FDA staff at both the central and district offices.

We reviewed AATB standards and accompanied an inspector on an accreditation visit to a tissue bank. We reviewed documents and data from the AATB and interviewed officials and staff from the association. We conducted interviews with senior staff from

30 organizations involved in obtaining, processing, and distributing human tissue.

We also interviewed officials and reviewed data, statutes, and regulations from New York, Florida, California, Georgia, and Maryland.

We conducted this study in accordance with the *Quality Standards for Inspections* issued by the President's Council on Integrity and Efficiency.

PROFILE OF OVERSIGHT FOR TISSUE BANKING

Oversight of tissue banking occurs at three levels. At the Federal level, the Food and Drug Administration (FDA) has primary responsibility to set and enforce standards to ensure the safety of tissue. Within the industry, the American Association of Tissue Banks (AATB) operates a voluntary accreditation program. At the State level, two States — New York and Florida — license and inspect tissue banks. Below we provide a description of each of these activities.

Food and Drug Administration

FDA's regulation of tissue dates to December 1993. Operating under its public health authority, the agency issued an interim final regulation in response to evidence about transmission of HIV to recipients of organs and unprocessed tissues from an infected donor.[4] In a second case, FDA inspectors found imported foreign tissue that tested positive for Hepatitis B. In July 1997, the FDA reissued this rule with minor modifications, and the new rule became effective January 26, 1998.[5]

The FDA requires that tissue banks must ensure that donor screening and infectious disease testing are performed for HIV -1 and -2 and for Hepatitis B and C. Tissue banks must maintain and make available to FDA inspectors records that document screening and testing for each donor of human tissue. FDA has the authority to order the retention, recall, and destruction of tissue that doesn't comply with these requirements.

FDA has conducted 188 inspections of 118 tissue banks since 1993. In more than half of these inspections, FDA inspectors found deficiencies that needed correction. FDA issued 26 notices of official action — the most serious level of deficiency, in which the agency requires the bank to take corrective actions. In 72 other inspections, FDA issued a notice recommending that the bank take voluntary actions to meet the requirements.[6]

FDA is in the process of expanding its oversight of tissue banking. Regulations to expand that authority, however, have not yet been finalized. The components of expanded FDA oversight strategy comprise three regulations:

- **Registration of all tissue banks.** This proposed regulation would require tissue banks to register with FDA and list their products. The proposed regulation would apply to establishments engaged in "recovery, screening, testing, processing, storage, labeling, packaging, or distribution of human cellular or tissue-based products."[7]

- **Expanded screening and testing for communicable diseases.** This proposed regulation would require donor screening and testing for diseases such as Human T-lymphotropic viruses (HTLV) and syphilis, and donor screening for Creutzfeld-Jakob Disease (CJD).[8]

- **Standards for "good tissue practices."** These standards, akin to good manufacturing practices required of medical device pharmaceutical manufacturers, would cover areas such as proper handling, processing, and tracking of tissue.[9]

American Association of Tissue Banks

AATB currently accredits 58 cadaveric tissue banks.[10] Tissue banks perform a variety of functions. Of these 58 banks, 54 retrieve tissue, 34 process tissue, and 56 store and distribute tissue; 51 of these banks retrieve musculoskeletal tissues, 37 retrieve cardiovascular tissues, and 20 retrieve skin. Five banks are for-profit (three tissue processors, one tissue distributor, and one retrieval agency). The other 53 accredited banks are non-profit organizations. Eleven banks are OPOs. The number of donors recovered by accredited banks has grown substantially, from 6,132 donors in 1994 to 17,725 donors in 1999.

AATB's standards are consistent with, but go beyond, FDA's requirements. For example, in addition to screening and testing for HIV and hepatitis, AATB requires that tissue banks test for HTLV and screen for CJD. The standards also address operational and organizational issues. These areas include qualifications of tissue bank personnel and technical issues, such as safety practices, equipment testing, facilities, labeling, and quality assurance.

Accreditation involves a review of a bank's written procedures and an on-site inspection. Since 1997, AATB has used contract inspectors to conduct accreditation visits.[11] Since 1997, an average of five new banks have sought accreditation each year.

A bank receives one of four recommendations. Banks that show no deficiencies receive immediate accreditation. A bank with minor deficiencies receives Level A accreditation, meaning that it must submit to AATB a written plan to correct the deficiencies found during the inspection. A bank with more serious deficiencies receives Level B accreditation, which means that it must take corrective action and be reviewed again through an on-site inspection. Finally, a bank could be denied accreditation outright. Accreditation is given for a three-year period, at the end of which the bank is subject to another review, including an on-site inspection. Since 1986, AATB has accredited a total of 98 tissue banks; 19 banks have been denied accreditation.[12]

State Regulation

New York and Florida are the only two States that operate oversight programs requiring that tissue banks be licensed and inspected. A few States, including California, Georgia, and Maryland, require that banks be licensed, either as tissue banks or as laboratories.

New York's licensure law dates to 1990.[13] Currently, the State licenses 13 allogeneic tissue banks located in New York and 36 located out-of-State.[14] New York inspects both in-State and out-of-State banks prior to initial licensure and every two years thereafter.

Banks are licensed along two dimensions. One is a functional dimension: whether the bank procures or processes tissue. The second dimension relates to the type of tissue which the bank works with — cardiovascular, musculoskeletal, or skin. A bank may be licensed for any or all tissues and functions. At present, 29 banks are licensed to procure and 9 to process cardiovascular tissue; 39 to procure and 20 to process musculoskeletal tissue; and 33 to procure and 19 to process skin.

Licensure requires an initial application and on-site survey. Banks do not pay a fee for licensure. Tissue banks must disclose ownership and key staff. Banks must update this information annually and report statistics on procurement, processing, and distribution.

In addition to meeting FDA requirements to screen and test for HIV and hepatitis, New York requires banks to test for HTLV and syphilis. New York also requires tissue banks to meet specific standards for each type of tissue — musculoskeletal, cardiovascular, and skin — that the bank procures, processes, or stores. These standards relate to donor qualifications, tissue retrieval processes, laboratory testing, and disposal of unused tissue.

Banks must report any adverse incidents to the State. Since 1991, the State has received 8 reports from cardiovascular, 13 from musculoskeletal, and 6 from skin banks.

Florida's law was enacted in 1992[15] at the urging of the State's OPO, tissue banking, and eye banking community. Florida currently licenses 20 cadaveric tissue banks; 9 are located in Florida and 11 are based in other States. Another 2 banks have submitted applications that are now under review. The State inspects both in-State and out-of-State tissue banks prior to initial licensure and every two years thereafter.

Florida requires tissue banks to pay an initial application fee of $1,000 and an annual fee of 0.25 percent of gross Florida revenues, with a minimum of $1,000 and a maximum of $35,000. The fees go to a State trust fund used for operating the licensure program, the State donation advisory committee, a donor registry, and donor education programs.

Applicants must disclose the bank's ownership, as well as information on equipment and donor selection and testing criteria. Florida requires tissue banks to comply with current FDA regulations. The surveying standards also address tissue tracking practices, emergency procedures, equipment standards, procurement processes, conflict of interest policies, community involvement, and labeling standards.

Florida requires tissue banks to report within 24 hours adverse events that could affect tissue recipients' medical conditions. Only three such incidents have been reported in the program's history.

LIMITATIONS IN OVERSIGHT OF TISSUE BANKS

Today's tissue banking system is complex and rapidly changing. Tissue is processed into new forms and products that are put to a variety of important medical uses. New technologies using human tissue emerge constantly. No new cases of disease transmission through human tissue have been identified since 1993. This absence points to significant strengths and accomplishments in the current oversight system which has focused on preventing the spread of communicable disease.[16]

However, continued vigilance and monitoring are needed: FDA inspectors have found deficiencies in tissue banks' screening and testing practices. Banks have failed to meet basic standards of the AATB and been denied accreditation. States have received notification of adverse incidents involving tissue. Appendix A describes some safety problems that FDA inspectors have identified during inspection visits and adverse events that have been reported to the State agencies. These problems include distribution of tissue from donors who tested reactive for hepatitis, bacterial contamination of tissue, and repeat testing of donors as a way of qualifying their tissue as suitable for transplantation.

In the course of this limited inquiry, we identified some important vulnerabilities and limitations in the current tissue banking oversight structure. Rapid developments and innovation in the tissue banking field mean that traditional oversight methods have not kept pace with growth and changes in the industry. Under these circumstances, thoughtful consideration needs to be given to the nature of any oversight approach.

Below, we outline limitations and vulnerabilities in the current approaches, and we offer a combination of options that, taken singularly or in combination, could provide a way of enhancing oversight of the tissue banking field.

FDA oversight

Some tissue banks have never been inspected by FDA.

We developed a list of 154 tissue banks, based on data from three FDA district offices, AATB, Florida, and New York. We found that FDA had never inspected 36 (23 percent) of these banks. In addition to the 154 banks we identified, there are likely others that operate in States without licensing programs.[17]

FDA has indicated that regulation of tissue banks is an unfunded mandate. In order to carry out these inspections, the agency has had to borrow resources from other programs, such as blood and plasma.

FDA lacks a prescribed cycle for reinspection of tissue banks.

FDA staff told us that their goal is to inspect tissue banks once every two years, but there is no required minimum cycle for these inspections.[18] Of 118 tissue banks that the agency

has inspected, 68 have been inspected only once since the FDA began its tissue program in late 1993.

FDA's compliance program acknowledges that there are insufficient resources to accomplish biennial inspections of all banks. As a consequence, the agency has established a priority list for followup inspections. The first priority for the program is reinspection of firms whose last inspection was classified as Official Action Indicated. This classification is the most serious level of deficiency, in which the agency requires the bank to take corrective actions.[19]

The number and location of tissue banks are unknown.

Information is lacking about the number of tissue banks in operation, and the types of tissue products that they produce. This lack of information limits the confidence with which assurances can be made that the supply of tissue is safe. These "unknown" tissue banks are likely to be new entities that may be in the early stages of operation. This situation does not inspire confidence that these banks are meeting basic standards of safety.

The FDA has issued a proposed regulation[20] calling for registration of tissue banks and listing of their products. Such a regulation would address directly this current limitation in knowledge about tissue banking.

The current scope of FDA's regulations is limited.

The agency's current regulations focus on preventing transmission of communicable disease. The regulations require tissue banks to conduct some donor screening and testing, to prepare and follow written procedures, and to maintain records. The regulations provide for FDA inspection of tissue banks, quarantine of imported tissue, and retention, recall, and destruction of tissue that doesn't comply with the regulations.

The current regulations, however, do not monitor other important aspects of tissue bank quality. FDA has proposed a regulation expanding donor suitability and testing requirements, and is developing a regulation on good tissue practices, akin to good manufacturing practices required of medical device pharmaceutical manufacturers. Until that regulation is finalized, tissue banks have limited requirements for quality and handling of tissue if they are not accredited by AATB or licensed by New York or Florida.

We were unable to document the extent to which banks that are neither AATB-accredited nor licensed in New York or Florida are involved in recovering tissue. The number, however, is likely to be substantial. For example, of the 154 tissue banks we identified, 67 are neither accredited by AATB nor licensed by New York or Florida.

Private accreditation

Many banks do not seek AATB accreditation.

At present, 58 tissue banks have AATB accreditation. Yet we identified another 90 banks that are not accredited. These banks are under no obligation to meet the standards or policies set by the AATB.[21]

Unaccredited banks include both large and small operations. For example, the country's largest processor of heart valves has never sought accreditation. Some OPOs that operate tissue banks are not accredited by AATB. Other unaccredited banks are small entities in the early stages of operations and do not yet feel that they can comply with the standards.

For many tissue banks there is no real incentive to seek accreditation. Hospitals and physicians regularly purchase tissue from unaccredited banks. The cost of accreditation may present a major barrier for smaller banks. For other banks, already subject to inspection by FDA and State authorities, a third inspection may seem burdensome.[22]

A number of steps could be taken to encourage a role for private accreditation of tissue banks. For example, FDA could provide technical advice and information that could be used in developing standards. FDA could also consider in what areas, if any, the agency could accept accreditation as showing compliance with FDA inspection regulations. To implement such a change, legislation would likely be needed.

State oversight

Only two States inspect tissue banks.

In many ways, these inspections go beyond FDA requirements. The State initiatives provide an important aspect of quality assurance. Yet the inspections are limited to banks that conduct business in Florida and New York. Those banks may be small, local entities that operate within each State, or they may be large national operations that are based elsewhere and that either process or distribute tissue in New York or Florida. For example, 15 of the 20 banks licensed in Florida also are licensed in New York, and 14 are accredited by the AATB; 29 of the banks licensed in New York have AATB accreditation. A few States, including California, Georgia, and Maryland, require tissue banks to be licensed by the State, either as tissue banks or as laboratories.

Other States could give consideration as to whether they wish to regulate tissue banking, and, if so, how they would coordinate with other entities to limit redundancy and regulatory burden.

Information on supply and availability of tissue

There is no national system for tracking the availability of tissue and where there may be a shortage. Each bank maintains its own inventory and distribution records. Concerns have been raised that some tissues, such as skin, may be in short supply, and that donated

skin is processed into products that may be used for procedures that are not medically indicated. It is not clear how much tissue goes for such cosmetic uses; because physicians and patients determine how these products actually are used, tissue banks that manufacture them do not have that information.[23]

Recent concerns about shortages of skin have led to two surveys related to its availability. A survey of burn centers, conducted by the American Burn Association (ABA), found that 32 percent of respondents had delayed or altered treatment over the past year, and about half reported that they had difficulty obtaining allograft skin. The AATB survey found that banks recovered skin from over 6,000 donors in 1999. It also found that banks generally can meet the local need for skin, but when skin is requested by facilities outside their local area, meeting those requests is more problematic. Only 3 of 20 banks supplying cryo-preserved skin, and only 3 of 12 banks supplying fresh skin, can always meet requests from outside of their local area.

These initial surveys suggest that further research may be warranted to examine the extent and implications of a potential shortage of tissues. They provide the first systematic information about tissue supply and availability. The two associations deserve great credit for collecting and publicizing these data. However, there are limitations related to the source and specificity of information obtained. For example, the AATB respondents were accredited banks only; the ABA data do not allow one to determine if any patient actually was unable to obtain skin needed in a surgical procedure. These shortcomings and the limitations of an initial survey can easily be overcome in future refinements.

RECOMMENDATIONS

The Food and Drug Administration should expedite the publication of its regulatory agenda that requires registration of tissue banks, enhanced donor suitability screening and testing, and the use of good tissue practices.

The FDA has been the lead agency within the Department of Health and Human Services for oversight of tissue banking. The FDA's current regulatory program focuses on preventing transmission of HIV and hepatitis by requiring that tissue banks test and screen donors to detect these conditions.

FDA has proposed and is refining three regulations that will enhance oversight of tissue banking. That regulatory agenda would require registration of all tissue banks, expanded screening and testing, and use of good tissue practices, akin to good manufacturing practices.

This proposed agenda is important for at least two reasons. First, at present FDA is able to inspect only those banks that it knows about. Requiring registration of all tissue banks would ensure that the agency has a comprehensive list of those banks that are in operation, as a first step in assuring their compliance with standards.

Second, many tissue banks are neither accredited by the American Association of Tissue Banks nor licensed and inspected by New York or Florida. Those banks that are not accredited or inspected do not have to meet any standards beyond the current FDA minimum requirements that they screen and test tissue donors for HIV and hepatitis.

Within its existing regulatory authority, FDA should take two steps to enhance oversight of tissue banking:

FDA should set a realistic, yet aggressive, date by which it would complete an initial inspection of all tissue banks.

As we show above, more than one of every five tissue banks has never been inspected. As we also note, the agency has indicated that regulation of tissue banks is an unfunded mandate, and that it has had to borrow resources from other programs to carry out current inspections. Nevertheless, we believe that it is important to establish a baseline of information. Such information would provide a minimum level of assurance that tissue banks are meeting basic public health and safety standards to prevent transmission of communicable disease.

FDA should determine an appropriate minimum cycle for tissue bank inspections.

A minimum cycle for inspections would help ensure that tissue banks are meeting standards on an ongoing basis. As we note above, FDA has established a priority list for

followup inspections to maximize available resources. We believe, however, that some minimum cycle, which the agency would determine, is important to ensure that tissue banks are subject to ongoing oversight.

FDA should work with States and with professional associations that have inspection and accreditation programs to determine in what areas, if any, oversight activities could be coordinated.

We recognize that resource constraints can put pressure on an agency's capacity to conduct inspections and reviews of tissue banks. In addition, we recognize that multiple inspection visits can place a strain on a tissue bank's operations. We believe that FDA, the industry, and the States with regulatory programs could benefit from examining where standards are in agreement, as well as places in which standards might conflict.

Following such an examination, determination could be made of whether formal partnership or other arrangements would be appropriate to maximize the effectiveness of the oversight process. Such arrangements could require that legislation be enacted.

COMMENTS ON THE REPORT

We received comments on a draft of this report from the Department of Health and Human Services. They are supportive of our findings and recommendations. The full text is included in Appendix B.

Our work in tissue banking continues. We will maintain an active watch on how the tissue banking community responds to the concerns that we have raised.

APPENDIX A

Examples of Safety and Quality Problems Found in Tissue Banking

- Routine acceptance of tissue for further manufacturing without accompanying records from procurement agency documenting that donor's serum specimen had been tested and found negative.
- Confirmatory testing repeated until negative result was obtained for Hepatitis B surface antigen and Hepatitis C antibody, as a means of potentially qualifying donors as suitable for transplantation.
- Acceptance of foreign tissue with donor records not translated into English and without documented medical/ social histories.
- Lack of adequate controls to assure product sterility. Lack of standard operating procedures to prevent cross contamination of human tissue during manufacture.
- Failure to assure tissue was quarantined until all infectious disease testing and donor screening reviewed by a responsible official, and donor found to be free of risk factors for/ clinical evidence of Hepatitis B and C or HIV-1 and -2.
- Errors in calculating a donor's serodilution status. In retrospect, tissue bank determined that the tissue should not have been accepted because of indicators recorded on medical/ social history.
- Tissue bank notified that a donor had been incarcerated in the year prior to his death, nine months after tissue was tested, processed, and distributed.
- Distribution and implantation of soft tissue grafts from a single donor with possible bacterial contamination. The grafts came from a donor with no evidence of risk for HIV or hepatitis (confirmed through serological testing). Contamination appears to have occurred either at recovery or during processing.
- Positive test for the Hepatitis C antibody found by distributor, even though others who had handled the tissue had found negative test results.
- Tissue processing errors, such as use of expired processing reagents.
- Release and distribution of tissue from donors who tested repeatedly reactive for Hepatitis B surface antigen.
- Improper donor testing by the tissue bank's contract lab for HIV, Hepatitis C antibody, and Hepatitis B surface antigen.
- Culture-positive tissue or tissue lots distributed, then recalled.
- Adverse reaction in a heart valve recipient.

From actual problems found by FDA inspectors and adverse event reports to States

Comments from the Department of Health and Human Services

APPENDIX B

THE DEPUTY SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

DEC 26 2000

TO: Inspector General, HHS

SUBJECT: OIG Report on Oversight of Tissue Banking

I commend the Office of the Inspector General (OIG) for its prompt yet thorough response to my request to review the status of oversight of tissue banks. I recognize that the report does not address ocular and reproductive tissue.

The OIG report notes that "no new cases of disease transmission through human tissue have been identified since 1993", pointing to "significant strengths and accomplishments in the current oversight system." The Department agrees that the FDA should expedite its planned rule making activities related to tissues, specifically the final rule to require registration of tissue banks and listing of tissues and the proposed rule to require adherence to good tissue practice. Further, the Department finds considerable merit in the OIG's recommendations for an intensified inspection program directed toward entities that procure, process, and store tissues. As the OIG report recognizes, however, oversight of tissue banking is an unfunded mandate for FDA. Unless appropriations increase, FDA will have to make difficult choices in regard to its oversight in other areas of comparable or greater public health significance in order to increase its activity in the tissue banking area.

