

**Committee:** Infectious Disease

**Title:** Improving Investigations of Transplant Transmitted Infections at State and Local Health Departments

**I. Statement of the Problem:**

Each year in the United States, more than 28,000 solid organs and 2 million tissues are recovered for transplantation, including heart, lung, liver, kidneys, pancreas, intestine, bone, skin, heart valves, tendons, fascia and corneas. Tissue and organ transmitted infections have long been recognized as a known risk for patients receiving tissue products and organs. Because of the urgent need for organs, some infections are allowed to be transmitted from the donor, but many other infections are unrecognized; a recent estimate is that approximately 1% of transplants are associated with potential risk of an unrecognized and unintended transmission. Infectious agents transmitted from solid organ donors to recipients in just the past few years have included viruses such as HIV, hepatitis C virus (HCV), lymphocytic choriomeningitis virus, rabies virus, West Nile virus; bacteria such as *Mycobacterium tuberculosis* and *Pseudomonas aeruginosa*; and parasites such as *Balamuthia mandrillaris*, *Strongyloides* spp., and *Trypanosoma cruzi*, the etiologic agent of Chagas disease. Many of these infections have been associated with a high mortality rate. Among tissues, disease transmission reports are less frequent and the risk is less known due to lack of surveillance; organisms that have been identified include transmission of HCV, Group A streptococcus, *Clostridium* spp., and *Chryseobacterium meningosepticum*.

In several cases of transplant transmitted infections, investigations have identified instances in which there has been limited communication among healthcare providers caring for patients receiving organs or tissues from a common donor, where the organs and tissues were distributed to multiple states. This can result in the delayed identification of transplant transmitted infections and subsequent potential treatment for the recipients. In addition, since there is no systematic requirement to collect and bank pre-transplant serum from recipients to assess whether a post transplant infection was acquired from the donor, investigations can be complex and challenging.

Epidemiologic and laboratory investigations of these infections are complex, involve multiple agencies and jurisdictions, and require a knowledge of organ and tissue procurement procedures and transplant medicine that are not typically found within state and local health departments. Thorough investigations of transplant transmitted infections can help prevent additional cases by expediting the identification of additional contaminated organs or tissues collected from the same donor. Additionally, improved recognition of transplant transmitted infections should result in more rapid treatment of the recipients of the implicated organs or tissues.

Organs and tissues are regulated by two different agencies; organs by the Health Resources and Services Administration (HRSA) and tissues by the Food and Drug Administration (FDA). Oversight of the transplantation of vascularized human organs such as kidney, liver, heart, lung or pancreas falls under HRSA, which contracts with a private, non-profit group, the United Network for Organ Sharing (UNOS) to maintain the Organ Procurement and Transplantation Network (OPTN); a national matching registry. Potential organ donors are screened for a limited number of infectious agents including HIV 1 and 2, hepatitis B and C, cytomegalovirus and Epstein-Barr virus.

Within the FDA, the Center for Biologics Evaluation and Research (CBER) regulates human cells or tissue intended for implantation, transplantation, infusion, or transfer into a human recipient as a human cell, tissue, and cellular and tissue-based product or HCT/P. Under CBER, potential tissue donors are screened for HIV types 1 and 2, HBV, HCV and *Treponema pallidum*. In addition donors of viable leukocyte rich HCT/Ps must also be tested for HTLV I and II and in some instances *Chlamydia trachomatis* and *Neisseria gonorrhea*.

Organ Procurement Organizations (OPOs) recover and place organs to transplant centers in coordination with UNOS. Tissue is recovered by various organizations and are processed in varying degrees by tissue banks. The processing depends on the tissue bank and the type of tissue recovered. Tissue banks distribute their products to hospitals, outpatient centers, and even dentists.

Screening cannot be done on all donors of tissues or organs for every potential infectious agent, nor is it practical. Transmission of infectious agents via tissues and organs will continue to be a rare although real problem. In order to allow public health and clinicians to better investigate transplant transmitted infections, it is important to have guidelines in place to ensure a coordinated and systematic response.

Similar issues have arisen concerning infections transmitted through the transfusion of blood products.

## **II. Statement of the desired action(s) to be taken:**

### ***Justification***

The purpose of this position statement is to support improved and standardized investigations of transplant transmitted infections by the public health and health care community. This would facilitate improved recognition of future cases of transplant transmitted infections, prevention of additional cases, and rapid initiation of appropriate therapy for patients with transplant transmitted infections.

Such improvements will require state health departments to develop procedures and expertise in complex investigations and establish contacts with the transfusion services and other stakeholders in the transplant community. It is crucial that CDC play a lead role in assisting state HDs in these efforts by developing investigation toolkits for transplant transmitted infections and by providing enhanced resources to the states in the form of personal consultations.

