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# Advisory Committee on Organ Transplantation

**Fall Meeting**

**November 2–3, 2006**

**Doubletree Hotel**

**Bethesda, Maryland**

**Thursday, November 2**

**Welcome and Introductions**

*Gail Agrawal, Chair of ACOT*
*Remy Aronoff, Executive Secretary of ACOT*

Mr. Aronoff welcomed the new Advisory Committee on Organ Transplantation (ACOT) members, and Ms. Agrawal led participants in a round of introductions.

**Working Group Recommendations on Centers for Medicare and Medicaid Services (CMS) Reimbursement**

*Suzanne Conrad, Iowa Donor Network*

Ms. Conrad reported for the work group on CMS reimbursement of organ procurement organizations (OPOs) for donation after cardiac death (DCD) and insurance coverage for living donors and presented the group's recommendations:

- *Recommendation 1*: When the next of kin has made the decision to pursue organ DCD, the CMS-designated OPO is responsible for expenses related to donation. ACOT recommends to the Secretary that the Medicare program allow these direct organ acquisition expenses to be reimbursable to the OPO under the Federal program. It would thereby remove a financial barrier to donation. Reimbursement to the OPO would begin at the time donation consent is given and continue until the time organs are recovered or the time a patient is returned to palliative care. At that time, responsibility for expenses would revert to the patient or the patient's insurance carrier.

Dr. Solomon asked if the reason the patient might be returned to palliative care would be because it was discovered that the operation could not proceed and, in this case, if it is fair to give the patient the expenses? The group discussed the fact that this is typical and that families are aware there is a chance that this will happen.

- The motion to adopt the recommendation was seconded; there was no further discussion on the recommendation. The vote was held and was unanimous.

Ms. Conrad read the second and third recommendations, which relate to coverage of those who are living donors:

- *Recommendation 2*: ACOT recommends to the Secretary that he promote collaboration between the transplant community and the insurance industry to adopt standards of coverage for living organ donors specifically relating to future adverse events (e.g., hernia repair, biliary tract reconstruction) resulting from the donation. The future coverage period would be limited to 10 years.
- *Recommendation 3*: ACOT recommends to the Secretary that he take action intended to provide Medicare eligibility for any living donor who loses insurability as a result of disability on the basis of previous organ donation.

the basis of previous organ donation.

Dr. Lorber asked about insurance portability and instances in which the complication occurs after the donor has changed insurance companies. Dr. Migliori stated that these liabilities go to the new carrier and, if the donor has problems getting insurance (or becomes unemployed or their employer goes out of business), the third recommendation would apply. He noted that it is rare for individuals to be denied insurance coverage because of their past donation. If all other commercial opportunities for coverage are denied, CMS would become the backup.

Dr. Vega asked if the work group considered a recommendation for instances in which living donors do not have insurance to cover pain medications postoperatively. Ms. Conrad responded that the work group did not address this situation; it appears that some centers pay and others do not. Dr. Migliori noted that the organ recipient's insurance is responsible for this and that at the time of discharge, the transplant center becomes responsible for this.

Mr. Hagman asked why the second recommendation contains the coverage limitation of 10 years, when donors are likely to need more coverage and have more problems as they age. Dr. Migliori noted that the work group had considered this limit for practical rather than other reasons. It was thought that the complications would primarily occur in the first year, but he conceded that the point is well taken. Mrs. Boone commented that she had also missed noticing the 10-year limit; she inquired about what would happen after that period was over. Dr. Migliori suggested that the recommendation be changed to recommend coverage be perpetual and remove the 10-year limitation.

Ms. Principe noted that the group appeared to be in agreement to take out the 10-year limitation. She asked about the awkwardness of potential donors having to submit a letter of denial from their insurance company. Dr. Migliori responded that such requirements would be developed under the standards created by the insurance company industry and associations such as the Health Insurers' Association of America, etc.

Ms. Agrawal accepted a motion to accept the recommendations, with an amendment to remove the 10-year limitation; the motion was seconded. There was no further discussion and the motion was unanimously accepted.

- **FINAL RECOMMENDATIONS FOR RECOMMENDATIONS 2 and 3:**

  *Recommendation 2*: ACOT recommends to the Secretary that he promote collaboration between the transplant community and the insurance industry to adopt standards of coverage for living organ donors specifically relating to future adverse events (e.g., hernia repair, biliary tract reconstruction) resulting from the donation.

  *Recommendation 3*: ACOT recommends to the Secretary that he take action intended to provide Medicare eligibility for any living donor who loses insurability as a result of disability on the basis of previous organ donation.

**Working Group Recommendations on Public Solicitation of Donors**

*Dr. David Conti, Albany Medical Center*

Dr. Conti presented the work group's recommendation:

- ACOT recommends that the Secretary of the Department of Health and Human Services (HHS) develop guidelines that intend to protect the ability of the Organ Procurement and Transplantation Network (OPTN) to continue to equitably allocate donor organs within a single national network and potential individual recipients from risks that can arise from public appeals (e.g., Internet Web sites, media campaigns, and billboard advertisements) for organ donors. These guidelines would serve as a resource for transplant centers, OPOs, and potential donors and recipients. ACOT further recommends that the guidelines take into account: (a) The distinction between deceased and living donors; (b) the necessity to ensure that money is not exchanged between donors and recipients; and (c) psychological motivations of donors resulting from public solicitation.

These recommendations grew out of the extensive discussions generated by the presentations at the last ACOT meeting in May and were conceived by the work group as guidelines, rather than as requirements. The goal is to help the public be aware of the risks and how to approach these risks, not to ban directed donations.

Ms. Agrawal suggested changing the word "money" to the phrase "valuable consideration" which is a phrase with legal meaning. Dr. Lorber asked if there is a common definition of "valuable consideration" and Ms. Agrawal reported that ACOT had discussed this question and made suggestions to the Secretary about clarifying the term. To date, ACOT's suggestions have not prompted action. Ms. Levine reminded the group that the Secretary is not authorized to issue his

prompted action. Ms. Levine reminded the group that the Secretary is not authorized to issue his own definition but, to the extent that it is hard to develop this area without a definition, the Secretary can seek help from the Justice Department and/or Congress. She commented that ACOT can reiterate that this lack of a definition continues to cause problems, which might be helpful.

The work group was asked to clarify the phrase "public appeal for live organ donors." Dr. Conti said that a lot of work has been done over the last 20 years to develop equitable and fair methods of allocating deceased donations. The appeal of public calls for organs has the potential to destroy this system and result in allocation of organs to patients who may not benefit the most from the particular organ, in both directed deceased and live donor situations. The bottom line is that public solicitation is dangerous to the allocation system, especially since it fosters public mistrust of the existing system. Dr. Solomon noted, on the other hand, that no one wants to hamper creative public education efforts about donation-education of doctors, patients, and the public is extremely important. Ms. Principe suggested adding language to stress the need for educational campaigns. Ms. Agrawal suggested adding language to ACOT's recommendation that the Secretary promote an educational campaign to inform the public of the risks of circumventing the existing allocation system.

The group discussed the fact that ACOT would not make a recommendation that would prohibit speech or impinge upon the First Amendment. The Secretary cannot either violate the First Amendment by prohibiting speech or various State and Federal laws that permit designation of organ recipients by donors. Ms. Agrawal commented that it is allowable to have reasonable restrictions on misleading speech.

The group debated sound versus unsound public appeals and mechanisms for protecting the integrity of the existing allocation system rather than restricting directed donation. Mrs. Boone said that it's hard to distinguish between good and bad solicitation and that asking friends and family members to give an organ is also solicitation. She reminded the group that, when it comes to living donor solicitation, centers and surgeons are not providing long-term followup for the donors to help gather data that might inform a person's decision to donate.

Dr. Vega said that the present allocation system is designed to allow the equitable distribution of organs from deceased donors. For living donors, there is no system that protects equity in allocation. In fact, centers tell patients to seek a living donor, which complicates the situation. People need to understand the difference between public solicitation for live donation versus solicitation of deceased donors. Dr. Conti agreed, stating that many centers and patients are looking for guidelines for what to do in these instances, so that it would be good for the Secretary to develop such guidelines.

Ms. Agrawal summarized the discussion by stating that the group as a whole is not ready to act on the recommendation yet. The issues behind this single recommendation might be clearer if it were to be split into a series of recommendations arising from ACOT's concerns. She asked the work group to continue working on this issue and to bring it back at the May 2007 meeting. Dr. Burdick added that it would be helpful to have more information about how the transplant program should clearly address the situation. Committee members agreed to do so, and ACOT members with specific concerns were asked to provide them in writing to the work group members. Ms. Levine will assist the work group with legal issues.

**Work Group on Medicare Part D**

*Kris Robinson, American Association of Kidney Patients*

Ms. Robinson reported that the work group has no recommendations to present; members will monitor both Plan D and Plan B over the next few months to see what problems occur with implementation. The workgroup has talked with CMS about its concerns about organ recipients who are covered by these programs. A lot of the challenges are coming at the pharmacy level. The work group wants to aggregate the information that is available to assess the situation. The OPTN Transplant Administrators will be contacted to learn more from them about specific transplant patient and transplant program concerns regarding Medicare Part B and Part D.

**Living Donor Bill of Rights**

*New business*

Mrs. Boone informed the group about a new living donor Bill of Rights, of which she has copies for ACOT members. Ms. Donna Luebke, of Cleveland's Metro Health Medical Center, spoke to the group. She said that live donors are finding that insurers have a 7- or a 30-day benefit, after which time coverage ceases. For example, her group has a donor member who was told that complications were covered by the organ recipient's insurance only for 15 days. There are many cases in which the organ recipient's insurance policy refuses to pay for the donor's health care. A self-employed donor recently lost her company because she cannot get insurance coverage. With respect to the discussion about public solicitation, there is a very real fear that this situation will

respect to the discussion about public solicitation, there is a very real fear that this situation will undermine both the living and deceased donor systems. The living donor Bill of Rights addresses actual issues that donors face.

Ms. Agrawal thanked Ms. Luebke for her remarks but said that this subject fits more appropriately under the "Public Comment" portion of the agenda. ACOT publishes its agenda publicly prior to its meetings and must be attentive to that written record so that members of the public can attend and hear what is on the agenda at any particular point. She promised that the group would return to this topic at the end of the day during the Public Comment period. Several ACOT members asked to see a copy of the document so they can discuss it after they have read it, and it was distributed to the group.