FDA has expedited development of the regulations needed to implement better oversight of tissue banks. A final regulation addressing registration of tissue banks and listing of tissues is nearing completion. FDA's proposed rule to require adherence to good tissue practice will be published in the near future.

Kevin Thurm

APPENDIX C

Endnotes

1. The FDA issued these regulations under the legal authority of section 361 of the Public Health Service Act. This section authorizes the Secretary to make and enforce regulations judged necessary to prevent the introduction, transmission, or spread of communicable diseases.

2. Since we obtained the FY 2000 data from FDA, seven additional inspections have been entered into the PODS data system. Because we cannot tell whether these are tissue banks as we define them here, or eye banks or some other type of establishment, we do not include these seven banks in our analysis.

3. When eye banks, hospitals, and other establishments falling under the FDA tissue establishment compliance program are included, the total number of inspections rises to 363 inspections of 251 establishments. These additional establishments include 79 eye banks, 29 hospitals, and 25 establishments, such as laboratories, that we classified as other entities.

4. 21 C.F.R., Parts 16 and 1270, added at 58 *Fed. Reg.* 65,514, December 14, 1993.

5. 21 C.F.R., Parts 16 and 1270, added at 62 *Fed. Reg.* 40,429, July 29, 1997.

6. Our analysis includes only those banks we identified as banks involved with procuring, processing, storing, and distributing skin, heart valves, and musculoskeletal tissue.

7. Proposed regulation at 63 *Fed. Reg.* 26,744, May 14, 1998.

8. Proposed regulation at 64 *Fed. Reg.* 52,696, September 30, 1999.

9. This proposed regulation has not yet been published.

10. The total number of AATB-accredited banks is actually 71; 11 of these are reproductive tissue banks, and 2 are based in Canada. In our analysis we use only cadaveric tissue banks located in the United States.

11. When AATB began inspecting banks in 1986, the association relied on volunteer staff from member banks to conduct inspections. The accreditation inspectors working with AATB since 1997 are former staff from FDA or the National Institutes of Health, who have experience in facility inspection. Using outside inspectors has helped to formalize the process and make it more professional. The contract inspectors are trained in audit and evaluation methodologies, and they have had years of experience in inspecting facilities. A second important difference is that the professional inspectors do not have any relationships with the banks they are inspecting; thus, they may be more objective in their evaluation.

APPENDIX C

12. Of the 19 banks, 8 were denied accreditation following Level B inspections. Five more failed to complete the process which requires a one-year waiting period after a bank receives a Level B accreditation. Inspections of four banks were aborted because of obvious non-compliance, and the inspections were not completed. Two banks would have been recommended for denial, but because current accreditation had expired, they withdrew from the process.

13. New York Public Health Law, Article 43-B, Sections 4364-4366; New York Code of Rules and Regulations, Title 10, Part 52. New York also licenses other types of tissue banks, such as hematopoietic progenitor cell banks, eye banks, semen banks, and tissue transplantation facilities.

14. New York actually licenses 60 tissue banks for procuring, processing, or storing skin, musculoskeletal, and cardiovascular tissue. Of these, 7 New York banks and 4 out-of-State banks procure or process autogeneic bone or infant foreskin, which are non-cadaveric tissues.

15. Florida Statutes, Title 29, Chapter 381.6021-381.6025; Florida Administrative Code, 59A (Health Facility and Agency Licensing), Chapter 59A-1 Certification of Organ Procurement Organizations, Tissue Banks, and Eye Banks.

16. It is important to recognize, however, that there are no requirements to track recipients of tissue. It is possible that cases of disease transmission could have occurred, but have never been reported to the tissue bank or to any government authorities.

17. The three FDA field offices are located in Dallas, Los Angeles, and Buffalo. We recognize that the number of banks we identify here (154) differs from the 148 banks we discuss below in the potential AATB universe. FDA can inspect any individual establishment involved in tissue banking; AATB accreditation applies to an entire organization. Thus, for example, a tissue bank that has a main office and two satellite offices would have one accreditation from AATB — but FDA inspections could be conducted at each of the three different offices.

18. In contrast, blood banks, mammography facilities, and medical device firms must be inspected every two years.

19. Food and Drug Administration, "Compliance Program Guidance Manual — Compliance Program 7341.002 - Inspection of Tissue Establishments," November 3, 1999, part II, page 4. The priorities for inspection of tissue banks are:

1. Firms whose last inspection was classified OAI (official action indicated).
2. Firms about which FDA has received surveillance information indicating there is a potential violation of 21 CFR 1270.
3. Laboratories that perform required viral marker testing for tissue banks.
4. Firms which have never been inspected and which are known to lack accreditation by a standard setting organization such as the American Association of Tissue Banks.
5. Firms which have never been inspected.
6. Firms whose last inspection was classified as VAI (voluntary action indicated).

APPENDIX C

20. 63 *Fed. Reg.* 26,744, May 14, 1998.

21. We recognize that the number of banks we identify here (148) differs from the 154 banks we discuss above in the potential FDA universe. FDA can inspect any individual establishment involved in tissue banking; AATB accreditation applies to an entire organization. Thus, for example, a tissue bank that has a main office and two satellite offices would have one accreditation from AATB — but FDA inspections could be conducted at each of the three different offices.

22. AATB accreditation contrasts sharply with the situation for hospitals, where accreditation by the Joint Commission on Accreditation of Health Care Organizations (JCAHO) carries a definite benefit. Hospitals that receive accreditation are deemed to meet Federal requirements for certification as Medicare providers. Thus, hospitals have a very strong incentive to achieve that status.

23. The American Medical Association's policy provides a useful framework for considering the differences between cosmetic and reconstructive surgery. That policy states that "*cosmetic* surgery is performed to reshape normal structures of the body in order to improve the patient's appearance and self-esteem. *Reconstructive* surgery is performed on abnormal structures of the body, caused by congenital defects, developmental abnormalities, trauma, infection, tumors or disease. It is generally performed to improve function, but may also be done to approximate a normal appearance." (Policy H-475.992)

Senate Permanent Subcommittee
On Investigations
EXHIBIT #_____11a_____

THE ORANGE COUNTY REGISTER April 16, 2000 Sunday

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THE ORANGE COUNTY REGISTER

April 16, 2000 Sunday MORNING EDITION

SECTION: NEWS; Pg. A01

LENGTH: 2351 words

HEADLINE: SPECIAL INVESTIGATION;
THE BODY BROKERS;
Legal and ethical issues are raised by generating millions of dollars from donated bodies. The rush to increase supply and profits leaves some families feeling misled or mistreated.;
Donors don't realize they're fueling a lucrative industry

BYLINE: MARK KATCHES; WILLIAM HEISEL; RONALD CAMPBELL, The Orange County Register:

BODY:
American businesses make hundreds of millions of dollars selling products crafted from donated human bodies, even though it is illegal to profit from cadaver parts, an Orange County Register investigation found.

Cadaver skin puffs up the lips of fashion models at $ 1,050 a shot. Dentists use ground bone about 200,000 times a year to treat their patients. Glossy catalogs advertise 650 products made from body parts.

A single dead body yields raw materials worth tens of thousands of dollars to businesses whose stock is traded on Wall Street and to nonprofit agencies that obtain the parts for them, records and interviews show.

Nowhere in the country are grieving families told that their gifts fuel a fast-growing industry predicted to hit $ 1 billion within three years. Neither are the millions of Californians who put a pink dot on their driver's licenses indicating their willingness to donate body parts.

"People who donate have no idea tissue is being processed into products that per gram or per ounce are in the price range of diamonds," said Arthur Caplan, a professor at the University of Pennsylvania's Center for Bioethics.

The products enhance millions of lives, according to industry trade groups. Cadaver tendons help athletes return to the playing field. Slings crafted from human skin solve bladder troubles.

Corneas prepared for implant allow the blind to see.

About 20,000 dead Americans became part of this manufacturing cycle in 1999, four times the number of bodies used for vital-organ transplants.

Organs can only be harvested from donors who are brain dead but whose heart and other organs are still functioning. Once the heart stops, organ donation is ruled out. Tissue still can be recovered.

The **tissue trade** now generates about $ 500 million annually.

"There is a profit," said Michael Jeffries, chief financial officer for Osteotech Inc., a leader in the bone business. "It's not an evil thing because the profit is put to good use. "

But trade in body parts has sparked questions from donor families and medical ethicists about ties between companies that sell body parts and nonprofit organizations that solicit them.

The tissue banks act as middlemen for their corporate partners.

Families are led to believe they are giving the gift of life.

They are not told that skin goes to enlarge penises or smooth out wrinkles, or that executives of tissue banks _ nonprofit groups that obtain body parts _ routinely earn six-figure salaries. The products are rarely life-saving as advertised.

"I thought I was donating to a nonprofit. I didn't know I was lining someone's pocket," said Sandra Shadwick of Burbank, whose brother died two years ago. Shadwick gave her brother's remains to a Los Angeles tissue bank. "It makes me angry. It makes me appalled. If it's not illegal, it ought to be. It's certainly immoral. "
Industry leaders say donations would plummet if families knew their gifts generate profits. One consequence would be a potential drop in the supply of vital organs.

"If donors were told at the time about profits, they wouldn't donate," said Jan Pierce, director of the Intermountain Tissue Center, a Salt Lake City nonprofit bank.

The Register began its investigation last November after allegations that the head of the Willed Body Program at the University of California, Irvine, profited from the sale of donated body parts.

After interviewing hundreds of people and reviewing thousands of pages of documents, the newspaper found that donated bodies follow one of two paths. They become either research subjects or raw materials for medical products that are sold commercially for profit.

It is more likely that body parts will be made into products.

IT STARTS AS A GIFT

The story begins with private acts of charity. California residents can indicate their intent to donate their organs and tissue on their driver's licenses. In addition, the industry aggressively recruits donors through Internet spam, billboards and television commercials. Government grants help pay advertising

costs.

The efforts are working. The number of donors increased 172 percent nationwide over the past five years, the American Association of Tissue Banks says.

Nonprofit tissue banks from Santa Ana to New Jersey screen possible donors and remove body parts. Up to 20 bones and tendons are harvested along with 4 square feet of skin and the whole heart.

In some cases, eyes, veins, jawbones, ribs and the spine are taken.

Bone is replaced with common PVC pipe to keep the body's shape for open-casket funerals.

The tissue banks then sell the body parts to companies that make products used by doctors and dentists. The tissue banks and companies share revenue.

A typical donor produces $ 14,000 to $ 34,000 in sales for the nonprofits, records and interviews show. But yields can be far greater.

Skin, tendons, heart valves, veins and corneas are listed at about $ 110,000. Add bone from the same body, and one cadaver can be worth about $ 220,000.

NO TESTS FOR FEDERAL LAW

The National Organ Transplant Act, approved by Congress in 1984, banned profits from the sale of tissue. But no company or tissue bank has been prosecuted.

"The law has never been tested in court. Nobody has ever decided what is selling and what isn't," said Jeanne Mowe, executive director of the American Association of Tissue Banks. Companies and tissue banks step around the law by charging
marked-up fees to handle and process the body parts. They avoid billing for the tissue itself. The law allows for reasonable fees to cover processing costs without defining reasonable.

Tissue banks also avoid using the word "sales. " But Judy Perkins, executive director of the University of California, San Diego, Regional Tissue Bank, calls fees a euphemism for sales.

The zeal to harvest tissue is underscored by the case of Heather Ramirez, a 19-year-old Arizona woman who died in an automobile crash.

Her parents accused the American Red Cross of stealing their daughter's bones, court records show. The family agreed to donate body parts, but expressly refused to give up the bones.

The Red Cross admitted in court records to altering documents _ making it appear as if consent has been given. The bones were returned after a two-year legal fight.

"Instead of having some closure after her death, it just became an unending saga," said the father, Greg Ramirez. "It was like she was dying over and over again. "
The Red Cross, which has its West Coast tissue center in Costa Mesa, chalks up the mistakes to human error. "We are certainly deeply saddened by this," said Red Cross spokesman Mike Fulwider.

BUSINESS IS BOOMING

The two largest for-profit companies in the tissue industry recorded a combined $ 142.3 million in sales last year, and each pays its chief executives more than $ 460,000 annually, records show.

The nation's four largest nonprofit tissue banks say they will generate a total of $ 261 million in sales this year. And prices are rising.

Patients pay $ 2,400 for a cornea at San Francisco's Pacific Eye Associates. The same eye center charged $ 1,000 four years ago.

Osteotech's trademark bone putty, used in spinal surgery, sells for $ 853 for 2 teaspoons _ about $ 100 more than in 1996. Industry officials say higher processing costs have led to steeper prices.

Costs can vary by hundreds or thousands of dollars. An Achilles tendon at a Seattle bank sells for $ 865. Georgia's CryoLife Inc., a for-profit firm, charges $ 2,000 for the same product.

"I know hospitals that shop for bone like you would a can of beans," said Perkins of the San Diego tissue bank.

The revenue helps nonprofit banks cover perks and salaries normally associated with private business. A Register analysis of 50 of America's largest nonprofit tissue banks shows top executives earning an average of $ 135,000 a year. One Los Angeles bank paid its top official $ 533,450 in 1998 and provides him a BMW, records show.

ENSURING A STEADY SUPPLY

The biggest deal in the industry was struck 13 years ago.

Osteotech opened its doors in New Jersey without access to bodies.

So the company spent $ 10 million to start a nonprofit tissue bank serving as its exclusive broker of human bones.

The publicly traded company is now the nation's largest producer of bone products.

As for the tissue bank? The Musculoskeletal Transplant Foundation is the world's largest.

The bank's chief executive, Bruce Stroever, predicts the industry will double, to $ 1 billion, by 2003.

"Osteotech couldn't go it alone and had to invent us," said

Stroever, who earns $ 350,000 a year running the nonprofit. "Neither one of us would be here without the other. "

In Florida, the opposite model occurred. The nonprofit University of Florida Tissue Bank spun off a private firm, Regeneration Technologies Inc., in 1998.

The nonprofit's top executive, Nancy Holland, doubles as the private company's vice president. She keeps both business cards on hand.

The tissue bank and private firm share office space and phone lines. The nonprofit tissue bank sends bone to the for-profit firm.

"It's a matter of subterfuge if you're hiding behind a nonprofit," said ethicist and law professor Lori Andrews of the Chicago-Kent College of Law.

Holland said telling potential donors about profits and ties to companies would complicate the consent process.

"We're already talking with someone who is in a state of grief, and we just thought it was too much information to impose on them at that time," Holland said.

Five months after the Register began asking questions, Tissue Banks International, a large Maryland chain, said that it plans to start telling prospective donors of for-profit links, but only in Southern California.

Although some industry financial figures are made public in dense reports filed with the Internal Revenue Service and Securities and Exchange Commission, key details are not revealed.

The American Red Cross won't say how much it pays Irvine-based Edwards Lifesciences Corp. to market heart valves that the Red Cross recovers. "Those things are considered proprietary," said Red Cross spokeswoman Blythe Kubina.

Beverly Hills physician Steven Burres founded Fascia Biosystems and sells trademark cadaver thigh tissue to cosmetic surgeons. He refuses to name his tissue-bank suppliers.

"If I was building antique chairs, you wouldn't care what lumberyard I got my wood from," he said.

Tissue banks contend most donor families do not want details.

Steve Oelrich, sheriff of Alachua County, Fla., agrees. He donated tissue from his teen-age son, who died in 1995.

"There are two things I don't want to know about this thing. One is the financial part, that they sell this and the hospital buys that. And I don't want to visualize what they do to your child," Oelrich said.

Tissue banks mine parts for 50 to 100 patients from a single

cadaver. After John Tabachka died in 1998, doctors implanted parts from the Pittsburgh-area volunteer firefighter into 422 patients.

"If he couldn't help you in life, he'd help you in death," Tabachka's widow, Sally, said.

The products can make a big difference to recipients.

When Jim Muth, 47, blew out his knee, the Yorba Linda man paid $ 7,500 to get tendons from a 19-year-old cadaver.

"They sell these things like nuts and bolts now," Muth said.

"They're just another part of the tool box. "

A year later, Muth is swimming, biking, walking and hopes to be running soon.

Strict federal laws ban any buying or selling of hearts, lungs, livers or other organs needed for transplant.

But the government has helped boost profits in the **tissue trade.**

The Clinton administration adopted rules in 1998 requiring hospitals to notify organ agencies of all deaths. That makes it more likely that families will hear from a tissue bank within four hours of a loved one's death. The rules are designed to increase the number of organ transplants.

But organ donors rose by less than 1 percent in 1999, according to the Association of Organ Procurement Organizations. The big beneficiaries are tissue banks and companies that showed gains in donors of as much as 40 percent, records and interviews show.

The government is trying new methods to increase organ and tissue donations.

Last fall, Vice President Al Gore announced $ 5 million in grants to organ and tissue agencies. Several grants target minority communities, which lag in donation.

Like many politicians and government officials, Gore said he was surprised by the size of the **tissue trade.**

"I did not know that the amount of money involved was as large as you have pointed out," said Gore in a recent telephone interview.

In Orange County, Chief Deputy Coroner Jacque Berndt explained why she doesn't charge the Orange County Eye and Tissue Bank to use the county morgue.

"They're a nonprofit, and their funds are limited in that sense," said Berndt, before learning the bank is part of a chain paying its chief executive $ 283,882 a year.

Berndt also was unaware of the Santa Ana bank's corporate ties.

The bank's Executive Director Larry Hierholzer said he ships skin to New Jersey-based LifeCell Corp. and heart valves to Georgia-based CryoLife. Both companies are publicly traded and have developed trademark products.

Berndt isn't the only coroner unaware of the business ties.

"I didn't even imagine this was such a high-paying business," said Sgt. Sharon Housouer, Imperial County's chief deputy coroner, who was approached by another tissue bank last year requesting access to her morgue. "It shocks me, but it really doesn't surprise me. I'm a cop. Nothing surprises me anymore. "

Register staff writers Liz Kowalczyk and Susan Kelleher contributed to this report.

GRAPHIC: COLOR PHOTO; BLACK & WHITE PHOTO; ILLUSTRATION; CHART; COLOR CAPTION; THE COLLECTOR; Vidal Herrera performs an autopsy at McAulay & Wallace Mortuary in Fullerton. He conducts autopsies and charges fees for body parts.; B&W CAPTION; NICK OELRICH; When the 19-year-old man died in 1995, his tissue was donated.; B&W CAPTION; STEVE OELRICH; Doesn't want to know details of what happened to his son's body.; B&W CAPTION; FINISHED PRODUCT; A technician at Osteotech Inc. displays bone dowels made from donated human bone. The company opened its doors 14 years ago without access to raw materials. It helped create a nonprofit tissue bank and is now a $ 75 million company traded on Wall Street.; ILLUSTRATION-CHART - THE $ 222,062 BODY (what it could cost to obtain all of tissue that can be harvested from one donor); ILLUSTRATION shows cost of individual body parts (e.g. cornea $ 4,800, heart valve $ 9,120; skin $ 36,522, etc.) (SEE MICROFILM OR GRAPHICS FILE); ILLUSTRATION-CHART - here's the route a typical tissue donation takes and its parallel financial journey (SEE MICROFILM OR GRAPHICS FILE)

LOAD-DATE: April 21, 2000

THE ORANGE COUNTY REGISTER April 17, 2000 Monday

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April 17, 2000 Monday MORNING EDITION

SECTION: NEWS; Pg. A08

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HEADLINE: SPECIAL INVESTIGATION;
THE BODY BROKERS;
PART 2 OF A 5-PART SERIES;
SKIN MERCHANTS;
ABOUT THE SERIES

BYLINE: The Orange County Register

BODY:
Register reporters began this investigation last fall after the University of California, Irvine, fired the head of its Willed Body Program for allegedly selling body parts for profit. The District Attorney's Offic is investigating.

