DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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STATEMENT OF

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"TISSUE BANKS: THE DANGERS OF TAINTED TISSUES AND THE NEED FOR FEDERAL REGULATION"

BEFORE THE

COMMITTEE ON GOVERNMENTAL AFFAIRS

UNITED STATES SENATE

May 14, 2003

FOR RELEASE ONLY UPON DELIVERY

INTRODUCTION

Good morning Madam Chairman and Members of the Committee. Thank you for inviting the Food and Drug Administration (FDA or the Agency) to participate in this hearing on human tissue. I am Dr. Jesse L. Goodman, and since January 2003, I have been the Director of the Food and Drug Administration's (FDA or the Agency) Center for Biologics Evaluation and Research (CBER). I am also a practicing physician and a researcher specializing in infectious diseases.

CBER is the FDA Center responsible for regulating many different types of human tissue and cells transplanted during various types of medical procedures. CBER also regulates blood, vaccines, and many other therapies.

I specifically mention blood because, although the challenges it presents are different from tissue, there are nonetheless similarities in terms of the risks of infectious disease transmission associated with these products. Some of the same approaches that have been used successfully to improve the safety of blood are also being used to make tissue safer. Examples include donor suitability, performing appropriate testing, assuring that materials are processed and shipped properly, and monitoring adverse events.

Tissues derived from humans present unique challenges. The risks of transmitting infection can be significantly reduced, but not completely eliminated. While we constantly strive to increase the safety of blood, tissue and other products that we regulate, no medical product or procedure

is one hundred percent safe. Education, training and appropriate regulation are important measures we employ to help reduce risk.

I want to thank the Chair and members of this committee for your continued interest in a topic that affects the lives of so many people. I also want to convey to the family and friends of Bryan Lykins just how sorry I am for their loss. I know there is nothing I can say today that will ease their pain, but I do want them to know that my colleagues and I at FDA are committed to making tissue transplants as safe as possible prevent such tragedies in the future.

BACKGROUND

The term "tissue" covers many products transplanted for medical uses, such as skin replacement following severe burns, tendons and ligaments to repair injuries, bone replacement, and corneas to restore eyesight. Tissue transplantation is a rapidly growing industry. The number of musculoskeletal tissue transplants increased from approximately 350,000 in 1990, to more than 800,000 in 2002.

Transplanted human tissue products have the potential to treat or cure a wide variety of health conditions. Over the past decade, advancing technology and improved techniques have expanded the therapeutic uses of tissue-based products. For example, we have seen significant advances in tissues to treat severe burn victims. These products have dramatically increased patients' qualify of life in ways that were previously unheard of. In addition to their important uses to restore and improve a variety of functions, these new techniques also hold the potential to provide therapies for diseases such as cancer, Parkinson's disease, hemophilia, anemia, diabetes,

and other serious conditions. Cells and tissues can also be used in combination with drugs or devices, and to deliver genes for gene therapies.

Many cellular and tissue products are regulated by FDA as biological products under both the licensing provisions of the Public Health Service (PHS) Act and the Federal Food, Drug, and Cosmetic (FD&C) Act. Several categories of human tissue used for transplantation are regulated as medical devices under the 1976 Medical Devices Amendments, including heart valves, dura mater (the brain covering) and some demineralized bone products. Most human tissues for transplantation, as defined in Title 21, of the *Code of Federal Regulations* (CFR) Part 1270, are regulated under the Agency's authority to prevent the transmission of communicable disease, section 361 of the PHS Act.

FDA has three primary goals with respect to human tissues: (1) to prevent the spread of communicable diseases; (2) to ensure that safety and efficacy is demonstrated for cellular and tissue-based products that are also drug, biological, and medical device products; and (3) to help enhance public confidence in these products so that, where appropriate, they can fulfill their great potential for saving and improving lives. We seek to accomplish these goals in a manner that will not discourage the development of new products.