This position statement is not intended to require that every health department investigate every transplant transmitted infection. Instead, it is to ensure that guidance is available for those investigations which are necessary to perform for public health purposes.

### ***Actions***

The CDC should develop toolkits containing materials that would facilitate, improve and standardize transplant transmitted investigations. These materials would provide guidance on specific pathogens, establish timeframes within which to conduct an investigation to attempt to prevent additional cases, delineate reporting criteria, and incorporate template letters that could be used to notify or make requests for information from physicians, OPOs, and organ/tissue recipients.

In addition, the CDC is asked to convene a high level meeting of representatives from the various agencies and organizations which have oversight for, or are involved in the collection, transplantation or monitoring of organs and tissues..

Because direct and timely consultation is vital during investigations of transplant transmitted infections, the CDC should ensure adequate staffing of appropriate subject matter experts to provide real time guidance during such events, particularly for interstate investigations that would benefit from federal coordination.

UNOS, through a contract with HRSA administers the OPTN. As such, OPTN should work with the CDC to develop complementary materials for OPOs and transplant centers to use when investigating organ transplant transmitted infections. FDA should work with CDC to develop materials for tissue banks and clinician users of tissue products for transplantation. Materials should be developed to ensure standardization and completeness, and to facilitate collaboration between the transplant services, public health, and healthcare facilities. Such material should be consistent with CDC guidance mentioned above.

### **III. Public Health Impact:**

The major benefits of thorough, standardized investigations of transplant transmitted infections are to:

1. Identify novel threats to organ and tissue transplant safety;
2. Identify patients who received organs or tissues from a donor identified with a potential transplant-transmissible disease;
3. Identify others that may have been exposed to communicable disease of donor origin;
4. Identify other potential modes of transmission in organ recipients (i.e, transfusions); and
5. Initiate appropriate and timely therapy for infected patients.

By providing investigational guidance to public health, the transplantation industry and health care providers, all stakeholders will be better prepared to recognize and understand

the scope of transplant transmitted infections, prevent additional cases and fully investigate transplant transmitted infections due to a previously unrecognized or newly emerging pathogen.

#### **IV. References:**

1. Federal Register: September 29, 2009 (Volume 74, Number 187)

#### **V. Coordination:**

##### **Agencies for Response:**

- (1) Thomas Frieden, MD, MPH  
Director  
US Centers for Disease Control and Prevention  
1600 Clifton Road, NE  
Atlanta, GA 30333  
404-639-7000  
[txf2@cdc.gov](mailto:txf2@cdc.gov)
- (2) Margaret Hamburg, MD  
Commissioner  
US Food and Drug Administration  
10903 New Hampshire Ave  
Silver Springs, MD 20992-0002  
1-888-463-6332

#### **VI. Submitting Author:**

- (1) Sally Slavinski, DVM, MPH, DACVPM  
Assistant Director Zoonotic, Influenza and Vector-borne Disease Unit  
New York City Department of Health and Mental Hygiene  
[sslavins@health.nyc.gov](mailto:sslavins@health.nyc.gov)  
212-788-4160

##### **Co-Author:**

- (1) Anthony Marfin, MD, MPH, MA  
State Epidemiologist  
Washington State Department of Health  
[Tony.Marfin@doh.wa.gov](mailto:Tony.Marfin@doh.wa.gov)  
206-418-5614
- (2) Katherine Feldman, DVM, MPH  
State Public Health Veterinarian  
Maryland Department of Health and Mental Hygiene

- KFeldman@dhhm.state.md.us  
410-767-5649
- (3) Sarah Patrick, PhD  
State Epidemiologist  
Missouri Department of Health and Senior Services  
Sarah.Patrick@dhss.mo.gov  
573-751-6127
- (4) Marion A. Kainer MD, MPH, FRACP  
Medical Epidemiologist/ Infectious Diseases Physician  
Director, Hospital Infections and Antimicrobial Resistance Program  
Tennessee Dept. of Health  
marion.kainer@tn.gov  
615 741 7247
- (5) Alfred DeMaria  
State Epidemiologist  
Massachusetts Department of Public Health  
Alfred.Demaria@state.ma.us  
617-983-6550
- (6) Ruth Lynfield  
State Epidemiologist  
Minnesota Department of Health  
Ruth.Lynfield@state.mn.us  
651-201-5422
- (7) Richard Danila  
Deputy State Epidemiologist  
Minnesota Department of Health  
Richard.Danila@state.mn.us  
612-676-5414