Sunday: ASSEMBLY LINE

Body parts are the raw materials behind a $ 500 million industry.

Skin, bone and tendons are treated like coal, timber and oil _ despite laws against profiting from tissue.

Grieving families are not told that nonprofit agencies that solicit donations of human tissue act as middlemen for for-profit businesses.

Monday: SKIN MERCHANTS

A carefully monitored system insures that donated internal organs go to people in dire need, but the body's largest organ, skin, is sold increasingly to plastic surgeons instead of to burn units where it is needed most.

Today: RESEARCHERS
Researchers are using the bodies of the dead as guinea pigs in car-crash tests and other experiments.

Shooting victim Justin Hartt, a Jehovah's Witness whose family objects to organ donation, had his lung taken after he died.

Animal rights protests encourage companies and researchers to use human tissue rather than rabbits.

Wednesday: GATEKEEPRS
The federal government loosely regulates the medical use of body parts.

Doctors and hospitals are not required to inform patients who received diseased transplants when tissue is recalled.

Thursday: PIONEERS

One family that made a fortune off donated human body parts represents what is good and what is troubling inside the **tissue trade.**

The tissue trade has given rise to entrepreneurs filling small niches, including a freelance autopsy service, companies that sell skeletons on the internet and a firm that tests tissue.

Jim Muth, below, is active again with the hlep of cadaver tendons.

GRAPHIC: BLACK & WHITE PHOTO; Jim Muth, below, is active again with the help of cadaver tendons.

LOAD-DATE: April 23, 2000

THE ORANGE COUNTY REGISTER April 18, 2000 Tuesday

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THE ORANGE COUNTY REGISTER

April 18, 2000 Tuesday MORNING EDITION

SECTION: NEWS; Pg. A01

LENGTH: 1950 words

HEADLINE: SPECIAL INVESTIGATION;
THE BODY BROKERS - PART 3 OF 5 - **RESEARCHERS** Rough research;
Bodies donated to science usually end up as medical subjects, but some also are used in crash tests and other product-safety studies;
Donor families usually aren't told the details;
INVESTIGATION: Tests on cadavers, for instance, helped in developing a safer generation of auto air bags.

BYLINE: RONALD CAMPBELL;WILLIAM HEISEL;MARK KATCHES, The Orange County Register

BODY:
Donated human bodies are replacing crash-test dummies and animals in sometimes-bizarre research projects that are largely hidden from the public, an Orange County Register investigation has found.

Like their counterparts in the body-parts industry, **researchers** at universities and in private business avoid telling families how their loved ones are being used. They fear donations would drop.

"There isn't a thing that should go on in these programs that is secret," said Don Cahill, past president of the American Association of Clinical Anatomists. "The donor population is altruistic for giving in the first place. That's why we should deal with them with honesty, dignity and forthrightness. "

"Instead," Cahill said, "**researchers** have taken this business underground. "

At least 17,500 bodies are donated to science in the United States every year, according to a Register survey. These bodies are in addition to the 20,000 cadavers used each year by businesses to make products.

Most of the bodies donated to science follow a traditional path: to medical schools, where students dissect them, or to medical conferences, where physicians practice their skills on them.

But each year, at least 4,000 bodies become the subjects of wide-ranging experiments, the Register found. Bodies are crashed to test vehicle air bags, heads are dropped to test helmets, and arms are dropped to test snowboard wrist braces.

These experiments are seldom discussed publicly and almost never disclosed to would-be donors or their families. Sometimes **researchers** don't even tell families they are taking parts from

their loved ones' bodies.

Since 1990, the Los Angeles County Coroner's Office has removed parts from hundreds of accident and homicide victims without consent. The coroner gave those parts to **researchers.** When some families found out, they felt violated.

One of the **researchers,** Russell Sherwin of the University of Southern California, used to ask permission from donor families, he said. He stopped doing that because too many objected _ hampering his research into the prevalence of the lung disease emphysema.

"My enemy is the public," Sherwin said, "and they are the ones I am serving. "

Most **researchers** rely on donations. Willed-body programs based at medical schools collect about 15,000 bodies annually. Roughly one body in 10 donated to willed-body programs is used for research.

Private agencies, such as the Maryland-based Anatomic Gift Foundation, supply an additional 2,500 cadavers a year to academic and commercial **researchers.**

"There is almost no body part that is not in demand," said Gina Dunne Smith, professional-services director for the International Institute for the Advancement of Medicine, a cadaver supplier in Edison, N.J.

SELLING LEADS TO ARRESTS
Employees at two universities allegedly sold donated bodies or body parts to **researchers** without approval.

University of California, Irvine, fired the director of its willed-body program, Christopher S. Brown, in September for allegedly selling seven donated spines to a Phoenix **researcher.** The Orange County District Attorney's Office is investigating.

In Los Angeles County, prosecutors have filed theft and embezzlement charges against Philip Guyett, former manager of the willed-body program at Western University of Health Sciences in Pomona. Guyett, who operated a private willed-body program on the side, allegedly sold a cadaver belonging to the university. He has pleaded not guilty.

Guyett told the Register that the demand for cadavers far outstripped his supply.

"I would get calls saying 'We're having a workshop for podiatrists, and we need 70 feet specimens in two weeks. Can you provide us with that?,' and I would usually have to say 'no,' because I didn't have that many donors," Guyett said.

"There is a legitimate demand, not some mad scientist out there trying to build a monster, but that kind of demand brings out the worst in people," Guyett said.

Although no reliable statistics are kept, most cadaver research

appears to take place at universities. It is funded by the federal government, as well as automakers, pharmaceutical companies and consumer-product manufacturers.

Physicians and other **researchers** use dead bodies or parts of them in situations where it would be impossible or unethical to use living people. Increasingly, they also are using dead humans in place of live animals, because of the public outcry against animal testing.

FAMILIES AREN'T TOLD

Donors or their families sign a form earmarking the body for research. They generally aren't told what that means.

That is partly because the potential uses are so vast and because pieces from an individual body may be parceled out months after death.

"Each organ may go to 20 different **researchers,**" Smith said.

But **researchers** also want to avoid sharing unpleasant details with donors or their families.

One of the biggest fields for whole-cadaver research is automotive safety. The National Highway Transportation Safety Administration, whose motto is "People Saving People," funds crash-test studies involving about 70 cadavers a year at seven universities.

"If you want safe cars you need good dummies, and if you want good dummies you have to test on cadavers," said Albert King of Wayne State University in Michigan, who has conducted crash tests on cadavers since 1966.

One of the schools that receives federal funds for cadaver tests is Ohio State University. It uses a few of the 150 donated cadavers it gets every year in crash tests.

"It's not something we advertise," said Margaret Hines, director of the Ohio State trauma research program.

Wayne State is more open with potential donors. A brochure it supplies to donors and their families lists "safety testing" as a potential use of donated bodies, said Barbara Russo, director of the school's willed-body program.

"If someone has questions, we will go into detail," she said.

"We don't hide that. "

She said the school's candor has not hurt donations. Wayne State gets about 175 cadavers a year and uses about 5 percent of them for research.

At Ohio State, Hines and her team dress the cadavers and strap them into car-like crash sleds. Then they slam, jerk and jolt the

bodies, using sensors to pinpoint injuries.

"The body is a complicated piece of machinery and difficult to replicate," Hines said. "Without these generous donations, we wouldn't be able to get accurate test readings about what happens in a car crash, and cars would be much more dangerous. " Automakers use cadaver tests to develop new safety features. The federal government uses them to set mandatory safety standards for all cars.

After dozens of small children were killed by deploying air bags three years ago, the federal government determined it could safely reduce the inflating pressure of the air bags by 20 percent to 35 percent. It based the new standard on crash tests involving 35 cadavers.

At Duke University, Barry Myers uses cadaver heads, necks and spines to study the body's reaction to falls and crashes. He repeatedly dropped 20 heads and necks a few inches to a few feet and measured the impact. He said his research has led to better bicycle helmets and safer cars.

"Look at car roofs," Myers said. "There is a very slender liner on the roof. Wouldn't you want a big fat pad up there to protect the neck? Don't pads protect necks? No. They break necks. "

WRIST BRACES TESTED

Utah **researchers** in 1998 tested a wrist brace for snowboarders by repeatedly dropping 12 arms from six cadavers. Their conclusion: Wrist braces reduced the potential for injury from minor falls but not more-forceful collisions.

The Univesity of Tennessee in Knoxville receives about 35 bodies a year for forensic research. **Researchers** have locked bodies in trunks, submerged them in water and left them lying in a field in various stages of decay to better understand crime scenes. The work has been widely publicized, and was even featured in crime novelest Patricia Cornwell's book 'The Body Farm,' but the school doesn't tell donor families how exactly the bodies will be used.

'We don't want to impose on these families in their time of grief the thought of Aunt Sally out there decomposing on the ground,' said Dr. Lee Meadows Jantz, one of the Tennessee **researchers.**

Researchers say their work on cadavers will save lives. They say they don't tell donors or their families exactly what they're doing because the truth would decrease donations.

"No two patients are going to agree on what kind of research is good and what kind of research is bad," said Wayne Grody, a pathologist at the University of California, Los Angeles, who has done AIDS research on donated hearts. "The greater good of humanity is best served by allowing research to go on unimpeded. "

CORONER DOESN'T ASK

The L.A County Coroner's Office believes so strongly in research that it has given organs and other body parts to **researchers** without families' consent at least 353 times since 1990, according to records reviewed by the Register.

"We do not need consent. That's the law," coroner spokesman Scott Carrier said.

California law does allow the coroner to remove tissues for scientific research. But the law also requires the coroner to "make diligent efforts" to find survivors and get their consent.

Carrier said the coroner doesn't believe that provision applies to tissue for research.

Orange County Chief Deputy Coroner Jacque Berndt said her department does not take body parts without consent.

Some of the families of people whose body parts the Los Angeles coroner removed believe their rights were trampled.

In 1998, the coroner removed the left lung from 17-year-old shooting victim Justin Hartt and gave it to Sherwin, the USC **researcher,** for his emphysema project. Neither the coroner nor Sherwin told Hartt's parents _ devout Jehovah's Witnesses who object on religious grounds to donating body parts.

"That, to me, is sacrilegious," said Justin's father, Merlin Hartt. "If they asked me I would have said 'no.' But no one ever asked. "

In 1996, the Los Angeles coroner removed one lung from 23-year-old Timothy Flanagan of Long Beach, who had been shot and killed while washing his 1984 Pontiac LeMans. The coroner gave the lung to Sherwin at USC. Neither the coroner nor Sherwin told Norma Taylor, who had raised Flanagan since boyhood.

"I'm sure this is important research, but it's important to show some respect for the family, too," Taylor said. "I can't believe this isn't against the law. "

When Jason Williams was killed outside his grandmother's front door in south Los Angeles two years ago, the coroner took part of his esophagus without consent.

"What they did is like stealing," said his grandmother, Laura Edwards.

"I just don't think the families truly understand what we're doing and what the benefits are," said Joseph Muto, chairman of the coroner's research committee. "Each research project potentially has life-saving capabilities. "
Harvesting body parts without consent might harm scientific research in the long run, said bioethicist Stuart Youngner of Cleveland's Case Western Reserve University.

"It rekindles the old body-snatching stuff that went on a couple centuries ago," Youngner said. "It's going to turn people off. "

Register staff writers Susan Kelleher and Liz Kowalczyk contributed to this report.

GRAPHIC: COLOR PHOTO; BLACK & WHITE PHOTO; MARKETING PUSH; This sign in Aliso Viejo is part of a nationwide campaign to increase donations. (COLOR); HARVEST YIELD; Vidal Herrera removes a brain from a cadaver during a private autopsy at McAulay & Wallace Mortuary in Fullerton. At the request of the family, the brain will be sent to **researchers.** (B&W); HOLDING ON; Laura Edwards clutches the ashes of her grandson, Jason Williams, who was gunned down outside her home. A portion of his esophagus was taken without her consent and used for research. "Here I have his ashes and they are not all they are supposed to be." (COLOR)

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HEADLINE: SPECIAL INVESTIGATION;
THE BODY BROKERS;
Scarce scrutiny;
Feds and industry say our tissue supply is safe, but inspections are rare, and statistics on tissue-linked illnesses don't exist.;
Safety standards vary among tissue banks

BYLINE: RONALD CAMPBELL; WILLIAM HEISEL; LIZ KOWALCZYK, The Orange County Register:

BODY:
Human-tissue transplants have caused AIDS, hepatitis and even rabies, but they're subject to less regulation than a kitchen toaster.

The U.S. Food and Drug Administration supervises tissue banks but says it doesn't know how many exist.

FDA and industry leaders say the nation's tissue supply is safe.

But an Orange County Register investigation found gaping holes in the safety net:

No hard statistics back up industry and FDA safety claims.

Regulators have focused on a handful of high-profile health threats but have not studied the long-term effects of tissue transplants.

None of the federal government's primary health investigators _ the FDA, the Centers for Disease Control and the National Institutes of Health _ routinely tracks deaths or illnesses affecting tissue recipients.

A cadaver suspected of carrying disease may be rejected by one tissue bank but accepted by another bank and its tissue sent out to patients.

There are so few inspectors that tissue banks can escape inspection for years, even if the most recent inspector found significant problems.

California, one of four states that regulates tissue banks, has not inspected any in nearly two years.

Doctors and hospitals are not required to inform patients who received diseased transplants when tissue is recalled so that they

can monitor their own health.

"There isn't even a way for FDA to communicate with all tissue banks," said Margerie Moogk, program director of Pacific Northwest Tissue Bank in Spokane, Wash. "You just aren't used to thinking about there being that kind of gap in regulatory authority, particularly (for) something that's going into the operating room. "

Congress considered regulating the industry 16 years ago. The nation's Lions Clubs, fearing that federal rules would hamper their eye banks, helped kill the proposal.

It took a series of medical surprises to shock the federal government into action.

The first came in 1991, when Colorado health officials learned about a 77-year-old woman with HIV. They could find only one possible cause for her infection: She had received a new hip bone from a cadaver in 1985.

The donor, a Virginia shooting victim, had tested negative for HIV when he died. Six years later, more-sophisticated tests conducted on frozen tissue samples showed he did have the virus.

Six other recipients of his tissue tested positive for HIV, and two of them died of AIDS, before experts connected the cases to the tissue donor.

A second surprise came in 1993, when the FDA learned that a few tissue banks were distributing untested or poorly documented human tissue from Russia and Eastern Europe. That prompted an emergency FDA rule requiring that every donor be tested for HIV and for hepatitis B and C.

Four years later, Japanese scientists nailed down a suspected link between transplants of dura mater, the outer lining of the brain, and Creutzfeldt-Jakob disease, a deadly neurological infection linked with mad-cow disease. The FDA followed up with a proposal for rigorous testing of dura donors.

Leaders of the tissue-bank industry say mandatory testing has virtually eliminated the threat of AIDS or hepatitis infection from tissue products.

A leading expert on Creutzfeldt-Jakob Disease, Paul Brown of the National Institutes of Health, said that because of the new FDA guidelines, "I don't think we'll ever see another case of dura-mater CJD in this country. "

The new guidelines came too late for Karen Bissell, who may have been the last American to contract Creutzfeldt-Jakob from a dura mater transplant. She received the transplant during brain surgery in 1992.

"We at the time had no idea that they had used this patch," her mother, Eleanor Bissell, said. "We had no idea until we went into the hospital last September (1998). "

Karen Bissell became ill in June 1998. The disease progressively stole her sight, her ability to walk and her consciousness. She died that September.

With these notable exceptions, human-tissue products have a superb safety record, industry leaders say.

For example, dentists have been using powdered cadaver bone to treat severe gum disease for nearly 30 years. It is the most-common medical use of human tissue, used in 200,000 patients last year, according to industry estimates.

"There's never been a single case of disease transfer," said Woodland Hills periodontist Robert Merin, president-elect of the California Society of Periodontists.

But Hessam Nowzari, director of advanced education in periodontology at the University of Southern California, argued that there is no proof for that assertion. If a patient developed kidney problems some years after gum surgery, he asked, would anyone think to link the two?

The FDA is focusing on the documented dangers of human tissue, not the theoretical ones. Its main weapons are surprise inspections of tissue banks and recalls of suspect tissue. Since 1993, it has conducted about 200 inspections and recalled more than 15,000 tissue products.

"We're trying to develop a framework keyed to risk," said Bill Hubbard, the FDA's senior deputy commissioner for policy. "We didn't want to overregulate these products, but at the time (in 1993) they were fairly unregulated. "

The FDA sets much-lower obstacles for human-tissue products than it does for more traditional medical products.

The FDA requires years of testing for new drugs and artificial medical devices. Once they are approved for sale, their makers must tell the FDA when a patient is hurt.

But tissue bankers have argued, and the FDA has agreed, that products made from the human body don't merit such scrutiny. Unlike drugs, they don't alter the body's biochemistry. Unlike medical devices, they don't change the body's normal functions.

So the FDA does not review the vast majority of products made from human skin and bones prior to sale. It does not know when a tissue product comes to market. It does not know when it harms a patient.

By comparison, even makers of consumer goods, such as toys and dishwashers, must tell a federal agency if they learn of a defect that could injure someone.

In December, the U.S. Consumer Product Safety Commission fined Black & Decker Inc. $ 575,000 for failing to report that toasters

had caused kitchen fires leading to eight injuries.

Had the company been selling contaminated body parts instead of toasters, the government's authority would have been limited to ordering a recall _ if and when it discovered the problem.

The FDA has proposed requiring banks to keep donor records for 10 years and show them to FDA inspectors. The proposal, awaiting approval by the federal Office of Management and Budget, would let the FDA trace tainted tissue to its source.

But the proposal doesn't go far enough, a 1997 report from the congressional General Accounting Office says.

"Without a requirement to report serious errors and accidents," the watchdog GAO wrote, "FDA is missing an opportunity to target facilities that may need additional oversight. "

In its reply to the GAO, the FDA said it lacked the money and manpower to review error and accident reports.

The tissue industry contends that strict oversight is unnecessary because its products are safe.

VOLUNTARY SAFEGUARDS

Tissue banks follow four steps to keep the nation's tissue supply disease-free:

Screening cadavers by asking the family about the person's sexual habits and possible drug use.

Testing the blood in donated bodies for, at a minimum, AIDS and hepatitis B and C. Some tissue banks test for other diseases.

Sterilizing tissue, either chemically or by freezing.

Handling the tissue in "clean rooms" to prevent transmission of disease from tissue-bank workers to the body parts.

These are informal standards, not required by law. In practice, these standards vary widely from bank to bank, allowing one bank to distribute tissue that another won't.

For example, in 1994, Pacific Coast Tissue Bank in Los Angeles accepted a cadaver that another tissue bank rejected, according to an FDA inspection report. A Florida tissue bank rejected the donor, a cocaine user, because he was so fat that the bank feared it couldn't rule out the presence of needle tracks on his arms.

Pacific Coast accepted the donor because the pathologist performing the autopsy couldn't find needle marks.

In April 1998 the New Jersey-based Musculoskeletal Transplant Foundation learned from another tissue bank that one of the foundation's cadavers had tested "repeatedly reactive" for the HIV p24 antigen _ an indication the body might have the AIDS virus.

The donor had passed the two HIV tests that the foundation requires, so its medical director continued distributing bone sections and powdered bone from this donor.

FDA inspectors discovered the situation during a routine inspection in June 1998 and demanded a recall.

"We stated that a positive test result for HIV should not be ignored and appropriate action should be taken to retrieve these tissues" from the hospitals that bought them, the FDA inspectors wrote.

Seventeen patients received parts from the donor, said Joel Osborne, the foundation's quality-assurance director. The foundation did not notify the patients or their doctors, leaving that up to the hospitals that bought the tissue. The foundation refused to name the hospitals, and the FDA could not provide them.