**Issues Related to Tissue Regulation**

*Tracy Schmidt, Association of Organ Procurement Organizations (AOPO)*
*Patricia Aiken-O'Neill, Eye Bank Association of America (EBAA)*
*P. Robert Rigney, American Association of Tissue Banks (AATB)*
*William Zaloga, New York State Department of Health*
*Celia Witten, Food and Drug Administration (FDA)*

Mr. Holtzman introduced the speakers to present on tissue regulation and gave an overview on the subject. He said that there is a connection between organ and tissue donation: When something untoward occurs concerning tissue in the United States, it affects organ donation rates as well. Negative publicity affects both areas. Many OPOs are also tissue recovery organizations and a large percentage of tissues recovered come from OPOs. There is, however, a lack of information about tissue and recovery in the United States. It is not clear what organizations are doing recovery, and it is relatively easy to enter the field, which is not well regulated (e.g., there are no mandatory guidelines). There appears to be a need to learn what entities are engaged in recovering tissues for transplantation and/or research. Ms. Agrawal stated that tissue banking and its regulation have been brought to ACOT's attention several times. While ACOT is specifically concerned with solid organs for transplantation, the public sees it all as the same field and area.

- *Mr. Tracy Schmidt, President, AOPO*

There are 58 OPOs in the United States. OPOs are interested in tissue recovery because these organizations are the gatekeepers for referrals for donations, and they also work on recovery as well, as the majority of tissues are recovered by OPOs. There is no centralized process or place for collecting data on this, however. Other than eyes, it appears that most tissue comes from OPOs. As noted, public trust issues affect both areas (organ and tissue); therefore, OPOs conduct much public and provider education on these issues. The AOPO had four recommendations for ACOT:

1. ACOT should encourage the establishment of an independent expert inquiry (e.g., by the Institute of Medicine) to assess the regulatory framework for both tissue and whole body donation. Such an inquiry would examine certification, accreditation, and what entities are currently in the field. The public is looking for organizations to protect them. Further, AOPO feels there is a need to limit recovery organizations to community-based organizations with nonprofit status, legally structured in such a way to support public trust. There is also a need to improve data collection on the national level, as there is currently no single source for data.
2. The FDA should have the role of requiring annual reporting of recovery activity (this could be Web-based reporting), and the establishment of industry-wide definitions—Mr. Schmidt noted that the definition of "tissue donor" is currently unclear and varies by location, which affects data collection. The goal would be to continue to improve the system to track the end-use of tissues.
3. CMS should use Hospital Medicare Conditions of Participation to ensure that hospitals and other OPOs are serving the public interest.
4. ACOT should seek public input on whole body donation programs for consideration by the whole committee. Some areas are having more problems than others and this feedback should be collected and considered.

Finally, Mr. Schmidt reported that AOPO is holding a summit meeting to include tissue processors, recovery agencies, AATB, AOPO, EBAA, and others. This meeting will be held on November 28, 2006, with the goal of improving public trust as an industry.

**Questions and Discussion**

Dr. Migliori asked, What proportion of tissue donations are managed by OPOs? Mr. Schmidt responded that about 80 percent of OPOs are doing tissue recovery work, although that is an estimate. Around 60–80 percent of all tissue recovered comes from OPOs. In terms of whether OPOs could do all of the tissue work and whether there is enough capacity, the answer is probably

yes, although that would vary by locale.

Dr. Solomon asked what the actual and potential risks are that are important to prevent. Mr. Schmidt answered that public trust and public safety need to be enhanced. In terms of public perception about donation as a whole—either whole body or tissue—30 to 40 percent of the U.S. public has concerns and is not fully committed to the idea of donation. Mistrust is a problem. Fraud and abuse are additional problems. Consent used to be a problem, but that has gotten better.

- *Patricia Aiken-O'Neill, President, EBAA*

The EBAA was founded in 1961 and currently has 83 member banks. EBAA members provide 97 percent of all corneal tissue used in transplantation. Members conduct 46,000 sight-restoring transplants annually and assist with significant medical research advances. There has been no transmission of systemic infection through transplanted eye tissue since 1987.

The EBAA was the first transplant association to establish medical standards, in 1980. EBAA's accreditation program includes a comprehensive education and technical certification program (which is voluntary, but all eye banks comply). In terms of data collection, eye banks are required to conduct tissue tracking as part of their accreditation requirements. Both the FDA and EBAA require banks to report adverse reactions in eye banking through an online system. The last phase of the comprehensive regulatory system was put into place by the FDA in 2005. It includes registration requirements, donor eligibility regulations (this concerns screening and testing), good tissue practice (GTP), and inspection and enforcement procedures.

To ensure the protective effect of FDA regulation across organ, eye, and tissue communities, EBAA seeks regulatory harmony between CMS and FDA when donors are shared. Specifically, EBAA recommends regulations to:

1. Modify Medicare Conditions for Coverage for OPOs relative to data retention requirements;
2. Modify the standard on adverse event reporting as part of an OPO written policy; and
3. Include an eye bank and a tissue bank representative on an OPO's advisory board (currently there is just a tissue bank representative).

EBAA also recommends that:

1. The Government allow sufficient time for the FDA's recently implemented regulatory structure (last published in June 2005) to work and to be appropriately evaluated; and
2. The Secretary write to State Governors to consider the adoption of Section 17 of the Revised Uniform Anatomical Gift Act (UAGA) of 2006.

Finally, EBAA's message is that, as partners in this process, our responsibility is to protect the donation process, to be accountable to the public, and to celebrate the miracle of transplantation.

- *P. Robert Rigney, Chief Executive Officer, AATB*

AATB welcomes the opportunity to present to ACOT and would also welcome an opportunity to meet with the ACOT tissue regulation work group.

United Network for Organ Sharing (UNOS) data from 2005 indicate that there were about 14,500 organ donors, and about 25,000–30,000 tissue donors that year; 5,000 (or 20 percent) are both organ and tissue donors. There were 28,108 organs transplanted in 2005; over 1 million tissue transplants occur in the United States each year and more than 1.5 million allografts distributed. In the last 20 years, there have been 10 million tissue transplants, while the last case of a viral transmission—of hepatitis C virus (HCV)—was in 2002, during the window period. The only other cases of HCV transmission were in the 1990s; tuberculosis has not been transmitted in 50 years; the last HIV transmission was 20 years ago, also during a window period.

In March 2005, AATB began to require nucleic acid testing for both HIV and HCV. There have been instances of bacterial contamination, of clostridium, in 2001, in which one person died. From 1998–2004, 14 cases of clostridium occurred, all from the same bank. They have massively changed processes since then. One case of fungal contamination occurred, in 1997. There has never been a case of cancer transmission.

The AATB believes the field is heavily regulated. Federal statutes that apply include the National Organ Transplant Act and the Public Health Service Act; regulations include those promulgated by the FDA, which has regulated tissue banks since 1993. State regulations also apply to tissue banks: Every State has some form of regulation under the UAGA. Also, private accreditation occurs through AATB; AATB member banks provide the overwhelming majority of tissues (95 percent) used for transplantation.

AATB's mission is to facilitate the provision of safe transplantable tissues of uniform high quality in

AATB's mission is to facilitate the provision of safe transplantable tissues of uniform high quality in quantities sufficient to meet the national need. The organization has established universally accepted standards to prevent disease transmission and to ensure optimal clinical performance of transplanted tissues and cells. AATB also accredits tissue banks and trains and certifies tissue banking staff. Six States require all of their tissue banks to be AATB accredited.

AATB standards were first published in 1984 and are now in their 11th edition. These standards address all aspects of tissue banking, including records, informed consent, containers, standards of practice, recalls, etc. These standards are references in more than 20 State statutes or regulations. AATB's Standards Committee regularly liaisons with other agencies including the FDA, EBAA, Centers for Disease Control and Prevention (CDC), and many others. The American Academy of Orthopaedic Surgeons has as a policy to use only tissue from AATB-accredited banks. AATB standards have served as a model for the FDA's current GTP regulations, New York Department of Health's tissue and cell standards, the European Union's Commission Directives, and many others.

AATB has also issued guidances (and are developing new guidance documents) to help the field. Guidances are in development on subjects that include donor family services, tissue donor screening, communicating with medical examiners, and other topics. AATB has also engaged in several important collaborations including projects with CDC, the World Health Organization, the Canadian Standards Association, and the Canadian Council for Donation and Transplantation, etc.

Mr. Rigney discussed cases involving tissues and tissue regulations. There was a clostridium death in 2001 (the Lykins case). In this case, AATB's time limits on retrieval were not followed and the AATB-accredited tissue bank refused the donor tissue. A nonaccredited agency took the donor and used a nonaccredited processor. In a second case, that of Biomedical Tissue Service, medical records were falsified, and consent forged by a nonaccredited organization. An AATB-accredited bank discovered these problems and brought in the FDA. In the third case, Donor Referral Services, a nonaccredited company, falsified medical records. This was discovered by an AATB-accredited processing company.

The AATB responds quickly and effectively when these cases come up. The organization's view is that AATB accreditation and standards are critical to preventing problems. The cases concerned nonaccredited tissue banks that violated AATB standards. Changes are needed to prevent such problems from occurring again.

At the ACOT May meeting, Mike Seely presented to the group on oversight issues for tissue banks; Mr. Rigney disagrees with the material that was presented by Mr. Seely at that session. We concur that safety is paramount and AATB requires an enormous amount of screening and testing. Any problems in tissue banking have to be addressed by the entire transplant community, however, not solely the tissue community.

AATB makes the following recommendations to ACOT:

1. First, do no harm (we advise that ACOT spend more time gathering information before acting);
2. Enact Federal criminal sanctions that would make it a crime to falsify donor consents or to intentionally falsify donor records;
3. Urge the enactment of the 2006 UAGA;
4. Require AATB/EBAA accreditation of tissue banks (use Joint Commission on Accreditation of Healthcare Organizations [JCAHO] or deemed status models);
5. Explore data collection requirements such as annual reporting by registered facilities; and
6. Investigate oversight and regulation of whole body donation for medical education and research.

**Questions**

Mr. Holtzman asked how many agencies are recovering tissue, how many are accredited, and what barriers exist to entering the business. The response was that AATB accredits 97 percent of tissue banks, some of which are located in Canada. The FDA could probably give more information on this subject as well. Several OPOs are accredited: 19 OPOs are accredited to do tissue recovery, and several also are accredited for processing. There is no barrier to opening a tissue bank, except that the operator has to meet many significant requirements. The inspectors appear at the facility pretty quickly, and it is hard to find processors to work with if they are not in compliance with regulations and standards. There are multiple levels of controls: By the FDA and by State and private accreditation agencies. TBAA is not averse to Federal regulations.

Mr. Holtzman asked if an organization went into business and was approved whether the FDA becomes concerned about issues such as falsification if the bank is not accredited by AATB. Mr. Rigney responded that the FDA can probably answer this better; FDA does not have the authority to regulate consent: This is regulated at the State level under the UAGA in each State. However,

regulate consent. This is regulated at the State level under the UAGA. In each State, however, AATB has extensive consent requirements and documentation requirements. Mr. Rigney clarified that TBAA has fewer standards on tissues for use in research settings, although they are trying to get more deeply involved with this subject. Most controversies have to do with nontransplantation uses.