With the increased use of human tissue has come a heightened need to ensure greater tissue safety and minimize the potential risks. Developments in the 1980s and 1990s prompted FDA to examine its approach to tissue safety. Several incidents illustrate the risks of infectious disease transmission when adequate precautions are not taken. During the 1980s, there were reports of multiple incidents of transmission of the degenerative neurologic disorder, Creutzfeld-

Jakob Disease (CJD), by dura mater allografts. A 1992 report documented that seven people were infected with HIV through transplantation of organs and tissue from a single donor. In the 1990s, possible transmission of CJD through corneas and eye tissue was reported and in 1999 a patient died from cardiac arrest during surgery to remove an infected corneal transplant. The probable source of the infection was contamination of the media used to store the cornea. Just last year, despite donor testing, there were three confirmed organ recipients and six probable tissue recipients who were determined to be infected by hepatitis C from a single donor's tissues. Tissues are also subject to contamination from other agents such as bacteria and fungi. These risks may have little to do with the donor; rather, they may relate to how the tissue is handled, processed and tested.

The overall risk of disease transmission through tissue transplantation is believed to be very low. However, more tissue transplants are taking place each year. Over 800,000 tissue transplants occurred in the past year. The public expectation for tissue safety is high and, as a result, FDA is taking steps to better understand, detect, prevent, and act upon threats to tissue safety.

As part of FDA's efforts to address tissue safety, in December 1993, the Agency published an interim rule for Human Tissue Intended for Transplantation (21 CFR Part 1270). This rule provided specific donor suitability and testing requirements for human tissues, including bones, musculoskeletal, skin, and ocular tissue. Like our actions to achieve blood safety, FDA was acting swiftly to counter the transmission of three serious disease agents: HIV, hepatitis B and hepatitis C. This rule also provided for the inspection of tissue banks and the recall and possible destruction of unsafe human tissue. When the final rule was published on July 29, 1997, a

guidance document on donor screening and testing was published to accompany and update the rule.

When the Agency put the 1997 tissue rule and guidance in place, FDA developed a plan to address tissues in a more comprehensive, but not unduly burdensome manner. The goal of this plan was to improve protection of the public health without imposing unnecessary restrictions on research, development, or the availability of new or existing products. We believe this will lead to safer and more efficient development of human cells, tissues, and cellular and tissue-based products, while increasing public confidence in those products. We designed our risk-based regulatory approach to tissues recognizing the importance of life-saving and life-improving tissues. This risk-based approach is intended to promote tissue safety in a manner intended to maximize benefits while minimizing risks.

RECENT DEVELOPMENTS

As you know, on May 24, 2001, my predecessor appeared before this committee at a hearing on the practices of the tissue bank industry. Let me report on Agency activities since that hearing in eight major areas, some of which are in response to FDA and CDC investigations into Mr. Lykins' case.

1. **Bacterial Contamination and FDA Guidance on Validation of Procedures for Processing Human Tissues**

   The death of Brian Lykins and other reports of infections in recipients prompted investigations by FDA and CDC. Extensive testing at CDC implicated CryoLife tissue in

the fatal infection and other reported infections. This led to a comprehensive inspection of CryoLife, Inc. (CryoLife), the tissue bank that processed the implanted tissue.

As an urgent response to these investigations, FDA decided that it was critical to take additional steps to control the threat of bacterial and fungal contamination during tissue manufacturing. Therefore in March 2003, FDA issued guidance for immediate implementation concerning the validation of procedures for processing human tissues. This guidance and the accompanying outreach to industry and professionals emphasized the important steps that we believe are necessary to reduce contamination risks. We believed that it was important that all of the tissue industry, and not just a single company, enhance their procedures to avoid the problems experienced at CryoLife.