Osborne said the foundation is convinced the transplanted tissue poses no danger. The p24 test is "prone to false positive results with cadaver serum," he said.

Notifying patients about the test result "could cause some very unnecessary worry, concern (and) mental anguish to patients," Osborne said. "The FDA seems to be blind to that. "

FDA inspectors audit the donor records that every tissue bank is supposed to keep, looking for cadavers that failed disease tests.

When they find a violation they can demand a recall.

But the demand for skin, heart valves, tendons and other tissues is so high that they rarely stay in a tissue bank's freezer for more than a few months. By the time inspectors discover a problem, years may have passed.

For example, the FDA inspected Los Angeles-based Doheny Eye and Tissue Transplant Bank in late 1997. It was the agency's first inspection of Doheny in three years, although a 1994 visit found "several significant deficiencies. "
This time they uncovered cadavers that tested positive or reactive for hepatitis B, hepatitis C, syphilis and HIV.

Under FDA prodding, Doheny issued a recall in December 1997 for products from seven donors distributed during the previous three years. Most of the tissue already had been implanted or destroyed.

"We immediately modified our practices" because of the recall, said Toby Bernstein, a spokeswoman for Doheny's parent company, Tissue Banks International.

Two of the five distributors that received Doheny tissue refused to join in the recall, according to FDA records.

One unidentified distributor said it sold Doheny tissue, knowing it could carry the hepatitis B virus, to an "implanting surgeon"

who knew the tissue was questionable. It is not known if the surgeon implanted the tissue or if he or she told patients about the risk.

The other distributor, Pacific Coast Tissue Bank in Los Angeles, said its own tests contradicted Doheny's tests, which had shown that two cadavers might carry the hepatitis B virus.

Different tests for hepatitis B can produce conflicting results.

The FDA argues that a positive or reactive result on any test should disqualify a donor.

At the time of the Doheny incident, FDA recalls were operating on shaky legal authority. New Jersey-based Biodynamics International, now Tutogen Medical Inc., won a 1995 court battle with the agency over its authority to retain or destroy tissue shipments.

That defeat prompted the FDA to back away from a planned recall order against Metairie, La.-based Southern Transplant Service, which had distributed tissue from 21 unknown donors without medical records, according to an FDA report.

The FDA adopted a permanent rule in 1998 after public hearings and says it now has legal authority over the industry.

The FDA is now attempting to "reinvent" its inspect-and-recall strategy. It has proposed requiring more tests of cadaver tissue and making tissue banks register their products.

Tissue bankers are wary of more FDA requirements.

"I don't have a problem with their concern," said Doheny President Ron Smith. But "sometimes they go a little overboard. We have a system right now that has proved very safe. "

The new FDA regulations won't change that system. The agency says it can't keep up with the industry's growth, so it plans to let trade groups, such as the American Association of Tissue Banks, do many inspections.

- Register staff writers Dena Bunis, Mark Katches and Susan Kelleher contributed to this report.

(SIDEBARS)

GLOSSARY
Dura mater Hard outer lining of the brain. Used as a patch in neurosurgery.

PVC pipe Common plumbing pipe used for aesthetic reasons to replace bones in cadaver donors. The pipe maintains the body shape after bone from the shoulder to the wrist and from the hip to the ankle is removed. It makes open-casket funerals possible.

Screening Questions are asked to determine if a prospective donor is

suitable for organ or tissue transplant.

Testing Blood analysis is done to determine whether donor shows signs of infection from any of several infectious diseases, including AIDS, hepatitis B and hepatitis C.

WHAT DO YOU THINK?

Q. Should tissue banks and doctors be required to track and report diseases and deaths from transplants?

Q. Should recipients of tissue transplants be guaranteed full information about recalled tissue?

Q. Should patients be told if they have body parts that have been recalled?

Q. What about your religious beliefs -- do you agree or disagree?

ABOUT THE SERIES

1: April 16
ASSEMBLY LINE
Body parts are the raw materials behind a $ 500 million industry.

Skin, bone and tendons are treated like coal, timber and oil -- despite laws against profiting from tissue.

PART 2: April 17
SKIN MERCHANTS
A carefully monitored system insures that donated internal organs go to people in dire need, but the body's largest organ, skin, is sold increasingly to plastic surgeons instead of to burn units where it is needed most.

PART 3: April 18
LABORATORY
Researchers are using the bodies of the dead as guinea pigs in car-crash tests and other experiments.

PART 4: April 19
GATEKEEPERS
The federal government loosely regulates the medical use of body parts. Doctors and hospitals are not required to inform patients who received diseased transplants when tissue is recalled.

PART 5: April 20 ENTREPENEURS
One family that made a fortune off donated human body parts represents what is good and what is troubling inside the **tissue trade.**

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Please join the online conversation at dialog.ocregister.com/

Fax us at (714) 796-5030; phone your comments to (714) 550-4636, category 4523; or write us at The Body Brokers, The Orange County Register, P.O. Box 11626, Santa Ana, CA 92711.

WHAT PEOPLE ARE SAYING
By e-mail, phone or fax, readers share kudos and concerns. Voices

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GRAPHIC: COLOR PHOTO; BLACK & WHITE PHOTO; CHART; ILLUSTRATION; COLOR CAPTION; RARE TASK; Regeneration Technologies prepares jaw bones for reconstructive surgery use. Most tissue banks don't.; B&W CAPTION; COLD STORAGE; The granddaddy of the tissue-product industry, CryoLife Inc. of suburban Atlanta, has more than a decade of experience dealing with regulators. Vice President Roy Vogeltanz stands in front of two of the company's heart-valve storage freezers.; ILLUSTRATION-CHART - human heart valves and what hospitals pay tissue banks for them; ILLUSTRATION-CHART - human tendons and veins and what hospitals pay tissue banks for them; CHART - CHRONOLOGY OF RECENT EVOLUTION OF ORGAN DONATION (SEE MICROFILM)

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THE BODY BROKERS;
Part 5 of a 5-part series;
PIONEERS;
Making death pay;
The **tissue trade** thrives despite laws against profiting from the sale of human parts. Those earning a living in the field make no apologies.;
Entrepreneurs gain when altruism, opportunity mix

BYLINE: MARK KATCHES;LIZ KOWALCZYK;RONALD CAMPBELL, The Orange County Register

BODY:
A family of Russian immigrants came to America with $ 90 and struck it rich in the body-parts trade.

Headed by patriarch El Gendler, the family grossed $ 24.8 million in salaries, bonuses and fees over five years turning donated human tissue into products, an Orange County Register investigation found.

Gendler co-founded the Pacific Coast Tissue Bank, a nonprofit that seeks donations from grieving families. He also co-founded with his wife a private, for-profit bone-processing firm that gets its raw materials from downtown Los Angeles-based Pacific Coast, records show.

"I make a good living," wrote Gendler, who declined to be interviewed in person. "But I work hard and have a lifetime of work invested. I am a top scientist, and I receive compensation as such. "

Industry critics and ethicists say the Gendlers represent the good and the troubling in the $ 500 million **tissue trade,** which thrives on a mix of altruism and money.

More than 175 companies and tissue banks nationwide operate in this fast-growing field, despite laws against profiting from the sale of body parts. The industry does not include agencies that harvest vital organs, such as hearts, livers and kidneys for transplant.

Few in the nonprofit tissue-bank business have been as successful as the Gendlers, who now hope to gain access to the Orange County morgue.

The family says its products have helped hundreds of thousands of patients live more comfortably.

They also are considered mavericks who are pushing salaries and perks to new heights in the nonprofit tissue-bank field, while discounting industry safety standards, records and interviews show.

The state attorney general is probing their business ties to see if nonprofit Pacific Coast directs too much money to the family's for-profit venture. And health regulators have cited the tissue bank for its handling of human tissue, inspection records show.

Lawyers for the Gendlers say the family is doing nothing illegal.

Money is made in the industry through product sales.

Tissue-bank executives and the for-profit companies emphasize that they are not charging money directly for body parts.

Instead, they charge marked-up fees for handling, processing and distributing the tissue. That distinction allows them to step around federal and state laws banning profits off body parts.

Pacific Coast generates an average of $ 26,600 from each donated body _ mostly from bone, according to Gendler. The tissue bank reported $ 6.2 million in revenue in 1998. Part of the money is used to pay salaries and perks to Gendler. Half the proceeds go to the for-profit company, which is owned by Gendler's wife, records show.

Here's how it works:

Gendler, the president of Pacific Coast, was paid $ 533,450 annually in salary and bonuses in 1997 and again in 1998, according to the tissue bank's federal tax reports. He is the highest-paid executive of a nonprofit tissue bank in the United States, according to a Register analysis of the industry. The average income for top executives at 50 of the nation's largest tissue banks in 1997 was $ 135,308. The world's largest tissue bank _ which generates 10 times more revenue than Pacific Coast _ paid its top executive $ 182,696 less than Gendler in 1998.

His son Eli Gendler earned $ 291,800 as one of the nonprofit tissue bank's two medical directors, records show.

Simona Gendler, the president's wife, runs the family business, Perfomat Inc. From 1994 to 1998, her company recorded $ 20.6 million in fees from Pacific Coast. The fees compensated her for grinding and processing human bone into Dembone, Lambone and other trademark products using her husband's patented methods.

Dentists use the products to treat gum disease and to fill small gaps in bone created when teeth are pulled. El and Simona Gendler formed Perfomat together, records show.

The private company lists its official address as a $ 2.47 million, seven-bedroom, seven-bath estate on a 22,248-square-foot lot a few blocks from Santa Monica State Beach. El and Simona Gendler own the home. Oliver Stone lives down the street.

A $ 60,600 BMW 740i _ bought with cash _ is owned by the nonprofit tissue bank. A $ 34,400 Mercedes is registered to Simona Gendler's company. Both cars were bought new in 1998, DMV records show.

El Gendler, 77, pays Pacific Coast $ 75 a month for use of the BMW, which has leather seats and a moon roof.

"I am almost 80 years old and it is difficult for me to drive unless I have a very comfortable car," wrote Gendler, adding that a Pacific Coast board member recommended the BMW. "The other alternative for me was to hire a chauffeur. "

Gendler's compensation is set by a seven-member board of directors that he chairs and which includes family members and longtime associates.

Board member Richard Huber, who recommended buying the BMW, said the tissue bank now needs to reassess its executive compensation, adding that Gendler's salary and perks present a public-relations problem that will be dealt with at an upcoming board meeting.

"We haven't paid attention to the public perception of this, and it's going to get changed," Huber said. "It's going to come across bad, and we should have protected him more. "

Huber also said the tissue bank will probably sell the BMW and buy a Lexus in the $ 30,000 to $ 40,000 range.

"He hates the BMW and he wishes he had the Lexus," Huber said.

"Now, he's looking bad and I'm the bad guy. "

Marc Richards, a Newport Beach attorney who represents Pacific Coast, conceded that the board is not aware of a better-paid tissue-bank executive in the country. But he added: "You're not going to find anybody who is as well-qualified. "

Richards noted that El Gendler does not have a company pension plan.

But donor families say they are troubled by El Gendler's income.

"How can they call themselves nonprofit when they make so much money? " asked Rita Sullivan, a San Fernando Valley resident. The bones of her daughter, Maria, ended up at Pacific Coast in 1998.

"How can they do that? I guess it's our own fault. We should ask more questions before we give away our tissue. "

Medical ethicists say Gendler's compensation and Pacific Coast's ties to Perfomat can damage a fragile industry that relies on the public's good will.

"Those kinds of excesses look bad when donated skin and bone is turned into things like a Mercedes," said Stuart Youngner, a bioethicist at Case Western Reserve University School of Medicine.

BONE IS THEIR BUSINESS

El Gendler was born in Lithuania to a pharmacist father and a dentist mother. The family was exiled to Siberia during World War II when Gendler was 18, Russian records show.

In 1952, he graduated from the Siberian Medical Institute in Tomsk. El Gendler later returned to his alma mater to become a department chairman. Simona Gendler was a department head at the Tomsk-based Institute of Vaccines and Serums.

El and Simona Gendler and their children emigrated to America in 1980.

Six years later, El Gendler and Dr. Tillman Moore, a surgeon at Orthopaedic Hospital in Los Angeles, incorporated the nonprofit tissue bank.

In 1991, El Gendler won praise in the media for sending bone to a Dallas surgeon who fashioned new skulls for separated conjoined twins.

The surgeon, Kenneth E. Salyer, said Gendler sends him bone at no charge about 10 to 15 times a year for children who need surgery to correct deformities.

"Any time I've called and asked him to help a child or asked him for information that would be helpful scientifically, he has been helpful," Salyer said. "He's open and cooperative and compassionate for the children I treat. "

GROUND 'DENTAL DUST'

The family for-profit business, Perfomat, holds trademarks for freeze-dried and demineralized bone products. Dembone is ground bone that insiders call "dental dust. " Nationwide, similar products are used in an estimated 200,000 procedures a year. The powder resembles grated parmesan cheese.

The Gendlers ship the products across the country, including to 17 hospitals and more than two dozen dentists and oral surgeons in Orange County.

Links between nonprofit tissue banks and private companies are common. But the deal between Pacific Coast and Perfomat is unusual because it involves family members. Pacific Coast pays Perfomat 50 percent of its revenue for processing.

Most large nonprofit tissue banks that operate in a similar way say their processing costs are lower. At LifeNet, the nation's leading producer of dental dust, 25 percent of revenue goes to pay bone-processing costs, officials say. Other tissue banks say their fees are closer to 20 percent.

In New Jersey, Musculoskeletal Transplant Foundation Chief Executive Bruce Stroever says his bank pays more than 50 percent in processing fees to Osteotech Inc., a publicly traded company. The

fees cover the cost of making Grafton, a proprietary paste or putty-like substance used in spinal-fusion surgery.

The fees Pacific Coast pays to the family business are now the subject of a state probe, said Deputy Attorney General Belinda Johns, who specializes in nonprofit cases.

Pacific Coast says on annual financial reports that the Internal Revenue Service and the state attorney general approved its relationship with Perfomat.

"I think he means we've never called him on it," said Johns, who reviewed Pacific Coast's state file in December.

As a result of that review, Deputy Attorney General James Cordi said, the state is "auditing" the relationship between the tissue bank and the company to see if laws governing nonprofits are being broken.

Pacific Coast could not exist without Perfomat, according to El Gendler. When the bank lost money in 1995, Pacific Coast borrowed $ 300,000 to solve "cash-flow problems," records show. The money came from Perfomat in the form of a zero-interest loan.

RUN-INS WITH REGULATORS

The Gendlers also have had a series of encounters with federal and state regulators.

They have been cited for having both goat and human bone stored in the same freezer, releasing bone for transplant after it showed signs of hepatitis infection, and taking bone from a suspected intravenous drug user after it was rejected by another tissue bank, inspection records show.

The Gendlers have disputed the citations, saying in most cases the Food and Drug Administration relied on inaccurate data.

Pacific Coast also saysthat 562,000 units of its tissue have been released for implant since 1987 with no known cases of disease or infection.

An FDA regulator was concerned enough in 1996, however, to telephone the state Department of Health Services telling the agency to consider suspending Pacific Coast's license, said Clint Venable, manager of tissue-bank licensing for the state.

The bank remained open because, Venable said, there was no public-health danger.

The FDA said it was unaware of the phone call, and its rules require extensive review "before any regulatory action is undertaken or referred to another regulatory agency. "

FDA inspectors cited some of the same hepatitis concerns this February, records show. The Gendlers say citations are a routine part of the business. But regulators have found problems at Pacific

Coast that are not typical in the industry, a review of more than 60 FDA inspection reports involving other banks shows.

Gendler wrote: "We have a good organization and we provide good services to the medical community at reasonable fees. "

.BUCKING STANDARDS

The American Association of Tissue Banks adopted standards for accredited banks that ban recovery of bone more than 24 hours after death. Pacific Coast harvests up to 48 hours after death, and the bank dropped out of the voluntary association in 1993 _ in part because of that rule, Gendler wrote.

Jeffrey Sandler, who runs Denver-based Allosource, said the industry adopted the 24-hour rule because of concerns about bacteria in tissue recovered past that point. He said the Gendlers could be in trouble if anyone gets sick from Pacific Coast tissue taken beyond 24 hours.

"When 99 percent of the industry follows the same standard, and there's one renegade out there doing it differently, what do you think his liability is? " Sandler said. "It could be huge. He's going against the prevailing industry standard. "

Gendler says his methods are safe.

"PCTB is able to take bone up to 48 hours due to a bone sterilization process that I developed," wrote El Gendler, who considers this process his greatest contribution to the tissue banking industry. "Most other tissue banks do not go through such intense bone sterilization and this is the reason they do not take tissue after 24 hours. "

Mission Viejo dentist Roger Kurthy said he has never had problems with Pacific Coast tissue, which he uses to treat root canals, tooth extractions and gum disease. He pays about $ 30 for a small vial containing 0.5 cubic centimeter of bone powder. He believes the products are sterile and safe.

Still, when told about the harvesting methods at Pacific Coast, Kurthy said he was bothered that the tissue bank does not follow the industry standard.

"It just doesn't feel good in your gut," Kurthy said. "As practitioners, it's something we should be told. We need to know these things. "
Pacific Coast's main wish in Orange County, records show, is to harvest bone between 24 hours and 48 hours postmortem.

Orange County Chief Deputy Coroner Jacque Berndt said El and Eli Gendler and two lawyers met with her last summer after first meeting with her boss, Sheriff Mike Carona.

The Gendlers offered to open a satellite office in Orange County to appease Berndt, who said she prefers having only local banks harvest tissue.

Her office has an exclusive _ yet unwritten _ arrangement with the Orange County Eye and Tissue Bank. The bank, with offices in Santa Ana, is part of the Maryland-based Tissue Banks International chain.

Pacific Coast is still waiting for an answer from Berndt, who has not decided what the county will do.

DID YOU KNOW?

About 140,000 spinal fusion procedures are done in the U.S. each year using cadaver bone.

GLOSSARY
Lambone: Membrane-like sheets of human laminar cortical bone.

Pacific Coast provides Lambone in three thicknesses. Dentists say it look like think brown paper.

Demineralized bone: Bone that has been chemically treated to remove calcium. It is used about 200,000 times a year to treat gum disease or fill voids left after teeth are pulled.

Harvesting: The process of taking bone and other parts from a cadaver.

Histology: Histology is the branch of biology concerned with the study of tissue. El Gendler was chairman of the Histology Department at the Medical Institute of Tomsk, his alma mater in Siberia, before coming to America.

If you missed any part of this series you can find it online at: www.ocregister.com/health/body/

Please join the conversation at dialog/ocregister.com/

Register staff writers Susan Kelleher and Natalya Shulyakovskaya contributed to this report.

GRAPHIC: ILLUSTRATION; COLOR PHOTO; CHART; Illustration of how the Gendler family got rich in the body business (A14); IMPORTED; Fetal skulls like these, $ 450 each, are among the human and animal bones sold by Skulls Unlimited, based in Oklahoma City, Okla. It is illegal to sell human skulls if the death occurred in the U.S. (Color photo-A01); HAPPY MOMENT; El Gendler with twin girls who were born in Lithuania near his hometown. The girls were born joined at the head and underwent reconstructive surgery in Dallas, using bone products invented by Gendler. (Color photo-A13); CORPORATE BASE; El and Simona Gendler own this Santa Monica estate on a 22,000-square-foot lot near the beach. The house doubles as the official corporate address for Simona Gendler's bone-processing company, Perfomat. (Color photo-A13); CHART/LST-Illustration of a skeleton and the typical prices tissue banks charge for each bone. (SEE MICROFILM-page A13); Illustration of speciality bone parts and cost (A13)

LOAD-DATE: June 06, 2000

Senate Permanent Subcommittee
On Investigations
EXHIBIT #_____11b_____

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Chicago Tribune

May 22, 2000 Monday, CHICAGO SPORTS FINAL EDITION

SECTION: News; Pg. 10; ZONE: N

LENGTH: 678 words

HEADLINE: **CADAVERS FOR CASH IN TEXAS: 'PEOPLE MAKE A LOT OF MONEY SELLING TISSUE'**

BYLINE: By Stephen J. Hedges, Tribune staff writer.