Dr. Conti asked why there are any nonaccredited tissue banks in the first place. Mr. Rigney replied that TBAA cannot figure out why banks don't get accredited, but their best guess is that this is due to the amount of time it takes (about 9 months) and the number of inspections required. Some of the banks that only do one type of work with tissues (e.g., they just store or they just process) may not think it's worth it to go through the work required to be accredited. Banks must be reaccredited after 3 years.

- *William Zaloga, Blood and Tissue Resources, New York Department of Health*

Dr. Zaloga presented on New York State regulation of tissue banks. In 1990, the State amended its public health law to incorporate organs, tissues, and body parts. The State has broad authority to regulate any tissue from recovery to final use. A State Transplant Council exists, as well as technical advisory committees.

New York has a long regulatory history with respect to tissues, including the following regulations: Clinical Laboratory and Blood Banks (1965); Hematopoietic Progenitor Cell Banks (1988); Semen Banks (1989); Human Milk Banks (1990); Article 43-B, "Organ, Tissue and Body Parts Procurement and Storage" (1990); General Tissue Banking Standards (1991); Tissue-specific Technical Standards (1993); and Guidelines for Collection, Processing, and Storage of Cord Blood Stem Cells (1997).

There are significant challenges to regulations. There are multiple parties involved in a very complex process. There are issues of consent, donor qualification, recovery, processing, and transplantation. One donor may provide organs and tissues for multiple recipients. The technologies are dynamic. Finally, there is intense media scrutiny of issues not well understood by the public. Problems with regulation of facilities include inadequate consent process; processing deficiencies; failures to perform required testing; and unlicensed operation (rogue facilities).

New York State regulation requirements address licensing, director and medical director requirements, medical advisory committees, general technical standards, tissue-specific standards, and nontransplant tissue standards. Standards focus on donor selection and testing; donor and recipient consent; record keeping; labeling; processing; distribution; and quality improvement. New York has cradle-to-grave tracking of tissues. Technical standards address many tissues including cardiovascular, musculoskeletal, eye, skin, etc. They are very detailed and consistent with professional standards such as those of AATB. New York State employs surveyors who are technical experts in the field, who review the banks' applications, and who conduct onsite inspection for quality assurance processes.

New York has established administrative requirements for tissue banks, including the educational level and experience of the tissue bank director; that the medical director must be licensed in their State of practice; and that there be a medical advisory committee consisting of five members with expertise in the field, including infectious disease (and, for reproductive tissue banks, genetics). Tissue banks may apply for a special exemption from a specific standard in cases of medical emergency or special medical condition, or for a methodology unique to the processor.

To maintain the license, the bank must maintain compliance with applicable sections of Part 52 and Subpart 58-5, as determined by periodic onsite surveys; report errors and accidents to New York State Department of Health; submit annual activities reports; provide denominator data; file an annual application renewal; and report changes in its director, medical director and/or owner and followup with new application.

In terms of addressing the significant challenges associated with tissue banks, New York adopts the following solutions. Because multiple parties are involved, the State requires strict oversight through licensure. To address the dynamic nature of this technology, the State maintains an active role in revising its standards. To meet the wide media scrutiny of this field, the State works closely on public education efforts with the public affairs office. In order to ensure an adequate consent process, New York requires the processor to specify the types of tissue to be used, and for what purpose. In order to ensure there are no processing deficiencies, the State focuses on contamination testing, validating methods, quality assurance, etc. In terms of the role of the funeral home directors, New York is considering restrictions to their ability to recover tissues. To ensure that banks do not fail to provide required tests, New York's surveyors (who are experts in the field) consult with the banks. To prevent unlicensed operations, the State follows up to ensure compliance.

**Questions**

Ms. Conrad asked if the New York banks are inspected by both the FDA and the State. Mr. Zaloga

responded that FDA regulations supplement, rather than inhibit, State regulations. Tissue banks have to comply with both sets of regulations. Mr. Frieson asked if the tissue banks are AATB certified. Some are; the ones that are not sometimes have deficiencies and need more help from the State to be in compliance. Ms. Conrad asked what the impact would be on State licensing and regulatory functions if AATB-certification was required for all tissue banks. Dr. Zaloga felt that New York's regulations parallel the AATB's and that the standards are very similar and complementary.

- *Dr. Celia Witten, FDA; Office of Cellular, Tissue and Gene Therapies; Center for Biologics Evaluation and Research*

Dr. Witten spoke about the FDA's regulation of human cells and tissues and cellular or tissue-based products (HCT/Ps). Centers with an interest in this field include: The Center for Biologics Evaluation and Research (vaccines, blood and blood products, human tissue/tissue products for transplantation, cells, and gene therapy); the Center for Drug Evaluation and Research (drugs, some biological); the Center for Devices and Radiological Health (devices for treatment, implants, and diagnostic devices); the Center for Veterinary Medicine; the Center for Food Safety and Applied Nutrition; and the National Center for Toxicological Research.

The history of the FDA's engagement is one focused on infectious disease prevention. In 1993, the FDA regulated human tissue intended for transplantation (interim final rule: *21 CFR part 1270*; final rule published in 1997). In 1997, the FDA announced a proposed, risk-based approach to ***all*** HCT/Ps. From 1997–2004, the FDA published three proposed rules; all final rules became effective May 25, 2005 and codified as *21 CFR part 1271*.

*21 CFR Part 1271* is a platform for regulation of all human cell and tissue products, defined as articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer to a human recipient. (Tissues for educational and nonclinical research are not covered by the regulations.) For certain HCT/Ps ("361 HCT/Ps"), part 1271 is the ***sole*** regulatory requirement. For HCT/Ps also regulated as drugs, devices, and/or biological products, part 1271 ***supplements*** other existing requirements.

Included are reproductive cells and tissue (e.g., semen, oocytes, and embryos); hematopoietic stem cells from peripheral blood and cord blood; cellular therapies (e.g., chondrocytes and islet cells); musculoskeletal tissue (e.g., bone, ligament, and tendon); skin; ocular tissue (e.g., cornea and sclera); human heart valves; and human dura mater. Not included are: Tissue/device and other combination therapies; vascularized organs (Health Resources and Services Administration [HRSA] has oversight); minimally manipulated bone marrow (HRSA has oversight); tissues intended for educational or nonclinical research use (not intended for transplantation); xenografts; blood products; secreted or extracted products (e.g., human milk, collagen, and cell factors); ancillary products used in manufacture; and *in vitro* diagnostic products.

Dr. Witten described the FDA provisions and regulations and the content of specific subparts. Subpart A explains what is regulated and what needs premarket review. Subpart B describes who needs to register, how to do that, and what information has to be provided. Subpart C describes donor eligibility, screening, testing, and exceptions, as well as relevant communicable disease agents and criteria for adding new ones. Subpart D describes current GTP—methods, facilities, and manufacturing controls to prevent communicable disease transmission—and lists many topics in GTP of the rule such as procedures, records, and tracking. Subpart E gives additional requirements reporting and labeling. Subpart F describes the FDA authority for inspection and enforcement. In addition, guidances are available from the FDA to aid in implementation of these regulations.

**Questions**

Ms. Agrawal asked if the FDA has any regulations on patient consent, and the answer was no. Dr. Migliori asked if people must use FDA-approved centers, in other words, if there was any way to avoid FDA oversight. Dr. Witten replied that you cannot distribute anything that's not approved. Mr. Holtzman asked if the FDA has a good handle on everyone who is recovering tissues in the United States. The response was that if someone is recovering tissue for something other than transplantation, they are not covered by the FDA. Second, in terms of the universe of facilities that are recovering tissues, the FDA only knows who reports to it and is on the FDA list; there may be entities that are not on the list. Third, in terms of whether the FDA knows about their operations, they are looking at this on both the recovery side and also with respect to implementation of the recent rules.

Dr. Vega asked why the FDA cannot require that any company involved in tissue for transplantation must be certified by AATB or another such body. Dr. Witten commented that this concept comes up often. The answer is that there is an issue of outside influence and conflict of interest. There is a legal line, which has to do with a group such as AATB being or not being an outside group, and how independent the groups are. Dr. Conti asked about a recent case in which tissue was processed by a facility that was not accredited by AATB and asked if the facility had been approved by the FDA. Dr. Witten said that she cannot comment on a situation that is under investigation.

Dr. Witten said that she cannot comment on a situation that is under investigation.

Ms. Conrad said that it's encouraging to hear that there are questions about implementation of the rule. One needed change is to address the case of facilities that have two locations that are under two different FDA offices—they are subject to two inspections at any time and this is very burdensome.

**Entertainment (Mis)education: Findings From a 2-Year Media Monitoring Study**

*Dr. Susan Morgan, Purdue University*

Dr. Morgan noted that ACOT's mission is to increase public confidence and assure the public that the system is equitable. One barrier to these goals is the media: Negative portrayals of organ donations affect the public's willingness to donate. To understand the role of the media, the Division of Organ Transplantation (DOT) provided funding to monitor the major networks and news channels for coverage of organ donation and the allocation system. The subject comes up quite frequently; on average, it appeared every 8 days just on the four major channels examined in 2004–2005. Thirty entertainment shows included story lines or subplots about organ transplantation, not including news programming, late-night television, or cable.

In a prior research study, family members who oppose donation cited the entertainment media (not the news) as the source of their negative views. Some nondonors use the negative media content to justify their not donating. They feel that the media fiction (such as the existence of a black market for organs) must be based on some kernel of truth; entertainment media thus reflects the public's worst fears about organ donation. This happens because the shows use accurate medical terminology, so viewers believe that everything else is accurate too. Many entertainment shows are based on real stories drawn from the news media, which also leads viewers to assume that all of the content is based on fact. In addition, there are few other sources for information about organ donation to counteract these views that, because of syndication and repetition, are seen over and over again by the viewing public.

It's important to remember how people cognitively process stories (including entertainment media stories). Magnetic resonance imaging demonstrates several facts: That stories are easy to remember; viewers suspend disbelief while hearing them; and that people forget the source of the stories (they can't remember that they learned something from a fictional show rather than the news). Also, when people watch television, they have the feeling they have seen it for themselves, and lived it vicariously; the more "into" a story someone is, the more factual the information seems to them. Specific myths often have to do with the black market, misperceptions about brain death, and fears about the inequality of the allocation system.

Public opinion studies reveal that 50–80 percent of people surveyed believe that there is a black market for organs in the United States. In fact, there are so many story lines about black markets, some of which last for a long time, that it's hard to set limits on which ones to look at. Dr. Morgan showed clips on this subject from *One Life to Live*, *Crossing Jordan*, and *Boston Legal*.

Fifty percent of people believe that one can recover from brain death, so why donate the organs if you might wake up otherwise. Dr. Morgan showed clips from *Grey's Anatomy* in which someone who has been declared brain dead later woke up.