2. Continuing CryoLife Investigation and Recall

The ongoing CryoLife inspection uncovered numerous, significant violations of FDA regulations. When CryoLife failed to respond adequately to the deficiencies noted during the inspection, FDA issued a Warning Letter to the firm. Again, the firm did not commit to all of the corrective actions FDA believed were necessary. On July 15, 2002, CDC informed FDA that it had received 54 reports of allograft-associated infections, almost half of which were associated with CryoLife implants. In response, FDA issued an Order for Retention, Recall, and Destruction to the firm on August 13, 2002. The order resulted in the recall of 7,913 tissue products. Further actions by FDA and CDC resulted in the firm committing to take the appropriate steps necessary to ensure the safety of the tissue it supplies. Under the Order, on September 5, 2002, FDA and CryoLife entered into an agreement designed to ensure that tissue the firm distributes would be free of contamination. The most recent

inspection of CryoLife was performed in early February 2003. Some improvements were noted, but significant work lies ahead. FDA continues to monitor the firm and to work with the company as corrective actions are implemented.

3. Inspections, Field Training and Enforcement Activities

A lynchpin for assuring the safety of tissues is assuring that tissue manufacturers and distributors are handling tissue appropriately and useing validated procedures to prevent contamination. FDA inspectors, organized under the Office of Regulatory Affairs (ORA), are the Agency's eyes and ears for assuring that proper procedures are in place and are being followed. Where appropriate, information from FDA inspections can and will be used to take enforcement action. However, it is preferable, wherever possible, to work with manufacturers to build quality into their procedures in an effort to prevent safety problems.

Working closely with ORA, we have upgraded and expanded our inspection activities. In fiscal year (FY) 2002, FDA held two extensive training sessions for the district investigators who perform tissue establishment inspections. Over 80 investigators were provided with detailed information on current and pending tissue regulations. To encourage consistent and effective inspections, FDA also published an updated compliance program guide in March of 2003, to assist our investigators and tissue establishments understand what will be addressed in a tissue establishment inspection. Training sessions for investigators are also planned for FY 2003 and FY 2004.

In FY 2001, FDA conducted 132 tissue establishment inspections, of which 51 resulted in the issuance of an FDA Form 483 report listing observations by an inspector of compliance

deficiencies or violations. In FY 2002, FDA conducted 165 inspections, and 48 of these resulted in the issuance of a Form 483 report. FDA plans to conduct over 200 inspections in FY 2003. These activities have resulted in 10 regulatory actions, including a mandatory recall order (CryoLife). There has also been an increase in recall activity, and most significantly the number of Class I recalls where there is a reasonable probability of serious adverse health consequences for recipients. In FY 2002 there were 10 Class I recalls compared to only one in FY 2000.

4. FDA Creates New Office

In October 2002, FDA created the Office of Cellular, Tissue, and Gene Therapies (OCTGT) to consolidate regulatory and review activities for tissues, cellular and tissue-based products, gene therapies, and xenotransplantation products. This office includes experts in molecular and cell biology, viral and nonviral gene therapy vectors, nucleic acid chemistry and genomics, proteomics, developmental and reproductive biology, stem cell biology and physiology, tissue and organ regeneration and medical and pharmacology/toxicology. OCTGT evaluates potential shortages to help assure the continued safe supply of needed products. This office works with CDC, NIH and other appropriate organizations to develop standards and methods for cellular therapies and participates in inter-center focus groups for collaborative reviews. Through this centralization of activity and expertise, FDA is working more effectively with our agency partners, conducting outreach, and regulating tissue products to achieve a safe and adequate supply.

5. Updating Donor Deferral Criteria to Respond to New Threats

In addition to laboratory testing, a critical component of enhancing the safety of tissues is excluding donors who may pose a higher risk of transmission of infectious diseases. The emerging challenges of prion diseases [such as CJD and variant CJD (vCJD)], for which there currently are no practical laboratory tests, pose a particular challenge, especially for nervous system tissues. Because of our concern about the potential transmission of these diseases by transplantation, implantation, infusion, or transfer of human cells, tissues and cellular, and tissue-based products (HCT/Ps), FDA issued guidance on June 14, 2002, regarding deferral criteria for donors potentially at risk of developing and transmitting these diseases. We published this draft guidance to present our current thinking about preventing the potential transmission of this disease by deferring donors with possible exposure. FDA intends to issue another draft guidance document for public comment that would include recommendations to screen and test donors for relevant communicable diseases other than CJD and vCJD, and combining both draft guidance documents into one final guidance of that time.