DATELINE: SAN ANTONIO

BODY:
Sun-baked and just two hours from the Mexican border, San Antonio might seem like a strange place for bustling aftermarket in the afterlife. But the city is a hotbed of human body parts.

There have been scandals over imported body parts from Russia, the distribution of diseased tissue and the harvesting of human bones and tendons without permission. The city's first tissue bank was forced to close in 1998 after its employees turned it in to federal authorities for purported safety violations.

None of that has slowed the tissue trade. Four tissue banks and one tissue broker currently operate in the area. County supervisors even take bids from tissue banks on the right to bodies collected by the medical examiner. Last year, the winning contract went to South Texas Blood and Tissue Center, which agreed to pay $180,000 annually.

"This is a business," said Vincent DiMaio, the Bexar County medical examiner. "People make a lot of money selling tissue."

Since 1983, DiMaio has moonlighted as a tissue harvester, cutting bones and other parts from the bodies that passed through his office. Always, DiMaio insists, permission was given by the family of the deceased. The county, though, has spent more than $100,000 settling two claims that he did not have permission.

DiMaio has received up to $47,000 a year from tissue banks, according to county purchasing records. Several DiMaio assistants also received $50 from the tissue bank each time they obtained a family's consent to harvest tissue.

Much of that tissue ended up going to Bone Bank Allograft Inc., a for-profit tissue distribution company founded by Joe and D'Lynn Mims. The Mimses say they started their corporation to place tissue in the hospitals where it is most needed.

"We do this because there is a need, and we provide a service," D'Lynn Mims said.

Medical sales weren't new to Joe Mims. In 1991, he was indicted for theft by a Texas grand jury in Lubbock for actions while he ran a medical supply company. The case involved the payment of "kickbac for preferential treatment" to a local hospital purchasing agent, according to documents filed by federal prosecutors.

The state dropped its case after Mims pleaded guilty in federal court for failing to report $54,121 in income. By 1993, the Mimses' tissue company had run into its own troubles. It was one of four Texas tissue distributors that had sold bones from Russia. U.S. Food and Drug Administration inspectors had determined that some of that tissue was diseased.

The Mimses recalled all 344 pieces taken from 17 Russian cadavers. Investigators found, though, that 98 pieces had been transplanted.

In an interview, Joe Mims denied ever being indicted. Later, the Mimses declined to return calls to discus the Russian imports.

About this time, the Mimses founded Legacy of Life, a non-profit tissue bank in Corpus Christi. They als started buying tissue for $3,500 a cadaver from Southwest Tissue Services, contracts show.

Southwest needed the business. It was paying Bexar County $73,800 and DiMaio $47,000 for tissue-harvesting services, county records show.

But it was unclear just how dire things were at Southwest until Aug. 26, 1998, when two FDA inspectors visited. Two days later, the FDA ordered Southwest to recall tissue that was contaminated with hepatitis and, in one case, the AIDS virus.

The tissue bank's own lab tests showed the tissue was contaminated, according to donor records obtained by the Tribune and interviews with a former top Southwest staffer.

David Fitzhugh, Southwest's director, didn't return phone calls from the Tribune. Southwest Tissue close its doors in November 1998, but the city's other tissue businesses are thriving.

The Mimses' Bone Bank Allograft recently won accreditation by the American Association of Tissue Banks, an industry group that represents 69 of the estimated 300 tissue banks. Last year, Bexar County ended the practice of direct payments to DiMaio from tissue banks. But it gave DiMaio a $48,000 raise, bringing his annual salary to $198,240.

LOAD-DATE: May 22, 2000

Senate Permanent Subcommittee
On Investigations
EXHIBIT # 12

RICHARD J. DURBIN
ILLINOIS

COMMITTEE ON APPROPRIATIONS

COMMITTEE ON
GOVERNMENTAL AFFAIRS

COMMITTEE ON THE BUDGET

SELECT COMMITTEE ON ETHICS

ASSISTANT DEMOCRATIC
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701 NORTH COURT STREET
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Jan. 9, 2001

Dr. Jane Henney
Commissioner
Food and Drug Administration
Parklawn Building
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Henney:

My staff met recently with representatives from the Department of Health and Human Services, the Inspector General's Office, and your agency for a briefing on improvements in the regulation of tissue for transplantation, including the new FDA rules for tissue banks.

As a member of the Agriculture Appropriations Committee, I would like information from your agency regarding the cost to the agency of fully implementing the new FDA rules. It would be most helpful if the agency could break out the costs in the following manner:

Registration and listing rules:	Cost in year 1
	Cost when fully implemented
Donor suitability rules:	Cost in year 1
	Cost when fully implemented
Good tissue practice rules:	Cost in year 1
	Cost when fully implemented

The Inspector General's report on the oversight of tissue banking states that at least 36 tissue banks have never been inspected by the FDA and that the agency is generally underfunded to perform these inspections and is forced to "borrow resources from other programs, such as blood and plasma"to carry out even those inspections that the agency now performs.

When the agency does conduct inspections, it has at times found serious deficiencies in tissue banks' screening and testing practices. The American Association of Tissue Banks also has an accreditation process and some tissue banks that have sought accreditation have been denied because they have failed to meet AATB's basic standards. These facts suggest that FDA should set up a regular schedule for performing inspections on all tissue banks but may need additional resources to do so.

Given the importance of the agency's broad mission to protecting the public from harm, we should work to avoid undermining other areas of oversight, while addressing the vital need to ensure that the tissue system in the United States is as safe as possible. Therefore, I would like to

receive a cost estimate for annual inspections for non-accredited tissue banks and biannual inspections for accredited tissue banks. I would also like to receive your agencies input on whether less frequent inspections could be safely implemented for those tissue banks that are both accredited and subject to state inspections.

Thank you for your prompt attention in this matter. I look forward to your timely response.

Sincerely,

Richard J. Durbin
United States Senator

Senate Permanent Subcommittee
On Investigations
EXHIBIT # 13

Advancing Excellence

The College of American Pathologists

Hearing on the Federal Government's Oversight Of Human Tissue Banks

Statement Submitted for the Record

Investigations Subcommittee
Governmental Affairs Committee
United States Senate

May 24, 2001

College of American Pathologists
Division of Government and Professional Affairs
1350 I Street, NW Suite 590
Washington, DC 20005
(202) 354-7100
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This statement is submitted on behalf of the College of American Pathologists. The College commends the Subcommittee's interest in addressing the federal government's oversight of human tissue banks and is pleased to comment on the important and complex issues related to the procurement, distribution and confidentiality of organ donation and tissue use.

The College of American Pathologists (CAP) is a national medical specialty society representing more than 16,000 physicians who practice anatomic and/or clinical pathology. College members practice their specialty in clinical laboratories, academic medical centers, research laboratories, as well as tissue banks. Pathologists obtain and interpret data as the result of the examination of tissue, blood, and other body fluids for diagnosis and patient care. They also perform a number of key activities in the procurement and distribution of organs and tissue. The College recognizes that tissue and organ procurement is a critically important resource for medical treatment, research, education and training. CAP believes that the donation of tissue and organs should be accomplished without compromising the rights and welfare of human donors.

Among its core values, the College is committed to advancing patient health and wellness. Because of this core value, the College supports all relevant laws pertaining to the procurement and distribution of organs and tissues, dealing honestly and fairly with patients, donors, donor families, and colleagues. Recognizing that organ and tissue donation is performed as an extreme act of altruism, it is the College's current policy that:

> The College of the American Pathologists holds that the procurement for research, education, quality control, test development or transplantation of organs and tissues derived from autopsies and surgical specimens, should never be motivated by or associated with financial gain. Organ procurement for profit adversely affects the professional stature of the pathologist and is contrary to the revered traditions of medicine generally. The College supports and encourages the use of appropriate tissues and organs for education, research, quality control, test development or transplant with the proper informed consent of the donor or responsible survivor, or by statutory authority. The provision of token reimbursement covering costs of shipping organs from one site to another is not contrary to the intent of this statement.

The College is currently reviewing its position in regard to the adequacy of the informed consent process for donors and donor families. We are committed to working with Congress, as well as the public and private sectors on these important issues.

Senate Permanent Subcommittee
On Investigations
EXHIBIT # 14

SUBMITTED STATEMENT

REGARDING TISSUE BANKING

TO THE PERMANENT SUBCOMMITTEE

ON INVESTIGATIONS

OF THE

COMMITTEE ON GOVERNMENTAL AFFAIRS

BY THE

NORTH AMERICAN TRANSPLANT

COORDINATORS ORGANIZATION

N O R T H
A M E R I C A N
T R A N S P L A N T
C O O R D I N A T O R S
O R G A N I Z A T I O N

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The North American Transplant Coordinators Organization (NATCO) is the professional society representing nearly 2,000 organ procurement and clinical transplant coordinators, and the largest group of transplant professionals in the nation. We thank the Permanent Subcommittee on Investigations of the Committee on Governmental Affairs for its examination into the current practices of the tissue banking industry and need for oversight of the industry.

THE NEED FOR OVERSIGHT

Recent concerns regarding the misuse of tissue and distribution have highlighted the fact that further oversight of the industry is needed than that is currently in place. The tissue banking industry has expanded and become more complex and costly. An estimated 750,000 bone and soft tissue transplants are performed each year. Twenty thousand donors and their families donated tissues last year. Medical progress and technology have allowed for new ways in which to use tissue from a variety of human sources in ways that seemed impossible only a few years ago. Processed tissue may be marketed and sold similar to other medical products. Tissues may be used for cosmetic purposes. It may be difficult to determine how tissue may be used at the time of consent of the donation.

Both advocates and patients acknowledge the need for new regulations regarding oversight of tissue banking practices because current external oversight is limited. Oversight and best practice standards for tissue banking have not always kept pace with new advancements in tissue transplantation. This has created dilemmas and tensions for informed consent, patient/donor needs and facility oversight. NATCO does not want to see problems that may occur with tissue donation and regulation impact negatively on organ donation. The number of individuals awaiting organ transplantation has grown to more than 66,000 persons on waiting lists today but organ donation has not met the need. Nearly 5,000 patients die each year while waiting for organ transplantation. Tissue donation oversight controversies cannot negatively affect those deciding to donate organs and tissues.

Oversight of tissues must assure that there is a provision for a safe, adequate and affordable supply of tissue and cell products. Opportunities for donation with the minimization of wastage for donated tissues and cells must be increased. A review of practices by the Office of Inspector General found that current oversight of the system is haphazard and has issued two reports with recommendations.

NATCO agrees with the recent regulation that requires tissue banks to register. NATCO hopes that criteria can be set forward that will allow for a date of completion for initial inspection of all tissue banks; guidelines for cyclical re-inspection of banks; and guidelines for operational aspects as well as screening and testing practices of tissue banks. The financial aspect of tissue banking should not overshadow medical ethics and ultimately patient concerns.

OVERSIGHT OF TISSUE BANKING – CURRENT PRACTICES AND NATCO RECOMMENDATIONS

Identification of Tissue Banks

The number and location of all tissue banks in the United States are unknown. This hampers progress in identifying tissue banks that may not be meeting standards or even seeking accreditation. Earlier this year, the FDA published a rule that would require the registration and listing of all tissue banks. NATCO believes this will assist in the initial steps to increase the quality of service provided by tissue banks to either eliminate those with unsatisfactory practices or to assure standards are met with cyclical reviews.

Inspection and Review of Tissue Bank Practices

Current oversight of tissue banks lacks comprehensive requirements to assure inspection by the FDA. NATCO endorses regulatory oversight that will result in appropriate supervision of the industry. The American Association of Tissue Banks conducts a voluntary accreditation program. Seeking this accreditation is purely voluntary. This accreditation process addresses donor screening and testing. It also reviews operational

and organizational aspects such as qualification of personnel, safety practices, quality assurance and equipment testing. Some banks have not met basic standards of the American Association of Tissue Banks and have been denied accreditation.

Inspection by the FDA of all tissue banks in the United States must be done. NATCO recommends that a date be set for the completion of initial inspections of all tissue banks. In addition, guidelines for cyclical reviews for tissue banks should be established. It has been reported that due to limited resources to carry out inspections in the past, money has been borrowed from other sources to carry out these inspections. Adequate resources should be allotted for initial inspections of tissue banks and follow-up inspections. Some tissue banks that have been inspected by the FDA already have been deficient in their screening and testing practices. NATCO recommends that guidelines be established to assure that the handling and use of human tissue meets quality standards for both the facility and services provided to the public.

INFORMED CONSENT

The National Organ Transplant Act (NOTA) and the States' Anatomical Gift Acts do not address what information tissue banks must provide in obtaining consent. NOTA requires organ procurement organizations (OPO's) to meet certain organizational and staffing requirements and to assist hospitals in establishing and implementing protocols for inquiries about organ donation by potential donors. These safeguards do not exist for tissue banks. Currently, tissue banks, their staffs and contractors who interact with donor families shoulder the responsibility for ensuring informed consent.

NATCO has officially endorsed the Bill of Rights for Families developed through the National Donor Family Council. This Bill of Rights includes the right to timely information regarding donation of tissue, including the conditions and processes of organ and/tissue donation. NATCO agrees with the recent OIG recommendations that endorses tissue banks give written materials to donating families at the time of the request or in the days immediately following a tissue request. Professionals must facilitate families'

questions and provide information at the time of request, donation or if questions arise later.

NATCO believes that full disclosure of the following must be included to provide full informed consent:

- Explanation of the tissue donation process including medical history, lab testing, communicable disease testing, medical suitability, and how tissue is recovered, processed stored and distributed.

- Donor families should be told what tissues can or will be recovered based on the suitability of the donor in order for tissue donation, and that the gift may take a different form than originally recovered

- Review of a completed consent form with the donor family before consent. A copy should be offered to the family. Other pertinent written material related to tissue donation should be offered to the family.

- Options to limit or restrict the use of the gift of tissue

- How the tissue will be stored, duration of storage and possibility that tissue may not be utilized

- A list and description of other companies and entities with which the bank has relationships for processing and distributing tissue. NATCO strongly disagrees that a company's concern for financial benefit should overshadow medical needs and principles. NATCO has also expressed concern in the past regarding possible financial irregularities in the tissue banking industry. Disclosure should respond to the sources of funding for tissue banks and other entities with which the bank has financial agreements

- NATCO urges that tissue not be referred to as a product. Rather, the gift and its packing should have an acknowledgement that it contains the gift of donated tissue.

- NATCO also agrees with the OIG recommendation that it would be beneficial for the Health Resources Services Administration (HRSA) to act as a resource to tissue banks to identify guidelines for consent requests, what written information is given by tissue banks to family and recommendations for staff training.

CONCLUSION

The membership of NATCO wants regulation and oversight of the tissue banking industry to move forward to assure quality standards in the handling of human tissue. NATCO also wants donor concerns regarding donation to be met completely. NATCO believes that the initial steps of recent FDA regulations and the OIG recommendations are laying the groundwork for this progress. NATCO looks forward to working with the members of this Committee, the FDA and other agencies to continue this progress.

Senate Permanent Subcommittee
On Investigations
EXHIBIT #___15___

STATEMENT OF
THE SOUTHEAST TISSUE ALLIANCE
SUBMITTED IN RESPONSE TO TESTIMONY BY
VALERIE J. RAO BEFORE
THE PERMANENT SUBCOMMITTEE ON INVESTIGATIONS
COMMITTEE ON GOVERNMENTAL AFFAIRS
UNITED STATES SENATE ON MAY 24,2001

The Honorable Carl Levin
Chairman
Senate Subcommittee on Investigations

My name is Lawrence Hopkins, I am the President and Chief Executive Officer of the Southeast Tissue Alliance, Inc., formerly the University of Florida Tissue Bank, Inc. (the "Tissue Bank") I am submitting this sworn statement in response to statements made by Dr. Valerie J. Rao before the Senate Subcommittee on Investigations on May 24,2001.

The purpose of this statement is to correct certain statements made by Dr. Rao to this Committee, which I believe are incorrect, and in many cases misleading regarding the tissue donor activities, which are conducted by the University of Florida Tissue Bank.

Dr. Rao states (Lines 59-62):

> Last April, I became concerned regarding several questionable practices by a tissue bank. My first concern was when Regeneration Technologies, Inc., through its association with the University of Florida Tissue Bank, would accept donors with non-metastasizing malignant tumors of the breast, colon, cervix, and lung.

This statement is false and misleading. The Tissue Bank does not engage in any practices that could be considered questionable by any regulatory agency, which oversees its activities. The Tissue Bank has never been cited by any regulatory agency as having been engaged in questionable practices and has always been held to be in compliance with published standards and regulations by The Food and Drug Administration, the State of Florida, the State of New York and the American Association of Tissue Banks. The American Association of Tissue Banks also accredits the Tissue Bank. The Tissue Bank has been inspected by all the above names organizations.

The Tissue Bank's Standard Operating Procedure 20-001 states that donors with non-metastasizing cancers are to be accepted only at the discretion of the Medical Director. The Tissue Bank's standard and practice adheres to and is consistent with the American Association of Tissue Bank's Standard D4.340 regarding acceptance of such tissue. The Tissue Bank's medical director is a highly respected and qualified pathologist and former professor of Pathology at the University of Florida School of Medicine. He is thoroughly qualified to make medical suitability determinations to ensure the safety of donor tissue.

Dr. Rao's opinion of the Tissue Bank practices is not based on any personal knowledge of fact. To my knowledge, she has not reviewed the published procedures of the Tissue Bank. I have formally extended an invitation to Dr. Rao to meet with the Tissue Bank to discuss our procedures but she declined to do so

> Dr. Rao states (lines 62-63): "They [UFTB/RTI] also accepted donors with septicemia, pneumonia, and intestinal obstruction."

This is a false statement. The Tissue Bank does not recover tissue from donors with confirmed septicemia, pneumonia. Questionable cases are reviewed by the Medical Director of the processing tissue bank who will determine if tissue is safe for transplantation based on laboratory testing and review of other pertinent donor medical information.

> Dr. Rao (lines 68-69) states: "... the use of sterile precautions are not observed during the excision and retrieval processes."

This statement is false. The Tissue Bank follows AATB standards with regard to the recovery of tissue, that includes aseptic (correct technical term for sterile precautions) retrieval of tissue as outlined in section D5.000 Retrieval Policies and Procedures, AATB Standards for Tissue Banking, 2001, and SETA's published Standard Operating Procedures.

> Dr. Rao (line 71) refers to the Tissue Bank recovery technicians and states: "The technicians do not have sufficient training and knowledge to observe changes which would be noted by a pathologist, yet they performed an autopsy-removal of the brain, which would obviously impair further medical legal investigation of the body of the deceased."

This statement is misleading and misrepresents a specific case to which she refers. The recovery technicians, in accordance with published procedures, removed brain tissue (biopsy) in the donor she questioned. This biopsy was obtained so that the medical director (pathologist) could conduct a safety test for Creutzfeld-Jackobs Disease (CJD). At the time of the recovery, the donor was not determined to be a medical examiner case. In a rare occurrence, the donor later became a medical examiner (autopsy) case because of a family request.

Respectfully submitted,

Lawrence A. Hopkins
President and CEO

Lawrence A. Hopkins, personally known, appeared before me this 14th day of June, 2001.

Kathy P. Birthisel
Notary Public
My Commission Expires April 4, 2005

KATHY P. BIRTHISEL
MY COMMISSION # DD 015575
EXPIRES: April 4, 2005
1-800-3-NOTARY FL Notary Service & Bonding, Inc.