Seventy-five percent of people believe that the medical/organ allocation is untrustworthy and unfair. Dr. Morgan showed clips on this subject from *The Simpsons*, *Grey's Anatomy*, and *The Unit*. Fourteen percent of people from one survey reported that they fear doctors will take their organs before they are dead. Dr. Morgan showed a clip from *Grey's Anatomy* on someone waking. People are also worried about being "cut up," which might reflect concerns about bodily integrity and the coldness of the medical system. Dr. Morgan showed a clip from *Grey's Anatomy*.

There are accurate portrayals in the entertainment media, also, although not many. Through the nonprofit contractor Hollywood, Health & Society, transplantation professionals, and the media work together to try to ensure more accurate portrayals. Examples of shows with more accurate and/or positive portrayals include *Num3ers* and *Scrubs*. (Clips were shown from these shows with more realistic portrayals of the organ transplantation process.) Such efforts to work with scriptwriters are important to improve what the public sees on this subject. This can help counteract the connection between messages and stories from television and people's preexisting fears about organ donations.

The way that the media presents organ donation has an impact on public attitudes about organ donation. It's important to remember that viewers suspend their critical thinking when they are engaged in the story-telling process so, if no counterarguments are seen by them in other places, damage can be done. People need to know that brain death is different from being in a coma; they need to know that the allocation system does not give preference to one group of people over another.

**Recommendations:**

**Recommendations:**

- *Advocacy:* Through a contract award, DOT has funded Hollywood, Health & Society to educate writers and producers on this issue.
- *Activism:* There is a huge group of professionals and recipients who care about this issue (including the 93,000 people on the list) who can be mobilized to speak out against inaccurate depictions. We should use the experience of the AIDS and breast cancer activists who waged efforts against inaccurate stories.
- *Attention:* We need to pay attention to this issue and reach out to shows and writers who need more education on this subject.

**Questions**

Dr. Conti remarked that the findings are stunning, especially with the shortage of organs that is occurring. He asked about specifics on how the HIV/AIDS and breast cancer communities' activism worked. Dr. Morgan said that it was basically a lot of angry people speaking out. Gay activists particularly used their unofficial contacts inside the industry to influence the stories and generate opposition against feeding public fears about HIV/AIDS. The bottom line is that writers don't want to generate a huge, angry response because it hurts them in the long run and brings the producers' and executives' attention to a particular show.

Dr. Scantlebury asked about the percentage of writers who are interested in being educated. HRSA

staff noted that more and more groups are calling for help on this issue. For example, *ER* is talking with staff today. Screenwriters call Hollywood, Health & Society, which then calls a participating entity responsible for providing more information, which could be an organization like CDC, HRSA, the National Cancer Institute, or someone from an individual transplant program.

Dr. Morgan commented that stories about problems connected to tissue transplant seem to be driving an increase in entertainment coverage of transplantation as a whole.

Recently story lines have appeared on *Nip, Tuck*; *Boston Legal*; *The Simpsons*; *Veronica Mars*; and others. It has spread to being included in shows other than crime and medical shows. Because no one is objecting, the stories are getting worse.

Larry Hagman described his experience being on *Nip, Tuck* and the plot of the current storyline. He said that his character dies, and his wife comes and takes the character's kidney.

Dr. Morgan added that viewers' responses about organ donations tracked with the content of the episodes that were being tested: The viewers report back as fact what was included in the show (that the allocation system is broken, that there is a black market or, more positively, that more people need to sign up as donors).

Dr. Solomon said, in thinking about how we can use activism to change this situation, we should consider how to capitalize on those who are on the list or have received a transplant or are families of recipients. We are organized as a system, but not as advocates. Dr. Morgan said that the first step is to educate and inform the providers and the professional community: People do not know that this is a problem. She is also working with Transplant Recipients International and other groups, and people seem interested in getting involved. It would be beneficial if OPOs and coordinators were to get involved in this and disseminate information to people on the list.

Dr. Scantlebury commented that DOT should look at this issue and put some funding behind it. We need to get the correct information back onto television and look at having spokespersons and public relations outreach. It was noted, however, that studies on coverage of mental health issues have found that a public relation or public education message inserted into a show with that content does not make much of a difference in perception. The way the brain interprets stories makes it important to insert the messages into the story line itself. Until the media is motivated to not ignore the accurate information, they will do so in favor of an exciting storyline. This is a business, but we should be clear that they should not make a profit at the expense of people's lives. We can be more proactive about this.

**UNOS Department of Evaluation and Quality Activities Update**

*Deanna Sampson, Department of Evaluation and Quality, UNOS*
*Walter Graham, Executive Director, UNOS*

Ms. Sampson spoke about OPTN membership standards, policy compliance, and enforcement. As everyone knows, there are not enough organs, so UNOS ensures that patients are appropriately listed and that organs are appropriately allocated. UNOS' contract with HRSA requires the existence of survey instruments, a peer review process, and data systems to conduct ongoing and periodic reviews of each transplant center and OPO to verify their compliance with the final rule and with OPTN policies.

In terms of the allocation analysis, 100 percent of allocations are reviewed, as are all member complaints and self-referrals. When it appears that there is a potential violation, UNOS gathers data, conducts a written inquiry, verifies responses with onsite visits, and takes the information to the review committee Membership and Professional Standards Committee (MPSC). The main potential problem areas are (1) that the recipient was not on a match run, (2) that the organ was offered and rescinded, or (3) that an out-of-sequence allocation occurred.
In 2005, 21,000 allocations were reviewed—1,084 inquiries were sent; 674 member self-referrals and 356 organ center referrals were investigated; 21 member complaints were explored; and 5 emergent issues identified. UNOS conducts field audits of each heart, lung, and liver program, each OPO, and other members as necessary. When UNOS goes onsite to a transplant center, staff examines candidates' medical records, data submission, data completeness, and patient notification. They verify that ABO typing was done twice prior to listing, and that ABO verification occurred prior to the transplantation. They also look at vessel recovery and storage.

Onsite work is divided into two score cards: (1) A clinical scorecard that looks at the accuracy of candidate listing status, ABO typing, ABO verification prior to implantation and (2) an administrative scorecard that looks at medical records being available for review, data entry errors, patient notification, and removal of candidates from the list. From 2000–2005, for liver programs across the country, compliance on the administrative scorecard was 89 percent and 95 percent for the clinical scorecard. For heart programs, compliance on the administrative scorecard was 90 percent and 94 percent for the clinical scorecard.

OPO reviews are conducted for consent for donation, ABO determination, serology testing, pronouncement of death, data submission, and accuracy. Site visits have been conducted for all OPOs and UNOS is developing scorecards for OPOs right now.

There were 109 referrals from the Policy Compliance Subcommittee to MPSC from July 1, 2005, to May 31, 2006. The referrals came from site survey results, member complaints, organ committee referrals, data submission, ABO discrepancies, allocation analysis, and metrics-driven findings. The actions taken on these cases during the due process period included deeming the facility to be a member not in good standing (7 cases); placing it on probation (3 cases); or sending a letter of warning, admonition, or reprimand (10 cases). Final action in these cases included removal of designated status to receive organs (two cases); deeming the facility to be a member not in good standing (one case); placing it on probation (one case); or sending a letter of warning, admonition, or reprimand (two cases). The committee also continues monitoring and may reaudit or conduct another site visit.

UNOS also conducts a metrics analysis to help identify any problems at a center or an OPO. This analysis looks for problems before a site visit occurs. There are about 20 metrics that serve as indicators that might suggest possible violations that need to be examined. The metrics for the waitlist are: Metric 1—modification or disparity in ABO; Metric 2—percent of heart 1A(e) and (d) greater than 14 days; Metric 3—total status 1A heart days; Metric 4—percent of liver status 1A; Metric 5—total status 1A liver days; Metric 6—M/P analyses; Metric 7—percent of patients at downgraded score; Metric 8—consecutive turndowns; and Metric 9—inactive programs with active patients.

Allocation metrics are: Metric 10—accepted for 1 patient, transplanted into another; Metric 11—allocations to candidates not on MR; Metric 12—percentage out of sequence placements; Metric 13—payback debts; Metric 14—0MM; and Metric 15—PTR code and data entry. Other metrics include: Metric 16—early deaths; Metric; 17—intraoperative deaths; Metric 18—graft and patient survival; Metric 19—percentage relistings; and Metric 20—data submission.

To date, the metrics have prompted 347 subcommittee reviews from July 1, 2005, through May 31, 2006. Of these, the recommended action was to place the facility on probation (1 case), have the facility voluntarily deactivated (3 cases); and continue to monitor the facility (128 cases).

Walter Graham, the Executive Director of UNOS, spoke about policy compliance and the future of enforcement. For a facility to come off probation, it must pass unscheduled, onsite visits, submit additional evidence, and pass additional audits. The harshest outcome is to be deemed a "member not in good standing." In these cases, public notice is given, in writing to the Secretary, OPTN members, and current and past patients. These personnel may not participate in OPTN work as

officers, board members, or committee members. Those in violation of Section 1138 of the Social Security Act can have their privileges suspended, cease receiving Medicare funds for any service (e.g., beyond transplants), and be prohibited from receiving organs or listing patients on the OPTN waiting list. In the last year, two hospital programs have lost their status.

Due process steps are taken unless there is imminent threat to the quality of patient care. In all other cases, steps include interview and a hearing. A formal report including a transcript is produced and the member can appeal the decision. When a member is on probation or deemed to be not in good standing, it has to fully comply with OPTN requirements to be reinstated. The board restores

membership; but if the Secretary was the initiator, the board cannot affect the decision.

All members that have been part of such actions have complied with ongoing monitoring Major changes have occurred because of the system. Sites have changed their leadership and personnel. In two hospitals, the CEOs were fired. Programs have been restructured and policy recommendations implemented. Experts have come in to help the sites solve their problems, for example, by restructuring the medical records office.

The MPSC process has resulted in 115 programs closing and withdrawing from the OPTN; these were facilities that were not able to correct the identified problems. Many people do not know that this has happened, because it's been very discreet; but there is aggressive monitoring of the system. In the future, changes will be made that will include helping patients and personnel report problems to the OPTN more quickly, such as through a patient call-in line, an e-mail address that can be used to report problems, and a confidential hotline for personnel.

Proposed bylaws changes for compliance that will likely be approved in December include: Increased surgeon/physician coverage; categorization of violations; changed evaluation of performance by looking at organ acceptance rates and waitlist deaths; referring doctors to local peer reviews by members; providing notice to OPTN of reviews and adverse actions by CMS, JCAHO, State agencies and vice versa, to improve communication; and reimbursement to the OPTN of costs over $500 for violations on the part of members.

More ideas include ways to let patients know there is a problem. The OPTN is beginning to discuss with DOT how to better alert patients. More patient education efforts are needed about what is available to them in terms of data and survival rates. The OPTN is sending patients information when they get onto the lists. We want more training programs, which might become mandatory. We want to add to the early warning metrics so that we can identify problems before they get too bad.