6. Dura Mater Proposed Rule

On October 22, 2002, FDA's Center for Devices and Radiological Health (CDRH) published a proposed rule to classify human dura mater as a Class II device. Class II means we know enough about the device category to establish controls for reasonable assurance of safety and effectiveness. A draft guidance document was published on the same day to support the proposed classification. The 90-day comment period for the proposed rule and the draft guidance document ended on January 21, 2003. The comments are currently under review.

7. Collaboration with CDC and Others

As I have discussed, incidents of infectious disease transmission by human tissue are not routinely reported. Current regulations do not require facilities to report incidents to FDA's MedWatch system, though voluntary reporting sometimes occurs. To date, only a limited number of adverse events relating to tissue have been reported to MedWatch. In order to achieve a more robust surveillance system, FDA is working with CDC to stimulate adverse event reporting and to investigate reported events. CDC has unique capabilities to conduct such surveillance and FDA is exploring ways to obtain adverse event information from CDC, as well as other health care delivery databases.

8. Training, Meetings and Outreach Activities

Working collaboratively with tissue manufacturers to identify new safety issues and improve tissue practices is critical to the success of our mission. With this goal in mind, FDA has dramatically increased outreach activities in recent years in an effort to anticipate and avoid safety problems. An addendum is attached to this testimony that describes the training, meetings, and outreach activities that FDA has conducted with tissue establishments, inspectors and professional organizations.

ENHANCED TISSUE SAFETY

FDA is committed to protecting public health by promoting greater safety of tissues used in transplantation. Greater assurance of safety in transplanted tissue will also be critical to public acceptance of this technology. The recent reports of serious bacterial contamination in tissues and West Nile Virus transmitted through blood and organ donors underscore the need for a

strong infrastructure to prevent and respond to new threats of tissue safety. In addition to the activities I have just described, FDA has advanced three regulatory proposals.

The first rule, proposed on September 30, 1999, would establish suitability determinations for donors of human cellular and tissue-based products. The second rule, proposed on January 8, 2001, would require manufacturers to follow current good tissue practices (GTP). The third rule, which became final on January 19, 2001, requires the registration and listing of tissue establishments.

FDA's regulations could enhance prevention and response in several ways:

- For the first time, a complete database of human cell, tissue, and cellular and tissue-based product establishments and products would be maintained. This would significantly increase the efficiency of FDA inspection and monitoring, and the effectiveness of communication about risks and related findings.

- Our proposed GTP rule would provide more comprehensive, detailed requirements designed to prevent bacterial and fungal contamination of tissues through appropriate manufacturing methods, facilities, and controls to enhance industry compliance.

- To prevent injuries and deaths, tissue manufacturers and FDA must identify, and rapidly respond to adverse events, particularly tissue contamination.

- Tracking requirements would make it possible for the Agency to quickly find recipients of implicated tissue. This would help ensure that when a risk is identified a timely and appropriate response can proceed.

- Requirements to screen and test donors for "relevant communicable diseases" would facilitate rapid implementation of new tests to detect emerging disease threats. This would enable us to rapidly respond to new infectious disease threats such as West Nile Virus as they emerge and as interventions become available to reduce risk.

FDA is committed to assuring the safety of tissues, and we are continuing to move forward to accomplish that goal. We also want to acknowledge the American Association of Tissue Banks (AATB) and other professional organizations for their work in publishing standards for tissue banks and advancing the safety of tissue transplants.