Senate Permanent Subcommittee
On Investigations
EXHIBIT # 16

Regeneration
Technologies, Inc.
One Innovation Drive
Alachua, Florida 32615 USA
Phone: 904.418.8888
Fax: 904.418.0342

June 8, 2001

Honorable Susan Collins
Chair, Permanent Subcommittee on Investigations
Governmental Affairs Committee
United States Senate
Washington, D.C.

Dear Senator Collins:

Regeneration Technologies wishes to submit the enclosed statement in connection with the Subcommittee's May 24, 2001 hearing titled "Tissue Banks: Is the Federal Government's Oversight Adequate?"

Regeneration Technologies also wishes to thank the Subcommittee staff of the majority, including Claire Barnard, Barbara Cohoon, Eileen Fisher and Dr. Christopher Ford for the time they spent with and the courtesy they extended to RTI in connection with the above hearing.

Sincerely,

James M. Grooms
President/CEO

Enclosures:

Affidavit and accompanying statement titled "STATEMENT BY REGENERATION TECHNOLOGIES, INC., BEFORE THE PERMANENT SUBCOMMITTEE ON INVESTIGATIONS, COMMITTEE ON GOVERNMENTAL AFFAIRS, UNITED STATES SENATE, May 24, 2001, Hearing Titled "Tissue Banks: Is The Federal Government's Oversight Adequate?"

AFFIDAVIT

I, Gerard H. Bencen, being duly sworn, do hereby state as follows:

(1) I am General Counsel to Regeneration Technologies, Inc.

(2) Regeneration Technologies, Inc., is a corporation that processes and distributes human tissue for use in tissue transplantation.

(3) Regeneration Technologies, Inc. is headquartered in Alachua, Florida.

(4) The attached document titled "STATEMENT BY REGENERATION TECHNOLOGIES, INC., BEFORE THE PERMANENT SUBCOMMITTEE ON INVESTIGATIONS, COMMITTEE ON GOVERNMENTAL AFFAIRS, UNITED STATES SENATE, May 24, 2001, Hearing Titled 'Tissue Banks: Is The Federal Government's Oversight Adequate?'" is intended for submission to the Permanent Subcommittee on Investigations, Committee on Governmental Affairs, United States Senate, and is true and accurate to the best of my knowledge.

Gerard H. Bencen

Gerard H. Bencen, Esq
General Counsel to Regeneration Technologies, Inc.

IN THE CITY OF ALACHUA

STATE OF FLORIDA

Gerard H. Bencen, identified to me, did personally appear before me, a Notary Public for State of Florida, on this 8 day of June, 2001, and upon his oath stated that the facts set forth in the above affidavit, including the above-titled document, are true to the best of his knowledge and belief.

Anna Marie Martin

Notary Public

NOTARY PUBLIC STATE OF FLORIDA
ANNA MARIE MARTIN
MY COMMISSION # CC 862390
EXPIRES: Aug 11, 2003
1-800-3-NOTARY Fla. Notary Service & Bonding Co.

My commission expires: _____

STATEMENT BY

REGENERATION TECHNOLOGIES, INC.

BEFORE THE

PERMANENT SUBCOMMITTEE ON INVESTIGATIONS

COMMITTEE ON GOVERNMENTAL AFFAIRS

UNITED STATES SENATE

May 24, 2001

Hearing Titled "Tissue Banks: Is The Federal Government's Oversight Adequate?"

Testimony of Valerie J. Rao, M.D., Chief Medical Examiner, District Five, Leêsburg, Florida

Regeneration Technologies wishes to respond to several false and/or misleading statements Dr. Rao makes in her testimony before the Subcommittee at the May 24, 2001 hearing titled "Tissue Banks: Is the Federal Government's Oversight Adequate?" Regeneration Technologies, Inc. (RTI) is a leader in the use of natural tissues and innovative technologies to repair and promote the natural healing of human bone and other human tissues. RTI is the nation's largest processor and distributor of precision-tooled allografts (human-donor tissues processed or shaped to precise specifications for use with standard surgical instruments). RTI-processed allografts are used in a wide variety of procedures to improve patients' lives, including spinal vertebrae repair, musculoskeletal reconstruction, fracture and periodontal repair, heart valve disorder and others. In 2000, RTI distributed 159,000 allografts for over 107,000 surgical procedures. RTI was founded in 1998, is based in Alachua, Florida, and distributes its allografts in all 50 states.

In the first full paragraph on page 2 of her testimony Dr. Rao states: "Autopsies are the only means by which diseases such as tuberculosis, histoplasmosis, degenerative diseases of the brain, unsuspected malignancies, viral myocarditis, non-A, B, C Hepatitis, diseases of unknown etiologies, and other potential transmissible diseases can be detected and those donors excluded from the donor pool."

This statement is incorrect. In fact the diseases Dr. Rao lists are most often detected in a clinical setting, at which time their presence becomes part of one's medical record. At RTI those records are thoroughly reviewed as part of the donor screening process. In addition, RTI directly tests all tissue submitted for donation, at which time any latent evidence of the presence of those diseases would be revealed. If RTI determines that a disease that Dr. Rao listed exists, RTI rejects the tissue in accordance with RTI's *Universal Donor Acceptance Criteria.*

In the third full paragraph on page 2 of her testimony Dr. Rao states: "Last April, I became concerned regarding several questionable practices by a tissue bank. My first concern, was when Regeneration Technologies, Inc., through its association with the University of Florida Tissue Bank, would accept donors with non-metastasizing malignant tumors of the breast, colon, cervix, and lung."

This statement is misleading if intended to imply that RTI's policies with respect to malignancies depart from current practice in the tissue industry. In fact, RTI follows the Standards of the American Association of Tissue Banks with respect to this criterion. Specifically, standard D4.340 *Malignancies* requires that "Donors with a history of malignancy shall be evaluated by the Medical Director or licensed physician designee for suitability in accordance with the tissue bank's SOPM. The evaluation shall include: the type of malignancy, clinical course, and treatment prior to acceptance of a donor. The evaluation and reasons for acceptance shall be documented in the donor's record."

RTI Standard Operating Procedure PZ0003 clearly indicates that donors with non-metastasizing cancers are to be accepted only at the discretion of the Medical Director.

If Dr. Rao's statement is intended to imply that the practice described places allograft recipients at risk or is somehow otherwise improper, it is contrary to current medical opinion, upon which AATB Standards and RTI SOPs are based.

In the third full paragraph on page 2 of her testimony Dr. Rao goes on to state: "They [RTI] also accepted donors with septicemia, pneumonia, and intestinal obstruction." This statement is false. RTI does not accept tissue for transplantation from donors with septicemia, clinically relevant pneumonia, or intestinal obstruction. Tissue recovery does not constitute tissue acceptance. Tissue is first held in quarantine at RTI until all necessary information and supporting documentation are available for RTI's Medical Director to determine whether to accept or reject a donor's tissue.

In the third full paragraph on page 2 of her testimony Dr. Rao goes on to state: "...they [RTI] do not perform routine blood or bone marrow aspiration cultures, which is done to detect for possible diseases." This statement is misleading because it implies that RTI does not test for diseases detectable by culturing methods. RTI performs cultures of the tissue *directly*, rather than the *surrogate* culturing method Dr. Rao seems to recommend. RTI has determined that *direct* culturing is the most sensitive technique for detecting bacterial and fungal contamination. Directly culturing the tissue, because of its greater accuracy, is standard industry practice. Furthermore, if blood cultures are available from the hospital, RTI uses them to evaluate a donor's suitability. If a culture indicates septicemia, RTI rejects the tissue.

In the third full paragraph on page 2 of her testimony Dr. Rao goes on to state: "They [RTI] do not require an autopsy, and hence do not know the cause of death in the donor." This statement is false and misleading. It is misleading if intended to imply that RTI does not use autopsy results to evaluate the suitability of a donor. RTI requires Medical Director review of every autopsy report performed on a potential donor. The statement is false if intended to imply that RTI does not know the cause of the donor's death. In fact RTI requires that the cause of death be known in each case prior to acceptance of tissue for transplantation. If the cause of death of a donor cannot be determined, RTI rejects the tissue.

In the third full paragraph on page 2 of her testimony Dr. Rao goes on to state: "... the use of sterile precautions are not observed during the excision and retrieval processes." This statement is false. RTI requires that tissue be recovered using "aseptic technique" (the proper terminology for "sterile precautions"). Moreover, UFTB is an AATB accredited tissue bank and as such follows AATB guidelines on aseptic retrieval of tissue as outlined in section D5.000 *Retrieval Policies and Procedures*, AATB Standards for Tissue Banking, 2001.

Regeneration Technologies, Inc.

Instead of being singled out for criticism based upon isolated, anecdotal allegations, RTI should be credited with advancing a technology that reduces disease transmission, improves ease of use of donated tissues during surgery, and expands the beneficial use of donated tissue.

RTI has worked closely and successfully with many of the nation's donor agencies to increase tissue donations. Based on industry reports, RTI's network of agencies recovers approximately one third of all tissue donated in the United States. In 1999, an estimated 3.6 million deaths could have yielded tissue that is eligible for donation, although less than 0.04 percent resulted in donated tissue. Yet, in areas of the country where RTI's network of affiliated agencies are active, tissue recovery rates have increased as much as tenfold.

Organ donations have increased significantly in those areas as well. In 1999, RTI's affiliated tissue recovery agencies had the highest per-population organ donation rate in the nation – 23 percent higher than the second-highest rate. During the period 1998-1999, RTI's affiliated agencies increased organ donations by 53 donors, while the total U.S. donation rate grew by only 44 donors. There are several reasons why directed efforts to increase tissue donations also increase organ donations. First, while hospitals must by law maintain an organ donation program, some two thirds of deaths occur outside of hospitals. Thus efforts to increase organ donations that center on hospitals reach a comparatively small audience of potential tissue donors. Second, nearly 50 percent of deaths yield tissue eligible for tissue donation, while only a select few persons are eligible to donate organs. Moreover, there are far more tissue recovery agencies than organ recovery agencies. Thus efforts to increase tissue donations in communities reach a much wider audience than efforts to increase organ donations – an audience that includes potential organ donors.

Surgeons have used allograft tissue for decades as a biological solution for their patients' injuries and illnesses. However, the number of allograft implantations remained small until companies like Regeneration Technologies took the delivery of allograft a step further by offering implants that are shaped or processed to exacting specifications, which enables physicians to implant allografts to enhance the lives of hundreds of thousands of patients nationwide.

In 1996, RTI's research and development team (then the University of Florida Tissue Bank) developed precision-tooled allografts (producing one that year). Today, RTI makes 30 precision-tooled allografts and more than 100 conventional allografts in six market segments: spinal, sports medicine, oral/maxillofacial, general orthopedic, urological and cardiovascular.

RTI's precision-tooling innovations not only reduce the time surgeons use to spend shaping an allograft and, correspondingly, the time the patient is anesthetized, but also eliminate the second site surgery required when the patient's own tissue (autograft) is recovered and used in surgery. Many of RTI's precision-tooled allografts correspond to the ways surgeons have cut, shaped, and used allograft tissue for decades. Not only do RTI's tooled allografts provide a ready-made solution for surgeons, they also offer a sterile solution. By processing allografts under aseptic, clean-room conditions and in accordance with both FDA donor screening and testing requirements and individual state requirements, RTI strives to make surgery faster, safer and more efficient for the surgeon and patient.

Of utmost importance is honoring the donor's gift of tissue by using it to maximum effectiveness for improving patients' lives. RTI strives to meet this goal. Its research and development staff work hand-in-hand with surgeons across the country to develop new uses of allograft in an effort to honor the gift by maximizing the number of patients who are helped by each donation. Through its combination of precision-tooled, bone paste and other processed allografts, RTI processes are state-of- the-art in their ability to optimize the use of donated tissue.

FDA Regulation of The Tissue Industry

RTI supports appropriate FDA efforts to regulate the tissue industry. RTI filed comments on FDA's 1998 proposed regulation titled "Establishment Registration and Listing for Manufacturers of Human Cellular and Tissue-Based Products" (63 Fed. Reg. 26744, May 14, 1998) and on FDA's recently proposed regulation titled "Current Good Tissue Practice for Manufacturers of Human Cellular and Tissue-Based Products; Inspection and Enforcement; Proposed Rule" (66 Fed. Reg. 1508, January 8, 2001).

The Benefits of Allograft Tissue

For years, scientists have searched for a biological solution for tissue and bone injuries. RTI believes the solution was here all the time – the use of allograft. Allograft tissue is more compatible than metal or synthetic implants and can be remodeled by the patient's own bone over time. As noted, allograft also eliminates the second surgical site and the additional pain involved with it. Surgeons therefore often prefer allografts to tissue from the patient's own body (called autograft). Use of allograft also eliminates the chance of second-site infection and possibly prevents longer hospital stays. Allograft tissue can be particularly beneficial for elderly patients, who may suffer from osteoporosis and therefore do not have enough tissue for an autograft.

In addition, allograft tissue eliminates the need to replace a synthetic graft as the surrounding bone and tissue grow. Allograft tissue is therefore especially beneficial for young patients. Allografts can also remain in the body for life and, unlike blood, need not be "typed" and are not rejected by the body.

Informed Consent

Tissue banking is built upon the altruism of the donor and the donor's family. RTI believes that tissue processors, which rely on tissue banks for donated tissue, have a responsibility to honor that gift by using it to benefit as many patients as possible consistent with supplying tissue that is safe. RTI also believes communities take proper steps to ensure that donor families give informed consent prior to the donation.

The most important consideration in informed consent is the impact on donor families. The consent process is owned by each "community," whose participants may include the tissue bank, the organ procurement organization (OPO) and the eye bank, or a combination of the three. Informed consent forms should be standardized across the nation and any additional government regulation devoted to informed consent should be based on the donor families' and communities' needs.

Regeneration Technologies has developed informed consent standards for its affiliated donor recovery agencies that respect the donors, their families and community standards. RTI audits those agencies for compliance with those informed consent standards. Under those standards, for example, each donor family is given the opportunity to ask for more information throughout the interview process and is given a contact should it want additional information at a later date.

Regeneration Technologies' BioCleanse™ System

One innovation that helps make tissue safer is RTI's BioCleanse™ system. In 1997, RTI committed to develop this new standard of tissue safety and quality because traditional aseptic methods of cleansing tissue could not eliminate the risk of disease transmission, including HIV, Hepatitis B and C and microbial diseases such as syphilis.

The BioCleanse™ system is a patent-pending, pharmaceutical grade, computer-controlled, validated, multi-step tissue sterilization procedure that eliminates the known risks of those diseases. The BioCleanse™ system also eliminates from the tissue blood, fat and cellular debris where those diseases can reside, while retaining the beneficial properties of the tissue.

The risks of transmission of HIV and Hepatitis B and C in allograft tissue are very real. Of the 45 allograft tissue recalls FDA listed on its Web site for the year 2000, encompassing over 1,700 grafts that required removal from the market, nearly one third were for risk of transmission of HIV or Hepatitis B or C. An additional two were for tissue from donors who had been incarcerated (a risk factor for HIV and Hepatitis), and eight were for tissue from donors who had not been properly evaluated (i.e., whose HIV/Hepatitis status may not have been known).

The BioCleanse™ system thus brings advanced technologies to the tissue industry to increase the quality and safety of allograft tissue by using processing techniques that can better supply allograft tissue for the estimated 500,000 allograft transplantations performed annually.

It's important to note that BioCleanse™ is a safety step that follows screening and testing. Tissue recovery agencies screen donors for risk of HIV, Hepatitis B and C and other diseases, in accordance with FDA requirements and current industry practice. Tissue recovery agencies also perform a risk assessment on every potential donor that involves interviewing family members and evaluating the donor's medical records. All collected tissue is then serologically tested for the presence of any viral or bacterial disease before the donation is medically released and processed at RTI using the BioCleanse™ system.

RTI began distributing tissue with the BioCleanse™ system in March 2000. BioCleanse™ has an outstanding safety record with over 70,000 implants without a reported case of disease transmission or adverse reaction. An additional measure of safety is important because of the real risks of transmission of HIV, Hepatitis B and C and other diseases in tissue processed using only donor screening and testing.

For-Profit and Non-Profit Tissue Processing Entities

During the hearing, concerns were also raised about "excess profits." RTI is a for-profit company, which allows it to raise capital for innovation. The infusion of capital from the sale of stock or equity provides a for-profit tissue processor like RTI with significant financial resources to support the development of state-of-the-art facilities and research and development. Research and development brings innovations that can increase the safety and maximize the uses for donated tissue. U.S. law permits reasonable fees to be charged for services associated with the recovery, processing and storing of tissue and for the development of tissue processing technologies.

Nearly all U.S. donor tissue recovery agencies are non-profit entities. Tissue processors reimburse those agencies for tissue recovery costs. Those costs typically include promoting tissue recovery in communities to increase donations, educating hospital and other institutional staff on tissue donation and implantation, and direct costs such as technician salaries and training, equipment and transportation.

Tissue processors include both for-profit and non-profit organizations. Like for-profit and non-profit hospitals, for-profit and non-profit tissue processors operate under the same basic business model. That is, they obtain tissue from donor recovery agencies, process it and distribute it, and pay salaries and other costs associated with those activities. For-profit tissue processors file corporate tax returns and pay corporate taxes. Non-profit tissue processors, like other non-profit organizations, file IRS Form 990s.

For-profit and non-profit tissue processors might even have cross-contractual, joint venture or other business relationships with each other. For example, a for-profit organization might process tissue under contract for marketing under the name of a non-profit organization, perhaps using the sales force of a for-profit organization. For-profit and non-profit tissue processors can partner with the same organ procurement network.

Tissue processors distribute their products to hospitals, which, of course, may be for-profit or non-profit. The industry's trade group, American Association of Tissue Banks (AATB), includes both for-profit and non-profit organizations as members. All tissue processors are subject to the same FDA standards.

As noted, tissue processors, whether for-profit or non-profit, charge fees for their services relating to the costs of obtaining, processing and distributing tissue to hospitals. Costs include those of tissue recovery and cleansing, packaging and storage, processing (including precision-tooling), and research and development. For-profit and non-profit tissue processors' fees are competitive since they distribute their products to the same entities – hospitals (whether for-profit or non-profit).

As noted earlier, one of the advantages of the for-profit business model is capital infusion. Capital infusion from the sale of stock or equity provides a for-profit processor with financial resources to support the development of state-of-the-art processing facilities and research and development. Those innovations can increase the safety and maximize the use of donated tissue.

Conclusion

Regeneration Technologies, Inc. supports appropriate and science-based regulation of the tissue industry to make human tissue safer. RTI is proud of its record in processing safe precision-tooled allograft tissue through its BioCleanse™ system, which eliminates known and very real risks in human tissue by inactivating HIV, Hepatitis B and C and other diseases as well as eliminating blood, fat and debris from tissue that can carry those diseases. RTI has been pleased to work with the FDA throughout RTI's development and validation of the BioCleanse™ system and looks forward to working with FDA in the future to improve the safety of human tissue.

Senate Permanent Subcommittee
On Investigations
EXHIBIT # 17

Regeneration Technologies, Inc.
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June 4, 2001

BY FEDERAL EXPRESS

Valerie J. Rao, M.D.
Lake County Medical Examiner
Lake County Florida
809 Pine Street
Leesburg FL 34748

Dear Dr. Rao:

We are writing in response to statements you made before the United States Senate Permanent Subcommittee on Investigations on May 24, 2001. Many of the statements you made were false. Other statements you made were misleading with respect to how you characterized the manner in which Regeneration Technologies, Inc. (RTI) conducts conor screening and cadaveric tissue recovery. Attached is a discussion of these spurious statements. We insist that you revise your testimony submitted to the US Senate Governmental Affairs' Permanent Subcommittee on Investigations, and that you issue a public retraction of the false and misleading statements. In addition, we re-extend our previous invitation for you to visit RTI to obtain first hand understanding of our tissue practice.