**Questions**

Dr. Migliori noted that the process described by UNOS makes transplant quality something that is unmatched elsewhere in American medicine. It's very transparent and a good way to educate people about the system and the protections contained within it. It will enhance confidence, as we make referrals that patients will receive the best care possible from the best source. He noted that the National Transportation Safety Board (NTSB) does this kind of quality assurance well, in terms of flight safety, and offers good models. Mr. Graham responded that the Chair of the NTSB is a former UNOS employee, so there are good linkages with that agency.

Mr. Frieson asked about the "hook patient," that is where a kidney comes in to the center, but isn't well suited for transplant. The answer was that the OPTN looks at every matched run sequence, where the allocation occurred, and the turn down reasons. There are cases in which the patient gets the offer but then someone else gets transplanted. However, the intended patient is not always able to receive the organ, in which case it would be offered to another patient.

Mr. Frieson asked about status 1A patients who seem to stay on the list forever. This is a metric that UNOS checks; there was such a case a few years ago, of someone who was on the list for a

long time. The OPTN can look at programs and see how long a person stays on an urgent status listing and ask for explanation of what is happening with those patients. There have been instances where the OPTN has identified violations-one center is on probation; another one closed their program, fired their staff, and transferred all of their patients to another program.

Mr. Hagman commented that he had had that exact experience. A hospital in Los Angeles closed but he had not received any prior notice in advance of the closure. Patients were scrambling to find new places for both transplantation and followup. The OPTN staff responded that, in that instance, the OPTN was on the phone with the hospital CEO and suggested that the hospital announce the pending closure to the public, but it got leaked before that could happen. The OPTN had taken action against that program because of systemic problems and the Secretary closed them down for good. Their liver program wasn't participating in the compliance process and there had been misallocation, followed by a falsification of medical records and false information provided to the OPTN and the patient. A whistleblower revealed the problems to the OPTN and legal actions have occurred because of this.

Mrs. Boone suggested that information packets be provided to both patients on the waitlist and living donors. Mr. Graham committed to provide this information for living donors. He noted that, at most recent living donor committee meeting, there was a presentation about an outside organization offering a registry in four hospitals that have had good experience with both followup and self-reporting of data from donors. The OPTN is committed to finding a solution to this need. Dr. Migliori agreed that it is important to consider living donor outcomes, which are important to know in order for people to truly make informed choices. He urged the OPTN to consider building quality assurance outcomes data for living donors so this factor is also attended to.

Ms. Principe commented that cultural diversity is a factor and that it's important to be careful about how people perceive concepts and information. She urged the OPTN to look at this with deliberation. Mr. Graham agreed that patient education materials are most informative when they are created in the target language rather than being translated. Mr. Graham also noted that the OPTN has a relationship with the Virginia Commonwealth University's language department to help the hotline when needed.

**New Science in Organ Transplantation**

*Dr. Kenneth Chavin, Medical University of South Carolina*

Dr. Kenneth Chavin presented on new science in transplantation. We are now in a world where facial transplants are possible; there is now a registry with 18 hand transplant patients, which is an operation that was first conducted in 1998. He noted that immunosuppression to prevent rejection is very important in these cases There have been six cases in which patients lost their transplanted hands when they failed to take their immunosuppression medications. Nerve regeneration in these cases is still poor, but motor function is better than it is with a prosthesis. Nonetheless, social and psychological concerns about well-being still remain for these patients. Now we do not worry about how to do transplants, but how to optimize them; we are in the phase of making a good thing better.

Composite transplant has not had an impact on patient survival; graft survival is acceptable in compliant patients. While unparalleled research potential exists in this area, Dr. Chavin knows of only one research grant that is funding it. There is greater support for clinical research, including much funding from NIH and other Federal grant support. Grant support for clinical research includes the tolerance network, the living donor network for liver transplant, diagnosing rejection, and the Organ Donation Breakthrough Collaborative.

The collaborative has resulted in an increase in the number of organs available; it's working and more organs are being donated. The question is what kind of organs are they, and how we can make these organs last longer. If we look at different categories of standard criteria donor (SCD),

DCD, and extended criteria donor (ECD), we can see that in all groups have increased their numbers. However, the question remains whether we have increased the number of good donors or reduced the incidence of delayed graft function. Ultimately, ECD has highest delayed graft function, then DCD and SCD. We need good kidneys that function well, and not all of them are going to. We have to figure out which ones are best.

In terms of DCD liver donations, the numbers are going up and coming from older donors. Where liver cells are not working as well, graft survival is lower for DCD, compared to ECD donors. The livers are not equivalent. We are transplanting more people, but some of the organs are not the same quality. Use of ECD and DCD organs is disseminating rapidly, but the science of this area needs to continue to be studied. There is a higher risk and the question is whether it is acceptable.

In terms of living donation, data from the Dutch Transplant Foundation shows that it has a 50-percent efficacy. It's an easy solution for a cross-match positive. When we think about living liver donations, however, we must remember that it's a big trauma for the donor. It's a serious operation. We need to think about who is most appropriate to be conducting the operations. The Adult to Adult Living Donor Liver Transplant Cohort Study (sponsored by HRSA, the National Institute of Diabetes and Digestive and Kidney Diseases, and the American Society of Transplantation Surgeons found that the number of cases a hospital performs is crucial to patient survival. If a hospital does more than 20, they do much better (better even than with DCD). There is a learning curve.

There is also new immunosuppressant news from the World Congress. For example, steroid withdrawal programs are coming along, generated by the need to get people off immunosuppressants. For costimulate blockade with belatacept, death with loss of graft is now less at 1 year, which is headway.

In the kidney world, if we can prolong kidneys longer, the patient does not have to go back on dialysis or get a new kidney transplant, so it helps even more people. With new chronic allograph nephropathy, patients improve. Long-term results from the University of California at San Francisco show that, globally, people do well with this regime. Costimulation blockade has been tested in Phase II and it is clearly efficacious. In addition, there is a new way to administer cyclosporine-inhaled cyclosporine. Aerosolized cyclosporine is helpful and increases the number of years patients go without complications.

Then, on biomarkers: We are using genomics and proteomics as a replacement tool. There are new markers for urine samples for kidney recipients and it is possible to use FOX03 relative to the proteins. Finally, on T cells: As we apply multiple molecules to T cells, we can better see potential rejections. This will help us detect rejections, and fewer rejections are good for everyone.

**Questions**

Mr. Holtzman said that it's estimated that 20 percent of adult livers can be split; given that 15 percent of those on the waiting list are pediatric recipients, why not require the livers to be split and get rid of all of the pediatric cases on the waiting list? Dr. Chavin said that, actually, the policy has changed so that now children do get preference, although it depends if they are at a center that does splits and where the donor is. Dr. Lorber said that his recollection is that the mortality among pediatric cases waiting for livers is very low.

Dr. Leffel asked if genomic markers are going to be applicable to other solid transplants. Dr. Chavin noted that the turn-around time for this analysis takes several days, so it is currently too long. If it can be reduced down to a few hours, then we can use markers and can develop organ-specific markers.

**General Accounting Office (GAO) and Inspector General Studies**

*Dr. James Burdick, Director, DOT*

Dr. Burdick updated ACOT on several items. The collaborative has been successful in increasing the number of donors and transplants. There is a concern that the transplant programs are not being as effective as they could be at using the new "abundance" of organs. He wants to emphasize that the collaborative's message is one of action and we want the field to be focused on action.

The GAO is looking into the problem of noncompliant programs; they have met with the DOT and have begun their study. The Inspector General may come in, as well. The GAO is also studying pediatric immunosuppressants; HRSA and CMS will both be involved in this.

On the subject of the media, Dr. Burdick reported that he had just spoken with writers from ER about liver donation; they were interested in getting it as right as possible. Most of the contacts that are part of the Hollywood, Health & Society group are situations where the screenwriters approach us, rather than the other way around. We are also working with the OPOs to conduct public events/education in conjunction with programming that occurs as a result of these efforts.

Finally, ACOT members viewed a preliminary version of a movie celebrating the anniversary of organ transplantation.

**Public Comment Period**

- Donna Luebke: She is a Nurse Practitioner from Cleveland, OH associated with Metro Health Medical Center. She is also a living donor and advocate, as well as an educator. As discussed earlier, we have drafted a Living Donor Bill of Rights. It outlines issues that living donors face and what their care should look like. People self-refer and professionals refer patients to us. When a donor has a complication that is not addressed in postoperative period, or they have insurance problems, that's when they come to us. We work with centers to help the donors.

*The meeting adjourned at 4:15 p.m.*

**Friday, November 3, 2006**

**Followup and Next Steps for ACOT Groups**

Ms. Agrawal noted that it does not appear that there is consent yet on tissue regulation. The FDA is not focused on it, and it's unclear to what extent the private accreditation side is, either. There also seems to be very little, if any, regulation of tissue that is procured for things other than transplantation.

Ms. Conrad stated that there is a concern about whole body donation, where there seems to be less oversight except at the institutional level. The Iowa Donor Network often gets questions about whole body donation. She said her OPO had not previously explored the facilities in their area in depth, however, they are now beginning to collect information to assess their quality. She will bring the information back in May to ACOT.

Mr. Holtzman said that the tissue work group members are meeting soon; the sense is that people feel that regulation is necessary. Part of the issue is that it is not known who is recovering tissue. There will be a push to identify the players and then to explore whether there is a need for certification and/or accreditation. It would not be inappropriate for ACOT to recommend something on this subject, whether that is to encourage studies about who is recovering tissues for research or transplantation and/or recommendations for certification/accreditation to protect the public from inappropriate players.

Dr. Leffel reminded the group that, in the eyes of the public, donation is donation and all of the

areas affect one another. Likewise, transplantation is transplantation. ACOT should not shirk the issue. Tissue transplantation, stem cell transplantation all will become bigger issues in the future

issue. Tissue transplantation, stem cell transplantation-all will become bigger issues in the future.

Ms. Conrad noted that they are starting to be evaluated on how many organs they give to research facilities, so it is necessary to know who these facilities are and what their quality is. There are a lot of smaller organizations, some of which are for-profit organizations, about which very little is known. Dr. Migliori commented that if the reward for a research organ becomes bigger than the reward for a transplantation organ, it will become a problem.

Ms. Principe applauded ACOT for taking on this issue and for arranging the presentations. It's unfortunate that tissues and organs are separated. There needs to be more collaboration and oversight. It's surprising that there are tissue banks and facilities that are not under certification and that it's voluntary to be certified. She would recommend taking a close look at the voluntary certification process in tissue banking and doing something about it. In New York, there have been issues with tissue banks and how they affect transplantations as a whole. It is true that it's all the same to the public.