CONCLUSION

Hundreds of thousands of tissue transplants occur annually. Most of these are successful and free of adverse events. The future of tissue and tissue-based technology is promising. However, tragic events such as Mr. Lykin's death indicate that we must continue to do more. FDA will continue to improve tissue safety and refine our approach as new technologies and products become available. In addition to the proposed regulations, we have significantly increased inspections, oversight and outreach, even as we advance new regulations. The Agency continues to hold workshops and public meetings on issues affecting human cellular and tissue products to identify the need for guidance and to promote regulatory compliance in order to facilitate the development and availability of safe tissue products. FDA is committed to preventing the transmission of communicable diseases to ensure the safety and effectiveness of cellular and tissue-based biological and medical device products. When a patient has a

procedure involving a tissue product, we want to do our part to make sure that patient can be as confident as possible that the product will be as safe and free from any preventable risk of contamination.

Commissioner McClellan, my staff, and I look forward to working with the Committee both now and in the future to address tissue safety and ensure the Agency is taking all needed steps to prevent injuries and illnesses associated with contamination of tissues. I will be glad to answer any questions.

ADDENDUM

OUTREACH / WORKSHOPS / MEETINGS

Publications:

- Wells MA, "FDA Proposed Oversight of Human Reproductive Cells and Tissues used in ART, American Infertility Assoc. – In-Focus, Spring 2002

- Lazarus EF: Adoptive immunotherapy, the Food and Drug Administration and you: a regulatory approach to donor lymphocytes. Cytotherapy 4:5, 449-449, 2002

- Lazarus EF, Browning J, Norman J. et al: Sustained decreases in platelet count associated with multiple, regular plateletpheresis donations. *Transfusion* 41, 756-761, 2001

- Lazarus, EF and Klein HG: Apheresis, In Rich RR, Fleisher TA, Shearer WT et al (eds): Clinical Immunology, 2nd Ed. Harcourt Publishers, London, 2001

- Solomon RR, contributing author to: Lanza R, Langer R, Vacanti J (ed) Principles of Tissue Engineering, 2nd Edition. Chapter 65 – "Regulatory Considerations," KB Hellman, RR Solomon, C Gaffey, CN Durfor, JG Bishop, Academic Press, San Diego. 2000

- Lazarus EF and Klein HG: Hemapheresis and cellular therapy. In Hoffman R, Benz EJ, Shattil SJ et al (eds): Hematology: Basic Principles and Practice, 3rd Ed. Churchill Livingstone, New York, 2000

- Wells MA – "Overview of FDA Regulation of Human Cellular and Tissue-Based Products," *Food and Drug Law Journal*, Volume 52, No.4, October 1997

- Wells MA, "The Regulatory Reach of FDA: A Novel Plan," *Regulatory Affairs Focus*, Volume 2, Issue 9, September 1997

General/Ongoing Interactions with Industry:

- FDA presentations/participation at American Association of Tissue Banks (AATB) and Eye Bank Association of America (EBAA) Annual and Mid-year Meetings
- FDA presentations/participation at AATB Reproductive Tissue Council Meetings
- FDA presentations/participation at Food and Drug Law Institute (FDLI) and Regulatory Affairs Professional Society (RAPS) meetings

- FDA presentations/participation at American Society for Reproductive Medicine (ASRM) annual meetings
- FDA site visits to tissue establishments
- FDA consultant to the CDC/Industry Task Group developing the model certification program for embryo laboratories under the 1992 Fertility Success Rate and Certification Act
- FDA liaisons to ASRM's, National Coalition for Oversight of Assisted Reproductive Technologies (NCOART)
- FDA liaisons to AATB Standards and Medical Advisory Committees
- FDA liaisons to EBAA Medical Standards Committee
- FDA liaison to American Association of Blood Banks (AABB) committee for Hematopoietic Progenitor Cell Standards
- FDA liaison to AABB committee for Umbilical Cord Blood Standards
- FDA liaison to AABB committee for Cell Therapy Standards
- FDA liaison to joint professional organization work group for drafting Hematopoietic Progenitor Cell Product Circular of Information
- FDA liaison to NCCLS immune cell functional assay work group

Meetings within the HHS/FDA:

4/17/03	Biologics Cadre conference call
4/9/03	HHS Advisory Committee on Organ Transplantation (ACOT) Working Group

Meetings with other Federal/State Agencies:

2003	Multiple meetings with CDC re: SARS
2002-2003	Meetings with HRSA re: Vaccinia
2002	Multiple meetings with CDC and HRSA re: WNV
5/03	Federal Interagency Work Group on Hematopoietic Stem Cells
5/03	Meeting with WHO regarding cell and tissue regulation
3/01	Meeting with Health Canada, Rockville, MD, to discuss the Regulation of Human and Xeno tissues
6/98	Meeting with Japan Health Science Foundation
1998-2002	Multiple meetings of the DHHS Interagency Task Force on Assisted Reproductive Technology (FDA, DHHS, CDC, CMS)

1998 issues	CDC - Multiple meetings on coordination of reproductive tissue
1997	Trilateral meeting between US, Canada, Mexico- Mexico City
9/97	HRSA - Discussion of regulation of pancreatic islet tissue
9/97	New York State Dept. of Health - Meeting with Dr. J. Linden on coordination of Tissue Bank Inspections
7/97	Federal Trade Commission - Discussion of Stem Cell Promotion

Specific Events with Industry:

4/26/03	FDA invited speaker at the Northeast Regional Meeting of the Association of Reproductive Managers to discuss FDA's proposed regulation of assisted reproductive technology clinics.
4/22/03	FDA Presentation on "Science-based Testing for Biologics" at the National Research Council, Roundtable on Biomedical Engineering Materials and Applications
4/21/03	FDA Presentation at the Defense Advance Research Projects Agency (DARPA) on "FDA Regulatory Framework for Cell and Gene Therapy, including Engineered Tissues"
4/1/03	Keystone Symposia
3/28-31/03	AATB 7th Annual Spring Meeting, "Bacterial Culturing of Human Tissue Allografts: AATB Interaction with FDA and CDC" and "Infections Reported to be Associated with AATB-Accredited Entities: A Panel Discussion"
2/03	CBER Biologics Response Modifiers Advisory Committee Meeting on Hematopoietic Stem Cell Transplantation
12/02	Scheduled site visit at the Shady Grove Fertility Center
11/18/02	National Coalition for Oversight of Assisted Reproductive Technologies (NCOART) Meeting
11/9/02	University of Kentucky – Developing a Compliant Practice: The FDA comes to ART

11/4-5/02	Workshop on Development of Donor Screening Assays for West Nile Virus – ASRM participation
11/1/02	FDA discussion with CAP staff concerning comparison of standards with GTP proposed requirements
11/02	Workshop on Development of Donor Screening Assays for West Nile Virus (both blood and tissues discussed)
11/02	FDA Presentation at the AATB QA Workshop, New Orleans
11/02	Part 15 Hearing on Combination Products
11/02	FDA/ORA/CBER Tissue Training Course for FDA Inspectors
10/21-25/02	Human Tissue Establishment Inspection Training Course
10/16/02	ASRM Annual Meeting: FDA Update
9/21/02	FDA invited speaker to the 3rd Annual Embryology Summit Conference at the Mayo Clinic, Rochester, Minn. To discuss FDA's proposed regulation of embryology laboratories.
9/18-19/02	FDA/NIH/DHHS Workshop on Evidence Based Assisted Reproductive Technologies
8/02	AATB/FDA Workshop on Bacterial Contamination
6/02	TSE Advisory Committee – Validation of Procedures to Prevent Contamination and Cross-Contamination with TSE Agents; presentation of draft guidance on CJD/vCJD
6/02	FDA invited speaker at the 4th International Donor Registry Conference in Oslo, Norway, to discuss FDA's proposed regulatory framework for Hematopoietic stem cells.
5/9/02	CBER Biological Response Modifiers Advisory Committee meeting on Ooplasm transfer
3/24-26/02	AATB 6th Annual Spring Meeting – FDA Presentation on "Microbial Contamination and Cross Contamination Concerns During Processing of Tissue, an FDA Perspective"
1/02	TSE Advisory Committee—CJD/vCJD risk in tissue donors