RTI is a leader in tissue-based innovations that are used to repair and promote the natural healing of human bone and other human tissues. Our allografts are improving surgical outcomes in clinical settings throughout the United States. Tissues processed by RTI are used to repair and promote the healing of a wide variety of bone and other tissue defects, including spinal vertebrae repair, musculoskeletal reconstruction, fracture repair, periodontal repair, urinary bladder reconstruction and heart valve replacement.

Most importantly, in respect to your testimony, all tissues processed at RTI are medically released only after having met rigorous screening and testing guidelines that are more stringent than those promulgated by the State of Florida. Subsequent to the medical release of the tissue, RTI employs state-of-the art technology to process those tissues.

Your statements are puzzling, particularly because RTI has never dealt directly with you. You have never contacted us about your concerns or made any attempt to learn about our operations, despite our previous public invitation to you. The false and misleading statements you included in your Senate testimony, set forth below, demonstrate clearly that you have limited knowledge of RTI and its procedures.

Your derogatory statements regarding RTI have no basis in fact, and we demand that you retract them immediately and revise your testimony submitted to the US Senate Governmental Affairs' Permanent Subcommittee on Investigations. Should you wish to take the opportunity to learn about RTI and our procedures, we continue to extend our previous invitation for you to visit. If you wish to obtain any additional information on our tissue practices, please do not hesitate to contact us.

C. Randal Mills PhD
Director of Scientific Affairs
Regeneration Technologies, Inc.

Herman Baer, MD
Executive Medical Director
Regeneration Technologies, Inc.

Patrick Bianchi, MD
Medical Director
Regeneration Technologies, Inc.

Mack Tyner, MD
Medical Director
Regeneration Technologies, Inc.\

Jack McCarthy M.D.
Scientific Review Board
Regeneration Technologies, Inc.

Barry L. Eppley, MD, DMD
Scientific Review Board
Regeneration Technologies, Inc.

Harold K. Tu, MD DMD
Scientific Review Board
Regeneration Technologies, Inc.

N. Ray Lee, DDS
Scientific Review Board
Regeneration Technologies, Inc.

CM/mr

Cc: Governor Jeb Bush
Senator Rod Smith
John Anderson, Enterprise Florida
Representative Perry C. McGriff, Jr.
Representative Edward L. Jennings, Jr.
Senator Bob Graham
Senator Connie Mack
Congressmen, Karen Thurman
Permanent Subcommittee on Investigations
Michelle Oxman, Esq., AHCA
Lake County Commissioner Welton G. Cadwell
Dr. Stephen Nelson, Chairman of the Medical Examiner's Commission

Attachment

In line 47 of the testimony, you state that "[a]utopsies are the only means by which diseases such as tuberculosis, histoplasmosis, degenerative diseases of the brain, unsuspected malignancies, viral myocarditis, non-A, B, C Hepatitis, diseases of unknown etiologies, and other potential transmissible diseases can be detected and those donors excluded from the donor pool." This is incorrect. It is a basic medical fact that the specific diseases listed are most often detected in a clinical setting, at which time their presence becomes part of one's medical record. These records are available on all of our donors and are thoroughly scrutinized as part of the donor screening process at RTI before sign off by our medical directors, all of whom are medical doctors. Upon determination that a disease state exists, the donor is rejected according to RTI's *Universal Donor Acceptance Criteria*. Furthermore, as concerns your reference to degenerative diseases of the brain, not only do we exclude donors with transmissible neurological ailments, but RTI does not use any portion of the brain or tissues from the central nervous system in the allografts it releases for transplantation. To state, as you did, that autopsy is the only means by which the above-listed diseases and other transmissible diseases can be detected and excluded from the donor pool is simply incorrect.

Lines 59-62 of your testimony contain the statement, "Last April, I became concerned regarding several questionable practices by a tissue bank. My first concern was when Regeneration Technologies, Inc., through its association with the University of Florida Tissue Bank, would accept donors with non-metastasizing malignant tumors of the breast, colon, cervix, and lung." You misled the Senate when you implied that the policies of the University of Florida Tissue Bank (UFTB) and RTI are questionable and contrary to common tissue bank practice with respect to malignancies. In fact, the policies UFTB and RTI follow with regard to malignancies follow the Standards of the American Association of Tissue Banks (AATB). Specifically, AATB standard D4.340, titled *Malignancies*, requires that "Donors with a history of malignancy shall be evaluated by the medical director or licensed physician designee for suitability in accordance with the tissue bank's SOPM. The evaluation shall include: the type of malignancy, clinical course, and treatment prior to acceptance of a donor. The evaluation and reasons for acceptance shall be documented in the donor's record." RTI's Standard Operating Procedure PZ0003 clearly indicates that donors with non-metastasizing cancers are to be accepted only after this evaluation has been conducted by the medical director. The implication that this practice is improper or puts allograft recipients at risk is misleading, and contrary to current medical opinion, upon which AATB Standards and RTI's Standard Operating Procedures are based.

Lines 62-63 of your testimony state, "They [RTI] also accepted donors with septicemia, pneumonia, and intestinal obstruction." This statement is false. RTI accepts no tissue for transplantation from donors with septicemia, or clinically relevant pneumonia or intestinal obstruction. The recovery of tissue does not constitute medical acceptance of a tissue donor. After recovery, the tissue is held in quarantine at RTI until all necessary information and supporting documentation is available for RTI's medical directors to form a decision to accept or reject a donor. In

Attachment

your testimony, you misled the Senate by implying that accepting a donor for tissue recovery always results in releasing the donor's tissue for transplantation. Again, no tissue is accepted by RTI for transplantation from donors with septicemia, clinically relevant pneumonia or intestinal obstruction.

Lines 64-65 state, "...they [RTI] do not perform routine blood or bone marrow aspiration cultures, which is done to detect for possible diseases." This statement is misleading because it implies that RTI does not test for diseases detectable by culturing methods. RTI performs cultures of the tissue *directly*, rather than the *surrogate* culturing method you seem to recommend. RTI has determined that *direct* culturing is the most sensitive technique for detecting bacterial and fungal contamination. Additionally, directly culturing the tissue, because of its greater accuracy, is the standard of practice in the industry. Furthermore, if there are blood cultures available from the hospital, these are indeed used to evaluate the donor's suitability. If there are positive results indicative of disease, the donor is excluded.

Lines 65-66 state, "They [RTI] do not require an autopsy, and hence do not know the cause of death in the donor." This statement is both false and misleading. It is misleading in that it implies that RTI does not use autopsy results in evaluating the suitability of a donor and that autopsies are required in every circumstance. Rule 59A-1.005(37), Florida Administrative Code, indicates that a tissue bank's medical director or designees may exercise a waiver of an autopsy. RTI requires a review by a medical director, each of whom is a licensed MD, of every medical record on every donor, and a review of every report of an autopsy performed on potential donors. Your statement is also false in that it states that the donor's cause of death is not known. RTI in fact requires that the cause of death in each case must be known, and reviewed by a medical director, prior to being accepted for transplantation. Donors whose cause of death cannot be determined are rejected.

Lines 68-69 contain the statement, "... the use of sterile precautions are not observed during the excision and retrieval processes." This statement is false. RTI requires that tissues always be recovered using "aseptic technique" (the proper medical terminology for "sterile precautions"). Furthermore, UFTB is an AATB accredited tissue bank, and as such follows the guidelines on aseptic retrieval of tissue as outlined in section D5.000 *Retrieval Policies and Procedures*, AATB *Standards for Tissue Banking*, 2001.

Senate Permanent Subcommittee
On Investigations
EXHIBIT #18

VALERIE J. RAO, M.D.
DISTRICT FIVE MEDICAL EXAMINER'S OFFICE
809 PINE STREET
LEESBURG, FLORIDA 34748
(352) 326-5961
FAX: (352) 365-6438

June 7, 2001

C. Randal Mills, Ph.D.
Director of Scientific Affairs
Regeneration Technologies, Inc.
One Innovation Drive
Alachua, Florida 32615

RE: Testimony, United States Senate Permanent Subcommittee

Dear Dr. Mills:

I received your letter, dated June 4, concerning my testimony before the United States Permanent Subcommittee on Investigations. Let me thank you for your letter. In this letter, you are questioning the accuracy of some statements I made in my testimony. To the best of my knowledge and professional judgement, all of the statements you refer to are accurate and there is no need for their alteration or retraction.

Specifically, you state that an autopsy is not a definitive diagnostic procedure by which many clinically unrecognized and potentially transmissible diseases can be detected. This is contrary to the reports published and my experience of more than 20 years, actually, eviscerating and dissecting the deceased myself. I can cite cases in which a diagnosis of malignancy was completely missed. There have been cases diagnosed as carcinoma, metastatic in which there has been no cancer. Contrary to your statement, advances in clinical procedures have not reduced the value of autopsies. Even in university teaching hospitals, 10% of autopsies reveal a major diagnosis that if known before death might have lead to change in therapy and prolonged survival. Clinically missed diagnoses account for about 12% (Goldman, L., et al, N. Eng. J. Med., 308:17:1000, 1983). In deaths occurring outside hospitals, the discrepancies are larger. Unsuspected infectious disease can, in fact, be revealed by an autopsy (Buck, B., et al, N. Eng. J. Med., 2001, 344:310, and Buck, et al, Clin. Orth. 303:8-17, 1994). In a series of 1500 tissue donors, 57 were excluded on the basis of autopsy findings. In 20 of the 57 excluded cases, the exclusionary condition was unrelated to the clinical "cause of death" and was discovered only by autopsy, (Buck, B., AATB Workshop for Physicians on Safe and Effective Allografts, March 1996). Thus, to argue against the value of an autopsy as a diagnostic tool is to argue against the obvious. My concern is not what you die of but what you die with which then becomes a hazard for the recipient.

With respect to malignancies, infections, and intestinal obstructions, the information I based my statement on was derived from the "Donor Acceptance Criteria" which includes donor referral algorithms disseminated by the University of Florida Tissue Bank. Regarding malignancies, AATB criteria in effect at the time (AATB, Library of Congress Card Catalogue Number 87-71681) stated (Cl. 300) that donors should be accepted if there are:

- No infections or sepsis by history, physical examination and laboratory testing.
- Sterile blood cultures.
- No history of neoplasms other than basal cell carcinoma of the skin, carcinoma in situ of the uterus, or intracranial neoplasm.

The State of Florida rules (59A-1.003) likewise state, "Individuals with malignancies arising anywhere in the body shall be excluded from the donor pool. Any exceptions shall be approved by the Medical Director."

C. Randal Mills, Ph.D.
Page 2
June 7, 2001

I am fully aware that since the publication of the AATB Standard cited above these have been reviewed, but the revised standards did not become effective until April 1, 2001. I do believe that transplantation of tissues from donors with malignancies may pose an unknown risk to the recipient, although assessment of such a risk is left to each individual tissue bank. The current AATB Standards are not specific on the issue.

As far as blood cultures are concerned, they have demonstrated correlation between these and positive bone cultures (Martinez, O., et al Diag. Microbio. & Inf. Dis. 3:193, 1988). Thus, blood cultures may add in establishing donor safety.

Finally I note, in my testimony I dealt only with retrieval of tissues for transplantation from cadaver donors, not their processing. When giving a gift of life, I believe it should be without a blemish. This is the goal I have set for District Five. If in the future there is any question of tainted tissue in a recipient, I would not like to be the Medical Examiner who "co-approved" this donor.

Let me reiterate, my position. The reason they asked that I appear before this Subcommittee was to help improve the standards in the field of bone and tissue banking so the recipient lives a healthy and happy life. This was my goal and it should be for each and every one of us involved in this process.

Sincerely,

Valerie Rao M.D.

Valérie J. Rao, M.D.
Chief Medical Examiner

VJR/cm

cc: Governor Jeb Bush
Senator Rod Smith
John Anderson, Enterprise Florida
Representative Perry C. McGriff, Jr.
Representative Edward L. Jennings, Jr.
Senator Bob Graham
Senator Connie Mack
Congressmen, Karen Thurman
Permanent Subcommittee on Investigations
Michelle Oxman, Esq., AHCA
Lake County Commissioner Welton G. Cadwell
Dr. Stephen Nelson, Chairman of the Medical Examiner's Commission

JUL.25.2001 5:50PM AATB

Senate Permanent Subcommittee
On Investigations
EXHIBIT #___19___

American Association of Tissue Banks

The leader in cell and tissue banking for a quarter of a century
25th Annual Meeting, August 25-29, 2001, Washington, D.C.

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July 15, 2001 Via Facsimile, Hard Copy to Follow

Claire M. Barnard, Investigator
Permanent Subcommittee on Investigations
United States Senate
100 Russell Building
Washington, D.C. 20510

Dear Claire:

In reply to your request for information regarding the status of entities that were formerly accredited by the American Association of Tissue Banks (AATB), I submit the following.

Only one major entity continues to operate since it ceased to be accredited by AATB. That is the Pacific Coast Tissue Bank and its independent processor, Perfomat. Both are co-located in Los Angeles, California.

There are three small hospital-based banks still in operation: one is a skin bank, the New York Firefighters Skin Bank, located in New York Hospital/Cornell Medical Center, New York City.

The other two are surgical bone banks—small hospital-based operations that retrieve bone from patients, do not process it and re-implant the bone usually in the same patient from whom it was removed or in another patient. One of these is located in the hospital's blood bank (Southeast County Blood Center, Tallahassee, Florida) and the other in the hospital's operating room (University of Pennsylvania Medical Center, Philadelphia).

According to these small hospital-based operations, the cost of AATB accreditation was a major factor in their decision not to seek re-inspection. The other formerly accredited entities have either closed or merged with another AATB-accredited organization.

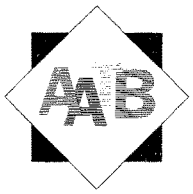
Would be glad to discuss this or any other issue with you in greater detail.

With best wishes, I am

Cordially,

Jeanne Mowe, Executive Director

1350 Beverly Road, Suite 220-A • McLean, Virginia 22101 • Web Site: http://www.aatb.org • Phone: 703-827-9582 • Fax: 703-356-2198 • email: aatb@aatb.org



American Association of Tissue Banks

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Charles Garrison, M.D.

July 30, 2001 Via Facsimile, Hard Copy to Follow

Claire M. Barnard, Investigator
Permanent Subcommittee on Investigations
United States Senate
100 Russell Building
Washington, D.C. 20510

Dear Claire:

Regarding my response of July 15, 2001, regarding the status of entities that were formerly accredited by the American Association of Tissue Banks (AATB), I made an error:

I stated that the University of Pennsylvania Medical Center, Philadelphia was no longer accredited; this is an error. The bank is accredited until August 2002; I misread the expiration date by one year. This leaves only two small hospital-based operations no longer accredited, rather than three

Hope the errata does not cause you any problems.

With best wishes. I am

Cordially,

Jeanne Mowe, Executive Director

1350 Beverly Road, Suite 220-A • McLean, Virginia 22101 • Web Site: http://www.aatb.org • Phone: 703-827-9582 • Fax: 703-356-2198 • email: aatb@aatb.org

Senate Permanent Subcommittee
On Investigations
EXHIBIT #___20___

Thursday, August 09, 2001 11:42 AM Fredrick G. "Woody" Caudle 301-577-4765

LIONS OF DISTRICT 22-C EYE AND TISSUE BANK AND RESEARCH FOUNDATION, INC.

9470 Annapolis Road • Suite 415 • Seabrook, Maryland 20706
(301) 577-7800 • FAX (301) 577-0218
www.lionseyeandtissuebank.com

Chartered in 1956

Chairman
Joseph F. Gaffigan

Chief Executive Officer:
Fredrick G. "Woody" Caudle

Chief Operating Officer
Roman A. Hitchev, MD, CPTC

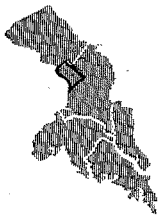
Technical Director
Kevin J. Sealy

Programs Director:
Diana C. Quinn, CHES

Medical Directors:
Lions Eye Bank
Dr. David B. Glasser
Lions Tissue Bank
Dr. Sanjiv Lakhanpal
Lions Preschool Vision Program
Dr. Salim I. Butrus

Community Programs:
- Mobile Health Units
- Preschool Vision Program
- Francis J. Garner Fund
- Eye Glass Program

Serving:
Calvert County
Charles County
District of Columbia
Montgomery County
Prince George's County
St. Mary's County



ACCREDITED EYE BANK ASSOCIATION of AMERICA

MEMO TO: Senator Carl Levin
Senator Susan Collins
Special Permanent Senate Subcommittee on Investigations
FROM: Fredrick G. "Woody" Caudle
CEO, Lions Eye & Tissue Bank
SUBJECT: Subcommittee Hearing, May 24, 2001
Testimony of Dr. William Minogue

On May 24, 2001, Dr. William Minogue, Sr. Vice President at Suburban Hospital in Montgomery County, presented testimony to the Senate Subcommittee on Investigations chaired by Senator Collins. Dr. Minogue testified as Chairman of the Board of Directors for the Washington Regional Transplant Consortium (WRTC), the designated Organ Procurement Organization for this region. During his testimony he gave an "Example of Inferior Tissue Banking" and stated, "Regrettably, not all organizations involved in recovery, processing and distribution of tissue share our [WRTC] concern to maintain and respect the integrity of the donation process and the sanctity of the donated gift." He later states that a "second tissue recovery agency" inappropriately or wrongly approached family and obtained confidential patient information. The agency in reference is the Lions of District 22-C Eye and Tissue Bank and Research Foundation, Inc. (LETB). We want to take this opportunity to correct the record.

The LETB is located in Seabrook, Maryland and serves three counties and the District of Columbia in the area in which WRTC is federally mandated to procure organs. The Lions Eye Bank was chartered in 1956 and recently celebrated its 45-year anniversary. In September 1998, our services expanded to include non-ocular tissue recovery. The LETB is a Charter Member of the Eye Bank Association of America (EBAA) and has continuously held accreditation since the inception of this program. LETB follows the American Association of Tissue Banks (AATB) standards and procedures and the Food and Drug Administration (FDA) regulations, and is licensed by the State of Maryland. LETB employs two full time AATB Certified Tissue Bank Specialists (CTBS). As demonstrated by Dr. Minogue's testimony, WRTC is not AATB or EBAA accredited and has been working with donor families approximately 13 years as compared to our 45 years of experience in the field.

During Dr. Minogue's testimony, he asked the Committee to "consider the following scenario." Dr. Minogue's statements during the testimony about this case are directly quoted and information the LETB wishes now to place before the Committee is in "bold italics". This information is intended to clarify and correct the record as to the accuracy of the testimony provided by Dr. Minogue before your committee on this one matter.

Dr. Minogue's statement: An elderly patient died at a local hospital. In accordance with the federal regulations, the hospital referred the case to the local OPO for potential donation. The OPO determined that this patient was not a candidate for organ or tissue donation and communicated this to the hospital and family.

Attached is a call referral report our Donor Service Call Center sends to us to review all calls referred. WRTC referred the case to us at 1805 on October 5, 2000. The transcript shows that WRTC provided us with information on the patient's death but failed to report that they had talked to the family or hospital. **(Exhibit 1)**

Dr. Minogue's statement: The decision was based on the generally accepted suitability criteria from tissue banks. Some time later, the OPO received an excited call from the local hospital. The hospital demanded to know why this patient was now being pursued for tissue donation when the family had already been told that their loved one was not a candidate for donation.

After the case was referred to LETB by the WRTC, our donor service specialists reviewed the case for possible cornea donation. Due to the age criteria, LETB ruled the corneas out and referred the case to the Anatomic Gift Foundation (AGF). At that time, the LETB had an agreement with AGF to refer potential research donation options to families where donation for transplant was not possible.