Mr. Holtzman concurred that ACOT should work on this at the next meeting. It seems that the FDA is moving ahead with practices and surveys; 6 months from now, we'll know more. The Inspector General may be getting into this from a regulatory side, too. It would be good to see firm recommendations come out of this.

Ms. Agrawal said that the work group will continue to work on this issue; interested parties who wish to be involved should contact Mr. Aronoff. It will be useful for Mr. Holtzman to report back from the working group on what happens at the upcoming November meeting (It would also be informative if the way the work groups report out is changed. At the May meeting, therefore, give a report that frames the issues that the work group looked at, describe the conversation that occurred in the work group, and then offer recommendations. In other words, there should be more background of the issues and options, as well as a more detailed rationale for the recommendations that will be made.) Mr. Aronoff said he would arrange a meeting of the tissue work group after the upcoming November Salt Lake City meeting on the subject.

In terms of public solicitation of donors, Ms. Agrawal asked if the group should separate into two subgroups on public solicitation for (1) deceased donors and (2) living donors. It may be duplicative, so the groups will have to coordinate, but the issues are very different.

Mrs. Boone reminded the group that it's almost a conflict to say we're going to solicit living donors but can't really gain any real informed consent due to the lack of long-term followup of these patients. It is strange that surgeons are not more concerned about this when they ask for consent.

Dr. Solomon concurred that the issues should be separated because the potential risks are very different. For living donors, the concerns are payment, commercialization, and the lack of followup. For deceased donation, the concerns are about fairness of allocation in the system. One area of confusion is directed donations; it should be further explored to determine if there is any possibility or necessity to limit this at all. We do not want to discourage live, directed donations; so, if you cannot limit living directed donations, then can you limit deceased directed donations? They are ethically very different and it may be possible to say that directed living donations are acceptable, while directed deceased donations are not morally justified. She asked about the free speech aspect.

Ms. Agrawal noted that, generally speaking, the constitutional protection of freedom of speech prevents the Government from limiting or restricting free speech except in narrow circumstances. Congress cannot limit organ solicitation. It might, however, be possible for Congress or the Secretary to say that there can be no solicitation of designation of organ donation in the ICU because of the fear of coercion. That might be a reasonable restriction under the Constitution.

Dr. Solomon said that there is a policy perspective that is outside of this entirely, and that is a national policy to preserve fairness in allocation of deceased donor organs. One can say, with this perspective, that there may be no directed deceased donations except under certain circumstances. When based on principles of fairness, this could work. If ACOT doesn't want to take that approach to set such a policy, then it can probably only provide guidance on how to explain it, and we need to scale down the goal. Ms. Agrawal commented that, however, both State and Federal laws allow directed deceased designations.

Dr. Lorber suggested that ACOT might want to make a strong recommendation to the Secretary that the whole idea of designation be reconsidered, knowing that it will take years. Maybe ACOT should think about short-term goals as it gets into the details of this, if it's in the public's best interest to change designation policies.

Ms. Principe said that the National Organ Transplant Act covers buying and selling organs as well as establishing the OPTN to ensure an equitable and fair allocation system. ACOT is obliged to consider both. On the exchange of money, it is difficult to know if this happens in reality or not. It's about education, particularly around solicitation, so that the public understands why it's important. Dr. Lorber responded that that's the perfect example of priorities. It would be easy to put together a

Dr. Lorber responded that that's the perfect example of priorities. It would be easy to put together a program that gets specific information to the public about the potential dangers of types of directed donations and solicitations. That would be constitutional.

Dr. Gruessner, who attended the meeting as a speaker, noted that restricting solicitation is difficult. Many donors do not know what they are getting into. Many people show up for donations because a priest or a minister tells them to go in and offer their liver, but they do not know what the long term-effects are and they don't know what the outcomes might be. In Japan, they've found that 15 percent of liver donors cannot be reintegrated into the society (e.g., the donor cannot attend school, work). Potential donors, regardless of how enticed they are, must know the true risks.

Ms. Agrawal said that there seems to be consensus to divide the work group into issues of public solicitation of (1) deceased donors and (2) living donors. She reminded members to let Mr. Aronoff know if they want to be in one of the groups. Also, a number of recommendations have been made by predecessors to this group; we will ensure that work group members get as much information as possible about the prior work of ACOT members on this subject. Finally, Ms. Levine will consult with the groups on the legal perspectives.

She asked if there is followup that needs to be done on the media presentation. Dr. Solomon commented that the take-home lesson was that the best way to respond to the negative media coverage is to create a grassroots advocacy campaign in which stakeholders annoy the broadcasting companies to change their ways. ACOT's legal and programmatic role is, however, unclear. HRSA could award a contract with Hollywood, Health & Society or other organizations to generate this campaign.

Dr. Scantlebury agreed that this is a subject worth attacking from a work group perspective. It would be valuable to connect with the appropriate people and see what can be done to counteract the negative shows. A work group can consider agencies and sectors of the transplant world that can assist HRSA with this. For example, Donate Life America is the national voice for organ donation and would be an appropriate organization to link to work towards dispelling this negative image. Mr. Hagman said that repetition is the best way to get something across to the public. In Florida, a recipient was successful in getting the State license plate to include the language: "Donate Organs Pass It On" on the official license plate. You see it everywhere and that repetition is really helpful in educating the public.

Ms. Agrawal asked members to let Mr. Aronoff know if they want to work on the media group. Given the total number of ACOT members and their other interests, Ms. Agrawal and Mr. Aronoff will assess whether there are enough members to work on this issue. In any case, we will not take it off

the table, but we will assess what to do first.

Finally, the recommendation on Medicaid Parts B and D was addressed. It seems to be an information problem with pharmacies and beneficiaries. It is unclear what the role would be of a work group, other than connecting with patient advocacy groups and/or pharmacy groups, on an education campaign. Ms. Robinson said that ACOT needs to be attentive to the situation in which patients give up and go without their medications, or can't get through on the hotlines. A HRSA staff member suggested that beneficiaries could be asked if they are transplant recipient when they register for Medicare coverage, and then it would be part of their beneficiary records and easier to track.

Dr. Lorber raised the issue of generic substitution (there are generics for only one immunosuppressive now, but there will be more later). The way that the FDA has chosen to evaluate cyclosporin's multiple preparations is problematic. None of the preparations are the same, and each is handled biologically differently. These are dose-critical drugs, which is relevant. Ms. Robinson concurred that this is an issue that makes a huge difference for the patient and is, further, about ensuring that the transplant is successful so that patients will not need a new transplant.

Ms. Agrawal stated that the work group will continue to meet; members should let Mr. Aronoff know if they want to be on it. The various work groups are responsible for deciding what they want to present or raise at the May meeting.

**Pancreatic Islet Transplantation: Status of the Field**

*Dr. Rainer Gruessner, University of Minnesota*

Dr. Gruessner presented on pancreatic islet transplantation. His background is in transplantation for diabetic patients. The field of transplantation for diabetic patients has evolved, and currently the research progress on islet transplantation is very high. He discussed what has been accomplished clinically.

The problem is that conservatively there are 80–90 million people who are diabetic. At least 1.5 million people are newly diagnosed with diabetes each year and it is the sixth-leading cause of death in the United States. There are geographic variations of end-stage renal disease (ESRD) in

the United States. Among whites—and a huge increase in the United States—overall. The problem is self-inflicted. We don't take care of ourselves and we eat too much, and the situation is getting worse.

An acute complication for diabetics' health is hypoglycemia; 25 percent of patients suffer at least one episode of severe, temporarily disabling hypoglycemia, often with a seizure or coma, in a given year. Four percent of deaths of Type 1 diabetics have been attributed to hypoglycemia. There is a hemoglobin level that is right for patients but, over time, the patients also develop other problems and the progression of secondary complications is likely.

There is a question about whether it's necessary to transplant the whole kidney, or if it's possible to use only the cells that produce insulin. Only about 2 percent of pancreatic cells produce insulin. So, it would be beneficial to transplant only the insulin-producing cells into patients with diabetes. The pancreas first rejects those cells that do not produce insulin; now we can detect this rejection early (in the first 5–6 days) and can reverse rejection in 95 percent of cases. Without this early detection system, however, it is necessary to rely on the patient's blood sugar levels, and it's much less successful.

Dr. Gruessner described the process for islet transplantation. It is better, safer, and easier for the patient; but we need to ask if the results are as good for patients. We need an integrated, complementary approach that includes both pancreas and islet transplantation. With ESRD, many patients will need both a pancreas and a kidney transplant. The immunosuppressant needed for pancreas and islet transplantation is the same; the only difference is invasiveness of the surgery. With pancreatic transplant, there is high efficiency, but it is major surgery. Islet transplant, on the other hand, is minimally invasive, but is less effective.

Pancreatic transplantation was first done in 1966 and has been rising steadily worldwide—there have been about 25,000 to date. Kidney disease patients are about 70 percent of the cases; pancreas transplant after a previous kidney transplant are about 10–15 percent; 5–10 percent have no kidney problems, but have diabetes problems instead. The 5-year patient survival is around 80–90 percent; this has gotten a lot better over the last 15 years. In terms of improvement over time of graft function, the marker of 50 percent of transplants working has improved since 1998. Combined procedure patients do best, as, for some reason, the kidney protects the pancreas. Reasons for the outcome improvements include technical improvements (e.g., a second operation was needed because of bleeding) and reductions in rates of rejection.

In terms of quality of life, when one looks at net life survival benefit, it is better for those who have diabetes and receive both a pancreas and kidney transplant. They do better than nondiabetic patients. Type 1 diabetics have the most benefit from transplant. Risk factors for death are (1) failure of the pancreas graft and (2) failure of the kidney graft. We have to keep the organs going and we have more time to do that with these organs than with the liver.

Looking at survival after pancreas transplantation in patients with diabetes and preserved kidney function, it's better for them to get the transplant than to stay on the list. The longer out they are from the pancreas transplant, the lower their risk of dying. With combined kidney and pancreas transplant, within 50 days, the patient's outcome is better than it would be staying on the waiting list. With pancreas transplantation after kidney failure, it is the same thing. In first year, the risk of death from transplantation is lower than that of staying on the list.

We take the islets from pancreas and put into the liver. It's not clear why the islets are in the pancreas to begin with-that's something we do not understand it yet. The pancreas can destroy its own system. If you put the cells in the liver, it's more forgiving, but it can be toxic to other tissues/cells such as islets.

There are three major obstacles to islet transplantation: (1) There is a shortage of donors; (2) there is at least a 50-percent loss of islet mass during isolation; and (3) there are difficulties in monitoring rejection (we don't have a surrogate for rejection yet, and patients develop hypoglycemia and other problems). It's hard to check the islet viability—you cannot biopsy a liver and take a huge chunk out twice a week and biopsy it, even if you could identify precisely where in the liver the islets are. Reasons that are postulated for why islets decline in function over time include: Intrinsic limitation of islets to repair injury, replicate, and survive; chronic rejection or autoimmune recurrence; the potential that immunosuppression interferes with islet replication/neogenesis; and the question of whether the liver is an appropriate islet implantation site.