12/01	CBER Biological Response Modifiers Advisory Committee on Risk Factors for Infectious Disease Transmission by Artificial Insemination
11/28/01	FDA Presentation at the AATB QA Workshop, Tempe, AZ
10/01	Workshop at RAPS Annual Meeting – Human Reproductive Cells and Tissues
8/29/01	FDA's Tissue Reference Group Workshop
6/01	FDA Presentation at the EBAA Annual Meeting, Tucson, AZ
5/3/01	FDA/EBAA Meeting regarding GTP Issues
4/16/01	FDA/ASRM Meeting – GTP Proposed Regulation
10/3/00	RAPS Meeting
8/14-15/00	Workshop: Unrelated Allogeneic Cord Blood Banking and Transplant Forum
8/2/00	Open Public Meeting - Human Bone Allograft: Manipulation and Homologous Use in Spine and Other Orthopedic Reconstruction and Repair
6/00	CDC Donor Suitability Workshop
2/10/00	FDA/ASRM Meeting Concerning the Donor Suitability Proposed Regulation
2000	Tissue Engineering course
11/17-19/99	AATB QA Workshop, New Orleans, LA - FDA Review of Tissue Bank Inspections; Status of Required Serology Testing; Update Regarding Proposed Regulations
9/99	ASRM - Presentation - FDA Update on Regulation of Reproductive Cells and Tissue.
6/99	EBAA - Presentation on Registration Proposed Rule and Donor Suitability Proposed Rule
6/99	Institute of Science, Law and Technology (ISLAT) informational meeting with FDA to discuss ART issues

4/8/99	Human Tissue Industry Seminar hosted by ASQ and Los Angeles District, Los Angeles, CA
4/99	RESOLVE consumer association informational meeting with FDA to discuss ART issues
3/99	AATB - Presentation on Donor Suitability Proposed Rule
12/98	FDA Science Forum on Proposed Approach
11/98	EBAA - Compliance with Final Rule
10/98	ASRM - FDA update on Regulation of Reproductive Cells and Tissue
9/10/98	Workshop: Hematopoietic Stem/Progenitor Cell Products: Discussion of Unrelated Allogeneic/Umbilical Cord Blood and Peripheral Blood Cell Banking and Transplantation
8/98	AATB Annual Meeting - FDA Update and Implications of FDA Regulation of Reproductive Tissue
7/98	AATB Informational meeting with FDA concerning establishment certification and standard development
6/98	EBAA Annual Meeting- Establishment Registration and Listing - proposed rule
5/98	AATB mid - year meeting - FDA - What's Ahead/CJD and Dura Mater
4/20/98	FDA/AATB Meeting Concerning Summary of Records
4/9/98	Videoconference arranged by FDA Southwest Region and Dallas District on the Regulation of Human Tissue Intended for Transplantation presented to EBAA members located in the Southwestern U.S.
3/98	Training and Review - Regulatory Issues in Tissue Banking
2/98	FDA presentation at CDC and RESOLVE (a federation of infertility patient associations) sponsored meeting "Approaches to A.R.T. Oversight: What's Best in the U.S."
12/23/97	Workshop: Ethical Issues in Cord Blood Banking