Joe Paparo was the technician on-call with AGF when this case was referred. At that time, Mr. Paparo also worked for LETB as a part-time tissue bank specialist. When WRTC referred the case to the LETB, they stated that we could approach for research after we indicated the age of the donor was not suitable for corneas. So Mr. Paparo proceeded to contact the family on behalf of AGF for research donation.

After contacting the family, Mr. Paparo learned that they were not interested in research donation, but very much wanted to donate for transplant. As a tissue bank specialist, Mr. Paparo reviewed the medical and social history and discovered donation for transplant was acceptable based on criteria given him. He then shared this information with the family. The family discussed the possibility of tissue donation for their loved one and called Mr. Paparo back indicating they wanted to donate for transplant.

Mr. Paparo obtained proper consent and attempted to locate a recovery suite to complete the case. After several unsuccessful attempts, Mr. Paparo contacted LETB COO Dr. Roman Hitchev for assistance. Dr. Hitchev contacted the hospital and explained that the OPO had ruled-out a medically suitable donor case and that the family wanted to donate. The LETB was attempting to carryout their wishes but needed assistance from the hospital in order to do so. After Dr. Hitchev placed this request with the hospital, a representative

from the OPO called Dr. Hitchev and stated that without an agreement with the hospital the LETB could not recover the tissue. Dr. Hitchev requested that the WRTC fulfill the family's wishes and do the case. The LETB was assured by the WRTC that they would procure the donor tissue. LETB later discovered the family's wishes were never fulfilled. **(Exhibits 2,3 and 4)**

Dr. Minogue's statement: The OPO investigated this case and determined that a "second tissue recovery agency" obtained confidential patient information without the hospital's knowledge. This "second tissue recovery agency" told the family that this tissue could be recovered for transplant purposes and that the family had specifically stated that they did not wish tissue to be recovered for use in medical research, though research donation was the only realistic option for a patient with this profile

In rebuttal to these statements I want to assure the Committee that the LETB at that time had an eye bank agreement with the hospital and had full access to patient information relating to donation. Additionally, WRTC acknowledged that we had access by the simple fact they referred the case to our organization, to include specifically stating research donation should be approached. We did, in fact tell the family that the evidence in the case showed by our criteria that the tissue could have been used for transplant, which would have fulfilled the family's wish.

We offered all possible options as is our duty and obligation to donor families. As to the research being the only realistic option for donation – WRTC, while experts in organ donation, are not sole experts in the standards of acceptable criteria for tissue donation. We can demonstrate this donor was a candidate for transplantable tissue that could have effectively enhanced a recipient's life.

Dr. Minogue further accused the "second tissue recovery agency" of pursuing the tissue for transplant even though the following medical conditions existed, which had caused the OPO to decline the tissue:

a. The patient was outside the generally accepted age range for donation.

Life Net, the organization that processes the tissue for WRTC, establishes WRTC's generally accepted age range. Their requirements are based on their current demand as a company, not on national need. This statement is a personal opinion of the OPO and Dr. Minogue and has no relevance to acceptable age of a donor. HCFA in its clarification of acceptable age range states that there may be no upper range limits for the donation of tissues including skin, non-weight bearing bone and connective tissue and some blood vessels. (Ref HCFA Q&A; Q 31)

b. The patient had a history of cancer that had rendered the tissue medically unsuitable for donation by OPO standards.

A thorough investigation of this case demonstrated the donor had prostate cancer that was removed "in situ" more than 10 years prior to his death. The cancer had not spread and was considered "primary" in the prostate only. Cancer is a rule out only in case of metastasis, as this case was not.

c. The patient had been dead for almost 24 hours when the "second tissue recovery agency" contacted the family.

This is not accurate. Our records show the call to LETB came at 6 PM. Mr. Paparo initiated the contact with the family at 7:10 PM. The next of kin called Mr. Paparo the next day at 2:30 PM with their interest in donation. At this point, the recovery had to be accomplished by approximately 4:30 PM. Our technicians were in place to fulfill the family's wishes when the OPO called and stopped the donation, but assured us they would procure the tissue and fulfill the family wishes – which they did not. **(Exhibit 4)**.

By well-established procedures and protocols incision must be done for safe recovery of tissue for transplant by the twenty-fourth hour following cardiac arrest. LETB carefully follows these procedures.

d. There was evidence of a recent infection affecting this patient.

The medical history indicated that this infection was effectively treated with antibiotics and again was consistent with the generally accepted medical standards for tissue donation. It should be noted that WRTC did not provide this information of a recent infection during the referral. It is incumbent upon the WRTC as the federally mandated referral "gatekeepers" to obtain and distribute complete and accurate information regarding a potential eye or tissue donor. **Exhibit 1]**

Dr. Minogue's statement: The investigation points to the following conclusions:
A "second tissue recovery agency" inappropriately obtained confidential patient information, without the hospital's knowledge or approval, and pursued the case for donation. The fact that the family had specifically stated that they did not wish to donate for research indicates that this agency was pursuing donation for transplant purposes or suggests that the agency was recovering tissue for research but not fully disclosing that intent to the family.

This again is not an accurate statement of the facts. Our agreement with the hospital signed in October 2000, allowed us to have patient information on potential donors. When the family indicated interest in donation we informed the hospital. **(Exhibit 2 and 3)** ***Further, when WRTC referred the case to our organization they are required to provide complete referral information as per our agreement. Dr. Minogue does not acknowledge that the original referral call provided by WRTC stated that WRTC suggested we approach for research. The family was well informed of our program and greatly appreciated the efforts we went through to fulfill their wish.***

Dr. Minogue's statement: The "second tissue recovery agency" was recovering tissue in our area for a publicly traded, for-profit, tissue bank

We are not sure why this is an issue as most tissue processing organizations are either for profit or provide tissue products to for profit companies. LETB openly informs its hospitals that the tissue procured is sent to Regeneration Technologies, Inc., The Alabama Tissue Program or Collegenasis. However, the LETB is a 501 (C) (3) charitable non-profit organization supported primarily by the Lions Clubs in our District. We can demonstrate multiple community outreach programs in health screening and indigent patient grants that we offer at no charge to our community.

Dr. Minogue's implication of dishonest practices by LETB is offending and one that we cannot let go unchallenged. We are a proud service organization with hundreds of volunteers who have served their community well for almost 50 years.

In summation let me reiterate our response to the inaccurate and misleading statements made by Dr. Minogue and submitted for the record. The LETB correctly requested a temporary privilege to recover tissue from this patient in a hospital where we already had an agreement to recover eye tissue and cornea. The fact that we did not notify the OPO that we were intending to recover tissue from this patient is immaterial. Once a matter is referred to LETB by the OPO there is no further obligation to report our actions unless the case involves organ transplants.

The donor family was completely comfortable with the procedures outlined by the LETB and grateful for our efforts to fulfill their wishes. We have statements from the family confirming these facts. They were not, as Dr. Minogue stated, "subjected to conflicting and confusing information" by the LETB.

As explained above we sought the permission of the hospital for a temporary privilege in order to fulfill the family's wish **– Exhibit 2 and 3.** ***The hospital was aware of our actions – we did have an agreement for eye tissue recovery with the hospital and therefore were certainly entitled to assist this family. And WRTC did refer the matter to us in the first place.*** **(Exhibit 1)**

The LETB personnel handled this matter, as we do all cases referred to us, in a professional and efficient manner. Our technicians are fully trained and experienced in both dealing with the family and handling the tissue. Through meticulous record keeping we were quickly able to identify the case Dr. Minogue featured in his testimony and are pleased now to have the opportunity to respond to his charges. The testimony he provided purposefully provided a very negative image to our organization. We would question his motives in attacking a successful organization that is dedicated to increasing the organ and tissue transplant rate. It should be noted that this OPO has opened an eye bank recovery program in an area that has been adequately served by our program for 45 years.

I should inform the committee that the OPO has recently retained an attorney and filed a lawsuit to attempt to collect payments they say are due on referrals to LETB. These referrals

regarding potential eye and tissue donors were incomplete and/or not in compliance with an agreement signed by our two organizations over a year ago. We have documented the consistent delay in forwarding referrals to LETB, often outside the safety timeline for procurement, as well as the cases where there was no referral at all or incomplete donor information on a referral as was the case cited above. These practices are not consistent with the agreement between our organizations; the MOUs hospitals have with both organizations, and with HCFA regulations.

OPO's are mandated and designated under Federal law, which states that they are the "gatekeepers" of all referrals provided by hospitals on deaths and imminent deaths. By law, the hospitals must work with the OPO for organs. They are, as a result, at a definite and perhaps unfair advantage when negotiating tissue and eye agreements with the same hospitals that are required to work with them. Conversely, there are eye banks and tissue banks that have in some cases (such as ours) been in existence for almost a half a century educating hospitals and donor families on the importance of donation. These successful eye bank programs established much of the criteria and standards in this industry and now are being overtaken by OPO's who wish to enter the eye and tissue banking industry.

The LETB found the testimony about competition interesting and self-serving. As Chairman of the Board of WRTC, Dr. Minogue advocated in his testimony that "we recommend giving OPO's oversight authority over all donation activities, including family contact, donor evaluation, recovery, processing and distribution." This would allow the OPO complete authority over all eye and tissue banks in their region. I have pointed out herein the inaccuracies of the OPO in this one referral and can demonstrate clear obstruction in many other cases. Dr. Minogue's recommendation will result in the elimination of long standing; successful eye and tissue bank programs through a monopolistic approach and preclude any redress on the part of the eye and tissue banks who are aggrieved.

We further fail to see how complete oversight of all donation activities by the OPO will increase organ donations, their primary responsibility. The LETB program feels strongly that in order to ensure a safe and productive organ supply for the thousands of critically ill patients that OPOs should solely focus on the extremely important task of alleviating the shortage of organs.

I want to thank you for your continued interest in our industry and reiterate that for LETB there is no greater goal than maximizing the gift of donated tissue and providing the best possible services to our community and donor families, services that have been well known in our community for over 45 years.

We would be happy to meet with you or your staff to answer any questions or provide further information.

Exhibit 1 – DRW Worksheet (10/5/00)
Exhibit 2 – Interoffice Memo from Roman Hitchev, MD, CPTC (10/7/00)
Exhibit 3 – Memo to Hospital (10/6/00)
Exhibit 4 – Lions Referral Worksheet (10/5/00)
Exhibit 5 – Report on Case (10/5/00)

EXHIBIT 1

DRW Worksheet

Patient Information 128797 | 10/5/00 | 18:05 | SJ

Referral Site	Referring Person	Referral Site Phone	Unit No
[redacted]	[redacted]	(202) 782-7085	MICU

Patient	DOB	Age	Gender	Ethnicity
[redacted]		82	Male	Caucasian

Admit Date	Admit Diagnosis	DOD	TOD	COD
9/27/00	Stroke	10/5/00	15:42	CVA

NOK	Relationship	Phone
[redacted]	Spouse	[redacted]

Funeral Home Information

Name of Home: Unknown

Phone:

Type of Viewing:

Medical History

Hx HTN, atrial fib, Prostrate CA (s/p SX).

MedRec Number:

Suitable for: ☐ MECase ☐ Autopsy ☐ Prior Approach ☐ Fl

Eyes	Peri	Dura	Skin	Bones	ST	H-V	Veins	Fascia	Brain Biopsy
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

OPO Information

☐ Donor Referral ☐ Liver
☐ Organ Offer ☐ Lung
☐ Kidney ☐ Heart
☐ Other

Referred Information

	Ref 1	Ref 2	Ref 3
Referred to	LD22	AGF/Joe	
Paged @		7:05:00 PM	
Responded @		7:10:00 PM	
Faxed @	7:01:00 PM		

Disposition: CRO

Coord	Date Closed
SJ	10/5/00

Notes

James WRTC Recd 18:03, INP-Admit date, DOB, NOK, med hx ; CRO due to age. SJ

Check List Information

Status	Task	Time
Yes	HD	18:31
No	DR	18:31
No	FH	18:31
No	MEH	18:31
No	CO	18:31
Yes	HC	18:28

14

EXHIBIT 2

interoffice
MEMORANDUM

[redacted]

To: Fredrick "Woody" Caudle, CEO
From: Roman Hitchev, MD, CPTC
Date: 10/07/00
Subject: [redacted]

This case (see attached documents) was ruled as non-medically suitable for transplant donation by the Organ Procurement Organization (OPO). However, due to the fact that it was referred to us by the OPO (name of referring person: [redacted]), we had the opportunity to evaluate in detail the potential for donation. In the course of the current and past clinical and medical history evaluation it appeared that there were no sufficient clinical factors for this case to be ruled medically unsuitable for transplant donation. Specifically, the history of cancer turned out to be history of Prostate Cancer, which was detected and removed "in situ" more than a decade ago with no relapses or further complications. The right-lung Pneumonia diagnosed on September 28, 2000 was actively treated with antibiotics. In light of these and other clinical findings, all consistent with the generally accepted medical standards for tissue donation, we made a decision to assist this family with their wishes for donation.

Due to the fact that we only have ocular tissue recovery agreement with the hospital we had to apply for temporary privileges in order to be able to carry out the wishes of the family. During the processing of our application I received a phone call from Guy David DeStefano, Director of Recovery Services of the Washington Regional Transplant Consortium (WRTC, the local OPO), who informed me that the hospital was denying us temporary privileges to do the case and they (the OPO, WRTC) were taking over the further coordination of this case. I brought to Mr. DeStefano's attention our clinical findings proving that the initial rule-out of this case (done by the OPO) does not rest on sufficient clinical/medical ground. I expressed concerns over the possibility of losing the case for logistical reasons due to the close window-of-opportunity expiration and/or depriving the family from their right to donate for transplantation. Mr. DeStefano assured me that they (the OPO) will complete the recovery for transplant purposes and will carry out the wishes of the family.

Later I learned that no tissue recovery had been performed by the OPO and the case had been aborted.

EXHIBIT 3

Memo

To: [redacted]
From: Dr. Roman A. Hitcheff
Date: October 6, 2000
Subject: Donation Request by the family of [redacted]

Dear Ms. [redacted]:

Thank you for your help in arranging the logistical details needed to carry out the anatomical donation of the family of [redacted] who expired at [redacted] Medical Center ([redacted]) on 10/05/00 at 1642 h. Pursuant to our telephone conversation I am sending attached the consent form signed by the family based on the provisions of the Uniform Anatomical Gift Act, as well as the referral documentation pertaining to the case.

We need permission to use the morgue of the [redacted] for a time period of approximately 2 hrs (between 1530 h and 1800 h, today, October 6, 2000). Due to the fact that death was pronounced 22 hrs ago, we are very close to the expiration of the window of opportunity for donation. In order for us to be able to carry out the wishes of the family and complete the altruistic act of donation, we need your understanding and prompt response.

This document is also to serve as a formal indemnification declaration on the part of the Lions of District 22-C Eye and Tissue Bank and Research Foundation (LETB), that the [redacted], its agents and employees, will be held harmless, and will be indemnified against any and all claims, suits or actions arising from the donation activities pertaining to this case.

Again, I would like to thank you and the leadership of [redacted] for the understanding and support in carrying out the highly humane request of this family.

Sincerely,

Dr. Roman A. Hitcheff, MD, C.P.T.C.
Deputy Executive Officer

cc: Fredrick "Woody" Caudle, CEO, LETB

attachments

EXHIBIT 4

LIONS Referral Worksheet

UFTB Referring Person: Sharon **Date: 10-5-00 Time: 7:10pm**

Referral Site: [redacted] **Unit: N/A**

Contact Person: [redacted]
Phone#: [redacted]

Patient Information

Patient: [redacted] Admitting Date:9/27/00 M.E. Case: No

Age: 82 Sex: M Race: C

COD: Stroke TOD: 16:42 DOD: 10-5-00

Medical History:
Prostate Cancer in late 60's early 70's, but removed without any problems. Suffered from a bowel infection post operatively- not from the cancer.
Diagnosed with R-Lung Pneumonia on the 28th of September. Treated with antibiotics.

Next-of-kin: [redacted]
Phone: [redacted]

UFTB Rule Out: yes / no
UFTB Accepted Criteria for:
Bone, Pericardium, Fascia Lata, Pelvis
Other: (Lions eye donor) yes / no

Disposition: Referred to AGF first, then family did not want research donation. Their only interest was in transplant. So, I worked it up for bone-upper, lower and soft tissue-pericardium, fascia lata.

Consent: yes/ no

Reason (no): N/A

Called UFTB to give status: Yes
Time: 2:30pm 10/6/00
UFTB Person: Sharon

Additional Notes for Follow-up: This case was first called in to AGF-Joe Paparo on-call. Sharon said that the doctor at the hospital relayed to her that the family might be interested in a research donation. UFTB ruled it out because of the age of the donor and the fact he had prostate cancer. However, they were not aware that the cancer had been taken care of years ago. UFTB also knows that [redacted] is a LifeNet hospital. After speaking with the family and finding out they were interested only in transplant, I called UFTB back to let them know that I was going to go for bone and soft tissue. I told them that we would have the body removed from the hospital to do the case.

I spoke with the son for some time Thursday night and he was determined to talk his mother into the idea too. I left the ball in his court that night and told him that I would call in the morning to see what their decision might be. After repeated attempts to recontact the family, I gave up the pursuit at 11:15am. To my surprise [redacted] the son, called me back and said they wanted to donate and we initiated the consent. The family was very willing.

When I found out that WRTC was blocking Lions from doing the case. I called [redacted] back to fill him in on the politics of what was happening. He was very understanding. The night before he complimented me on my approach and said that the hospital was very uneducated in what they told the family and he was glad that I had approached him. He also understood why we were unable to do the case. He is willing to write any form of letter for Lions, which might help our cause.

It is unfortunate that this family had to go through the motions of something very positive, only to have their thoughtfulness and generosity squashed by LifeNet and politically empowered tyrants.

Note: I now believe we could have salvaged this case by using another Funeral Home facility such as [redacted] or [redacted]. We have other MOU's that we should have called upon. We could have paid the livery invoice for the deceased trip to either F.H. and then to [redacted] for the cremation and services. I didn't think of this until the next day. This case really left a sour taste in my mouth. I certainly feel for the family and I will not let this happen again.

Signature of Requestor:

EXHIBIT 5

Report on 10-5-00

Referral Site: [redacted]
Referred by Sharon/ UFTB
Time: 7:10pm
Contact at [redacted]

Patient: [redacted] Admitted: 9/27/00 M.E. case: NO

Age: 82 Sex: Male Race: Cauc.

COD: Stroke TOD: 16:42 DOD: 10-5-00

Medical History:
Prostate CA in late 60's early 70's, but removed without any problems. Suffered from bowel infection post operatively-not from the cancer.
Diagnosed with R-lung pneumonia on the 28th of September. Treated with Antibiotics.

Next-of-kin: [redacted]
Phone: [redacted] UFTB accepted criteria

Consent obtained by Joe Paparo CST, CTBS
with [redacted]

Note: This case originally called in to AGF but family refused any donation towards medical research. (No research per [redacted]). So, I worked up the case for TX with Lions consent form.

Time: 2:30pm on 10/6/00 Family called me back wanting to do the transplant tissue donation. Consent obtained for Bone upper and lower with pericardium and fascia lata bilateral.

Additional Notes:

10/5/00–The initial referral I received was through AGF. I was told by the referring person that the family had an interest in donation. The donor's age ruled him out for an eye donation. Upon calling the family, I spoke to the son, [redacted], who had no interest in a research donation. It was obvious that this family wanted to do something good for others and in their time of need I decided to run the case for a tissue donation for transplant. I discussed this with [redacted] and told him his father was suitable according to Lions criteria. I also explained that Lions would pick up the cost to transport the deceased from [redacted] Hospital because of the politics involved, and the Lions Eye and Tissue Bank is only contracted to do eye recoveries there. So, after three phone calls with the son, [redacted] felt he and his mother were all for a tissue donation to Lions. He was very grateful for the information that I had provided to him and I felt he was comfortable with his decision.