A new procedure is allotransplanation involving no immunosuppressants and using two to four donors' islets. This was successful for 1 year; but 5 years later, the recipients are not insulin independent.

Many places in the United States are performing islet transplants; about 43 institutions worldwide have done it, with a total of 530 patients. There is not a lot of experience, given that small a number of patients. There is a multicenter trial of the Edmonton Protocol for islet transplantation occurring in 9 centers; however, only 36 patients were enrolled.

The study looked at the gain of insulin independence among patients over time; 21 of 36 patients were insulin independent. Twenty-five patients had to have more than one islet transplant and some needed three to four islet transplants, which takes many pancreases (and raises questions about allocation). Graft survival was disappointing, at 31 percent. After 2 years, their insulin independence decreases and patients need at least some insulin. We may also see adverse events over time, such as the development of fatty liver. This needs to be seen as an evolving therapy for a highly selective group of patients.

Single-donor islet transplant is being looked at, for allocation reasons. It is done at the University of Minnesota, where a six-patient cohort study is being conducted. Four of the six have been insulin independent for several years. There is a second study with eight patients, three of whom have been insulin independent for 4 or more years (the rest had to go back on insulin).In a third protocol, five patients are insulin independent after 1 year, but not enough time has passed to see if these results will hold up. Decline in function is still the main challenge. Trials are ongoing now among a consortium that views the end point as being less to reach insulin independence than to have hemoglobin A1c of less than 6.5 percent and no hypoglycemia. We have to understand what the insulin independence rates are and set reasonable goals.

Critical issues described include:

- Long-term results are still disappointing, while short-term results trail those of pancreas transplantation.
- Endocrine function with islet transplants is a controversial issue; it appears to be less of a problem than was initially thought, however.
- A UNOS registry is needed for transparency and accountability. There is no mandatory reporting yet, so people are reporting just their best data. The Collaborative Islet Transplant Registry reporting is not mandatory and only about two-thirds of all programs report.
- Standard acquisition costs (SACs) need to be revisited. It costs $20,000–$30,000 for acquisition in the United States. CMS is only reimbursing for islet transplant after kidney transplantation.
- Donor quality is a huge issue, more than for livers and kidneys.

ACOT could consider:

- SACs: We can't continue to pay so much for only a few centers to do this research; it has to be cheaper and more centers need access.
- SACs for whole organs versus islets: The process is more complex for whole organ than for islet transplantation. Less time is spent to remove the pancreas for islets than for whole organ transplantation. A solution for high organ acquisition cost is needed that will permit islet transplantation for research and, eventually, get to clinical use.

Allocation issues—islet and pancreas transplantation should not compete because:

- Donors with a high body mass index (BMI) are not favorable for pancreas transplantation, although they are ideal for islet transplantation. They do better because they have more islets.
- Islet transplantation could be used for those patients who are not suitable for pancreas transplantation or who have had many transplants and are not good candidates.
- One solution could be to do islet transplants in those who would predictably become insulin independent with a single donor.

The final question is, are we making an impact? We have a lot of diabetics and we need to identify those who will benefit the most from this kind of transplantation. Not everyone will benefit but, for those who will, it can be very helpful. We have made slow progress, and the organ acquisition costs have hampered the field.

**Questions**

Ms. Conrad asked if the pancreas needs to be flushed and if that raises the costs. Dr. Gruessner

concurred that it did need to be flushed and that there are costs from that process, but not costs at the same level as for removing the whole organ.

Ms. Conrad said that there are no application guidelines for islets and they are in competition with liver and intestine programs. It's hard for the OPO to make a call on where the pancreas should go —especially given that 50 percent of them are not viable—when there are pancreas patients on the list. Dr. Gruessner agreed but said that soon the islet and transplant patients will be on the same list and the problem will be solved. There are also discard rates for pancreases for transplantation of 10–15 percent of the time.

Dr. Scantlebury asked if a pancreas not suitable for transplantation can be used for islets. The answer is, Not really, because of the storage differences. The decision has to be made in the operating room or before. Dr. Scantlebury asked if was a system built into a region where there's no islet programs, to get them the islets outside the region. Dr. Gruessner responded that there is not; pancreases from patients with high BMIs would be good for this but the SACs are so high that it's hard for the centers to get them. They are wasted, when they should be made available at a lower cost.

Dr. Migliori commented that, with only 530 transplants occurring in 43 centers worldwide, this is still investigational. He asked if there is one operation or protocol being tested so that the field does not have to deal with so many different experiments. Unless a common methodology exists, it seems that we will throw money into a system with too much variation. Dr. Gruessner said that the CIT multicenter study is going in the right direction. The Phase III studies use very similar protocols and will have 100 patients being transplanted. There is no reimbursement for islet transplantation, however. The field would be further along if it resembled that of kidneys in the 1960s, and either private insurers or CMS paid for this.

**Organ Donation Breakthrough Collaborative Update**

*Dr. Alan Leichtman, University of Michigan*

Dr. Leichtman presented on the National Learning Congress: Organ Donation Breakthrough Collaborative and the status on organ transplantation since the initiation of the collaborative. He wanted to address the question of increases in kidneys donated as a result of the collaborative.

The biggest news is that more life-saving solid organ transplants are being performed and are being done at rates that exceed those that had been predicted from trends before the collaboratives began. In 2004, there was an increase beyond what would have been expected, based on the 2000–2002 increase for most organs. This additional increase in 2004 represents nearly 1,000 additional years of life.

The question is, has the increase in kidney transplantation largely reflected an increase in ECDs? Has the increase in transplantation come with a price in outcomes? Before the collaborative, there had been no growth in DCD organs; ECDs were the only growth. Since the collaborative, the trend has reversed: Two-thirds of the growth is in standard/or deceased criteria donors.

A second assertion that has been made is that the results are worse. In fact, looking at kidney patients' waitlist survival, posttransplant survival and graft failure, the trend is toward improvement in both graft and waitlist survival. For livers, the same thing is seen—either no difference or a trend to better survival. For hearts, the waitlist survival trend is improving and the posttransplant survival trend has also improved markedly.

### Questions

Dr. Lorber noted that, when one looks at today's SCDs (they are middle aged, around 50–55, and

they died from cerebrovascular accidents rather than trauma), they do not do as well after pancreas transplantation. Dr. Leichtman noted that there has been a change in the way that pancreases are allocated recently to shift those with a larger BMI to islet and those with a lower BMI and those who are younger to organ transplantation.

**Payment for Organs: Followup from May Meeting**

*Dr. Stuart Youngner, Case Western Reserve University*

Dr. Youngner discussed the issue of creating a regulated market in organs for living donors, which was also discussed at the May meeting. Dr. Youngner noted that there is a growing gap between the number of needed and available organs, and it is a given that it's a good idea to close this gap. Many attempts have been made to increase the pool of organs in the United States, including encouraging DCD (there have been some problems with this); presumed consent (there have also been problems with this approach); required request (this was a failure); promoting best practices (e.g., grants to study ways to increase donations and the collaborative—both of which have been largely successful); and allowing a market (today's topic).

First, it's important to note that there is resistance to organ donation. The subject touches on cultural, religious, psychosocial, and social taboos and feelings. Required request is a good example of this. The idea was to require professionals to ask families for organs. However, professionals are not actually good at this, and they don't like being told what to do so the idea backfired. Brain death is another example. There is a lot of resistance and confusion about the idea (as Dr. Morgan's presentation during this meeting made clear). If we had not established the concept of "brain death" before *Roe versus Wade* occurred, it would probably not be as accepted as it is now in this country. In Japan, for example, brain death is not accepted at all. The bottom line is

it is now in this country. In Japan, for example, brain death is not accepted at all. The bottom line is that a best practices model is a better way to encourage donations than is trying to change a national policy.

Let's say that you pay money for organs one way or another; a regulated market is more attractive than other forms of payment. The question is whether a regulated market would increase resistance or decrease the number of organs. First, do we already have a market in organs? Yes—already, many people make money in the field of organ transplantation, e.g., from drugs, surgery, and OPOs. Only the donor does not profit economically; everyone else is making money. The field is not running on altruism alone. It relies on the idea of altruism and the notion of a gift, but this symbol is nested in a market economy that includes health care, which is a problem.

The tissue industry is much more transparently a money-making exercise. Tissues are radically transformed (bones are made into screws, for example) and the commodification is much more obvious. Tissue products sit on shelves and have bar codes on them. They are inventoried and there are many for-profit companies involved in the field. In terms of acquisition costs for musculoskeletal tissues, their price on the market goes way up as they are transformed. The value is added into the tissue as a product. This is very stark in contrast to the "gift" of an organ.

What are the moral arguments against having a regulated organ market? First, some view that it would break a rule of some sort, such as the Ten Commandments. The rule in this case would be that the human body should not be commodified and that doing so is messing with, and somehow degrading, something that is sacred.

Another argument is that it would lead to a worse situation; this is a utilitarian argument about what the effect would be. It might generally lower respect for the human body or cause voluntary donations to decline. Another worse situation might be that it is part of the slippery slope to an unregulated organ market.

Finally, some argue that a market would lead to injustice and unfair distribution. The poor may be

coerced into selling their organs. Libertarians, however, think the poor should be allowed to sell their organs, since poor people are allowed/encouraged to do lots of other unpleasant things for money. In places like India, however, where this is allowed, the poor who sell their organs do not seem to benefit from it. Another issue is that poor donors might receive worse medical care (this conforms with what donors say already happens). Another argument about injustice is that we already spend what some might view as too much on transplantation and should invest more on other things like universal access to care.

There is a spectrum of market approaches:

- Rewarded gifting;
- In-kind expenses;
- Financial incentives;
- Regulated market;
- Futures market; and
- Totally free market-with tissue donors, they could hold an auction for their body parts.

When you look at the idea of paying for organs in the current United States, we have to keep in mind that the health care system is confused, confusing, unjust, and unstable. Doing a regulated market system under our current health care system is likely to be problematic. We have a society that is polarized politically, socially divided, and mistrustful of the medical system. We have a culture where market values over the last more than 30 years have invaded other spheres. All of those factors would affect the successes or failures of any market.

### Questions

Dr. Solomon asked Dr. Youngner to elaborate on the idea that a regulated model might lead to a slippery slope that stimulates a black market, when research indicates that the opposite might be true. The response was that as long as there is a shortage of organs, there is the potential to create a black market.

Mr. Holtzman asked what the political difficulties are with presumed consent compared to a market approach. Dr. Youngner replied that one has to have lots of education and allow folks to opt out easily. In Spain and other countries, they approach it differently and presume that donation is acceptable; but they respect the families and do not do it if the family objects. The success of this depends on how manipulative and aggressive the approach is. For example, in Ohio, you cannot say "no" on your driver's license to organ donation.