11/97	Meeting with Society of In-Vitro Biology - Proposed Approach
7/11/97	FDA/AATB - Discussion of Regulation of Demineralized Bone Matrix
6/23/97	Discussion of Regulation of Eye Tissue with EBAA
4/8/97	FDA meeting on Regulation of Eye Tissue with Eye Bank Representatives.
3/17/97	FDA Open Public Meeting for comments on the "Proposed Approach"
12/19/96	CBER/FACT meeting
12/96	FDA invited to discuss good tissue practices with AATB, EBAA and ASRM
12/12/96	FDA meeting with representatives on Cord and Peripheral Blood
12/11/96	FDA meeting with representatives of autologous and other cell therapies.
10/96	Heart valve industry - Discussion of regulation of heart valve allografts
12/13/95	Workshop: Cord Blood Stem Cells - Procedures for Collection and Storage
2/4/96	FDA meeting with representatives on conventional banked human tissue for transplantation, eye and reproductive tissue
10/95 and 3/96	FDA invited to discuss reproductive tissue donor testing, screening and establishment registration with ASRM and AATB
6/20-21/95	Tissue Workshop: Tissue for Transplantation and Reproductive Tissue: Scientific and Regulatory Issues and Perspectives
3/95	Workshop on Human Tissue Intended for Transplantation and Human Reproductive Tissue: Donor Screening and Infectious Disease Testing
6/94	Workshop on Human Tissue Intended for Transplantation

Planned Future Meetings with Industry:

10/03	Workshop at the ASRM Annual Meeting: FDA Regulations: What IVF Labs Need to Know
9/29/03	Center For Business Intelligence
5/28/03	International Society for Cellular Therapies –GTP Workshop (participation on organizing committee and presentations at the meeting)
5/15/03	Pittsburgh Development Center
5/12/03	Covance Laboratories, Inc.

FDA Investigator Training:

10/21-25/02	FDA Human Tissue Course for Investigators, Annapolis, MD
6/3-6/02	FDA Human Tissue Course for Investigators, Columbia, MD
2/9-11/99	FDA Central Region Human Tissue Course for FDA Investigators
3/12/97	Training Provided to Baltimore District Biologics Cadre regarding Inspection of Human Tissue Establishment
2/1-3/95	FDA Mid-Atlantic Region Tissue Bank Training for FDA Investigators, Baltimore, MD

Future Plans:

- "Human Tissue Inspection" course scheduled for 10/03
- FDA scientific workshops to gather information and data on ART practices
- FDA open public meeting to address questions concerning proposed rules on donor suitability and GTPS's (after publication)
- Continue dialogue with ASRM/SART and AATB
- AATB and ASRM have agreed to hold site visit program at semen banks and infertility clinics for investigators in the District Offices as an educational and cross-training opportunity for FDA investigators in advance of FDA finalizing in 2004 the new 21 CFR Part 1271 regulations that would include reproductive tissues and cell establishment.
- Continue Dialogue with EBAA, AABB, FACT and ISHAGE

Leveraging Initiatives with the Cell/Tissue Industry:

- Continue Dialogue with EBAA and ASRM regarding developing a draft guidance document to implement the donor eligibility (DE) and GTP rules specifically for their industry

GLOSSARY

AABB ……American Association of Blood Banks
AATB ……American Association of Tissue Banks
ACOT ……Advisory Committee on Organ Transplantation
ARM ……Association of Reproductive Managers
ART ……Assisted Reproductive Technologies
ASRM ……American Society for Reproductive Medicine
ASQ ……American Society for Quality
CAP ……College of American Pathologists
CDC ……Centers for Disease and Control
CJD ……Creutzfeldt-Jakob Disease
DARPA……..Defense Advance Research Projects Agency
DE ……Donor Eligibility
DHHS ……Department of Health and Human Services
EBAA ……Eye Bank Association of America
FACT……..Federation for Accreditation of Cellular Therapies
FDA ……Food and Drug Administration
FDLI ……Food and Drug Law Institute
GTP ……Good Tissue Practices
HRSA ……Health Resources and Services Administration
ISHAGE……..International Society for Hematopoietic and Graft Engineering
ISLAT ……Institute of Science, Law and Technology
NCOART……...National Coalition for Oversight of Assisted Reproductive Technologies
NIH ……National Institutes of Health
RAPS ……Regulatory Affairs Professional Society
RESOLVE……..National Infertility Association
SART ……Society for Assisted Reproductive Technologies
vCJD ……variant Creutzfeldt-Jakob Disease