Dr. Gruessner noted that the Iranian model was implemented as a regulated market because there were not enough donors. The idea was that they would only donate within their own country and not to foreigners. Over time, and in part because a new requirement that that recipient had to show

to foreigners. Over time, and in part because a new requirement that that recipient had to show "gratitude" to the donor, this regulated market turned into more of a free market. It takes a lot of discipline on the part of those who regulate the market to prevent this happening. In Japan, the market is very regulated and is moving very carefully. They do not accept directed donations not even among those who are biologically related or spouses.

Dr. Youngner noted that there is a question about donors who are altruistically donating, i.e., whether they are adequately well informed and getting enough care and appropriate followup. To introduce financial aspects before the registry is in place to track care and followup would be problematic.

Dr. Lorber said that the most cogent argument is not to go too far, too fast and to bear in mind the potential harm to organ transplantation if things go badly. The small, best practice research is powerful, and something that ACOT can promote. A presumed consent strategy could be defensible and helpful, with the caveats about education, opt outs, and support. It would be a minor change and that could be helpful. Dr. Arthur Matas has, likewise, proposed a demonstration approach that could assess the consequences.

Dr. Burdick commented that a factor, in terms of resistance, is the failure of the community to improve the systems. The collaborative shows that a presumptive approach can be really helpful. It matters how you approach the family and what you say in a positive way to encourage them to consent.

Mr. Hagman remarked that religious education shows that you can take a child under the age of 10 and convince them of just about anything. If we had a system of long-range education about, for example, smoking, exercise, and organ donation, we can make a difference over time. Dr. Youngner agreed, saying that you have to have a system that you are happy to teach children about. We have to make the system equitable, fair, and defendable to the children you are encouraging to be donors later in life. Mrs. Boone said that North Carolina has new curriculum changes that add organ donation information in the schools.

**Revision of the UAGA**

*Mr. Carlyle (Connie) Ring, National Conference of Commissioners on Uniform State Laws (NCCUSL)*

Mr. Ring discussed the changes to the UAGA, which have just been promoted recently. ACOT's recommendations about the UAGA were, in large part, the impetus for this revision. Three ACOT recommendations provided a stimulus; in particular, Number 10: Recommendation to engage in legislative strategies to encourage medical examiners not to withhold life-saving organs; Number 19: Recommendation to take steps to ensure that the donors' wishes are fulfilled; and Number 20: Recommendation that States update the law governing anatomical gifts. Changes in the law may improve the number of organ donors available, but it will not solve the problem entirely.

In 1968, the first UAGA was written and adopted by States within a few years. It was the first such act in the United States, as there had been no prior legislative experimentation. The 1987 act was enacted in 26 States; since then, many States have amended and modified it, so that version was less successful in establishing uniformity. The 2006 revised act harmonizes with Federal law to conform to improved practices and technology in order to address problems identified by ACOT.

NCCUSL was established to address areas of law in which uniformity among the States is desirable. The conference drafts and enacts uniform laws that are used by all States in the country. Examples of uniform acts include the Probate Code, Trust Code, and the UAGA.

The process used for this revision was to take the recommendations from ACOT and AOPO and create the Study Committee, which happened in 2003. The Drafting Committee members were appointed in 2004; this committee solicited feedback from stakeholders. Participating stakeholders included AOPO, National Association of Medical Examiners (NAME), HHS, UNOS, the American Medical Association, and many others. Drafting meetings were held with stakeholders participating, which was essential to the success of the process. Then, a word-for-word reading occurred, with debate, at two consecutive NCCUSL annual meetings. A vote is taken by the States on whether to promulgate that act; this was a unanimous vote.

The continuing principles in the new act include that the organ donation system should be an opt-in system, be voluntary, permit donor designation with first-person consent, and facilitate people opting in. It covers only donations from decedents (no living donors). Several principle changes have been made in the revision of the act, described below.

First, the revision honors donors' choice by barring others from interfering in the decision. In the past, the donor's desire could be overridden by the family. Now another person is barred (or "disempowered") from revoking the gift, if made by the donor. There are two exceptions: If a gift is made for a particular purpose and there are other purposes for which gifts can be made, you can do

a more expansive gift than that specified. Also, if the donor is an unemancipated minor, the gift can be revoked or amended.

The revision expands those who can make a gift (parents, guardians, and agents). The revision expands those who can make a gift if the deceased has not made a choice (agent, grandchildren, and special care person). Therefore, if the donor has not acted, other persons can now make the gift. It also expanded this list by adding health care agent, grandchildren, and other adults who have a health care concern. These individuals are listed in order of priority in terms of their power and the availability of the consenting person.

The act also defines "readily available" now in terms of these potentially consenting agents and how the consent can be given. It also discusses what happens when a spouse is emotionally incapable of making a decision. The revision ensures that majority of a "class" may make a gift decision; in other words, if the majority of one's siblings decide, then the majority rules. The act sets default interpretation rules for gifts; the parties have set intent and the donor's desire controls.

It also encourages and establishes standards for donor registries. It clarifies the earlier act about what entity receives the organs. If the named individual(s) cannot be a recipient, then the gift passes to the national allocation system and is given to the appropriate procurement facility or bank. It also includes a provision that sets standards for registries and encourages States to adopt such registries.

The act establishes access to gifts, registries, and medical records. It resolves the tension between health care directives and an anatomical gift. There is often inconsistency with a medical directive (e.g., to pull the plug) versus the desire to make an anatomical gift (in many cases, it is necessary to keep life-support systems operating for this to occur). For that limited period, under the new act, life support can continue while the donation is getting arranged.

It expands the rules for cooperation and coordination with coroners and/or medical examiners, and states explicitly that these entities will cooperate. If the medical examiner is going to deny a donation, he or she must write down the reason for the denial. If the medical examiner needs to personally appear when organ is to be taken, that visit's expenses are reimbursed by the procurement organization. The act now recognizes gifts made under other laws and clarifies that, if the gift is valid under another State or country's law, it can be implemented in the State where the person died. It also recognizes the validity of both electronic records and signatures.

The road to enactment is that the commissioners are charged with getting the act introduced into their State's legislature. It is anticipated that the act will be introduced in 37 States next year and that the remainder of States will consider it in 2008. Demonstrations of support are very important in getting the act passed in the States.

**Questions**

Ms. Conrad asked, What strategies can be used to counteract NAME's lack of support for the UAGA? Mr. Ring responded that they are working on generating support and meeting with the NAME leadership to get them involved. Also, they are thinking about a discreet amendment that would be both acceptable to other stakeholders and resolve NAME's concerns.

Dr. Migliori asked what is meant by "revoke and refuse" (section 8, paragraph B). Mr. Ring said that to "revoke" is when a gift has been made and the donor wants to revoke it. "Refusal" occurs when a gift hasn't been made, but a donor wants to prevent anyone from making a gift after he/she is dead.

Dr. Solomon said that, in terms of the ethics of end-of-life care, health care agents and caretakers

are important decision makers. The health care directives such as living wills have not asked about, or included information about, organ donation. Should there be a better dialogue with the end-of-life care field to add this information to living wills and such care? Many of the popular documents, e.g., (the Five Wishes) could be a catalyst for this discussion. Mr. Ring noted that, in Virginia, an advanced medical directive includes a suggestion that one confers authority to make an anatomical gift and provides space to note purposes. This varies by State. Dr. Solomon said that there is a perception that there should be a barrier between end-of-life care and organ donation, and this should be changed.

Ms. Agrawal said that many States have a specific form you have to use. The forms going around in the public sphere may not apply or be recognized in another State. In May 2007, ACOT could talk about this, as well as any other recommendations it may want to make to the Secretary. Mr. Ring responded that the new act clarifies that, if a gift is valid where it was made or the person resides, then it can be implemented in the State where the person died.

Dr. Lorber asked if ACOT had seen the revised act previous to this meeting. Ms. Agrawal said that this was the first time it's been discussed. Uniformity is important and the changes, especially around donor designation, are critical and probably would be supported by our members.

**Initial Discussion of Recommendations From this Meeting**

*None noted-see beginning of the summary for discussion and next steps.*

**Public Comment Period**

- National Kidney Foundation—the speaker, Dolph Chianchiano, said that the National Kidney Foundation is opposed to financial incentives. ACOT has not talked about the fact that new data demonstrate that 47 percent of those who die on the waiting list are on "inactive" status. These individuals would not have been considered for transplant in any case. The foundation will share this finding in more detail at the May ACOT meeting.
- CATO Institute—the speaker, Sigrid Frey-Revere, said that she was impressed by Dr. Youngner's discussion about possible pilot programs and asked if it is even possible to try market incentive programs. Ms. Levine responded that, if such a pilot program involved "valuable consideration" it would be prohibited, unless the law were changed to conduct a demonstration project. ACOT can recommend that such a change in statute be made by the Secretary. Ms. Frey-Revere asked if ACOT would be interested in asking Congress to make an exception to the statute. Ms. Agrawal replied that ACOT has made this suggestion to allow loosening of the definition in the past.

**Closing Remarks and Comments**

Dr. Leffel asked if the May meeting could include a Scientific Registry of Transplant Recipients update on the proposed implementation of the net lifetime benefit in renal allocation.

Dr. Migliori would like the May meeting to include an update from the collaborative on its efforts. His site has seen dramatic increase. They have had a 10-percent increase just in this year, and around a 26-percent increase in recent years. The collaborative's work should be recognized and endorsed.

Dr. Solomon asked if there were interest in forming a subcommittee of ethicists that would be independent from UNOS. This group could look at the new kidney allocation system and the economic benefit of prioritizing younger recipients. She would like to see a whole day devoted to this issue, outside of a formal ACOT meeting, with the goal of creating a structured way to evaluate this.

Dr. Gruessner said that the discussion is in flux and the net life survival benefit may not be the only consideration. There are other issues that will be looked at in January 2007. Dr. Lorber commented that he had been through an allocation debate in the past and anticipates that many stakeholders and special interest groups will have strong feelings. He advised ACOT to see how it plays out before going forward. Dr. Vega reminded the group that there was a new lung allocation revision in last 2 years. After the new allocation system was approved by the OPTN, a national meeting of stakeholders was held. It would be a good idea for UNOS to do that for the kidney allocation changes too.

Mr. Holtzman asked for an update on DonorNet 2007, which is to be rolled out by April 1, 2007.

Dr. Scantlebury said that she felt there was a need for one single logo promoting organ donation. There are so many of them it becomes confusing. Mr. Holtzman agreed that there seems to be a movement to get a common theme and vision on donation, given the electronic registries and the collaborative. Ms. Agrawal asked members who are interested in this subject to talk among themselves and the topic can be revisited in May.

*The meeting adjourned at 2:30 p.m.*

Next ACOT meeting is May 15–16, 2007 at the Doubletree Hotel in Rockville, MD.