

DRAFT ISSUE SUMMARY

BLOOD PRODUCTS ADVISORY COMMITTEE MEETING

MARCH 14-15, 2002

TOPIC 4.

Bacterial and Fungal Contamination of Human Tissue Intended for Transplantation

ISSUE

FDA seeks general discussion from the Blood Products Advisory Committee (BPAC) regarding mechanisms for preventing bacterial and fungal contamination and infectious disease transmission by human tissue intended for transplantation.

BACKGROUND

In November 2001, the Minnesota Department of Health received reports of three previously healthy persons who died unexpectedly following uncomplicated knee surgery, prompting the state health department to issue a one-week ban of elective knee surgery. [MMWR 50(6):1035-6, November 23, 2001]. All three patients had a rapid clinical course consistent with septic shock, and blood cultures from one of the patients yielded *Clostridium sordelli* (an anaerobic, spore-forming, gram-positive bacterium found in the human gastrointestinal tract.) This 23-year-old patient had received a fresh, human knee osteochondral allograft obtained from a cadaveric donor by a tissue bank. CDC's investigation revealed that the identical bacterium was isolated from the donor's contralateral knee and other non-implanted tissue, although the tissue bank cultures, prior to distributing the tissues, were negative. CDC then became aware of 5 other cases of septic arthritis (occurring in April 2001) due to *Clostridium septicum*, and these patients had all received allografts from the same tissue bank. CDC also reported on 4 cases of septic arthritis following anterior cruciate ligament reconstruction using tendon allografts, occurring in Florida and Louisiana in 2000 [MMWR 50(48):1080-1083, December 7,

2001]. A variety of bacteria were cultured in these 4 cases. Two cases had received tendons from the same donor, and these tendons had been irradiated. The two other cases received tissue from the same donor, and these tendons had not been irradiated, and were inadvertently released. Through epidemiological surveillance, the Centers for Disease Control and Prevention (CDC) have identified approximately 20 additional cases of septic arthritis (personal communication), the majority involving Clostridium. These will be discussed at the meeting.

FDA has been regulating human tissue intended for transplantation since 1993, when it issued an interim rule that focused on screening and testing the tissue donor for Human Immunodeficiency Virus (HIV), Hepatitis B (HBV) and Hepatitis C (HCV), because of concerns with importing tissue from donors who harbored these infectious agents. The interim rule also contained requirements for having written procedures and maintaining records related to donor screening and testing. The Interim Rule was finalized in 1997, and the requirements are codified at 21 CFR part 1270. Section 1270.31(d) of the final rule requires that a tissue establishment prepare, validate, and follow written procedures for prevention of infectious disease contamination or cross-contamination during processing. The “infectious disease” agents include HIV, HBV, HCV, as well as bacteria, fungi, and TSE-associated prions. FDA has recently proposed additional requirements for good tissue practices, which would control the recovery, processing, storage, packaging, labeling, and distribution of human cells, tissues, and cellular and tissue-based products, to prevent the introduction, transmission and spread of communicable disease agents and diseases to recipients of these products. The requirements would include controls over the facility, personnel, environment, equipment, supplies and reagents, process controls, process validation, labeling controls, and would introduce the concepts of tracking tissue from donor to recipient, and vice versa, and reporting of adverse reactions. Currently, FDA does not require reporting, and receives such reports voluntarily, through its MedWatch program.

The eye-banking and tissue-banking communities are also concerned about the possible transmission of infectious diseases to the recipients of human tissue. Professional

organizations have developed standards, which their accredited members must follow. For instance, the American Association of Tissue Banks Standards for Tissue Banking include standards for recovery using aseptic or clean techniques, validated processing methods to prevent contamination and cross-contamination, and microbiological testing of tissue, and reporting of adverse outcomes. These standards cover aerobic, anaerobic, and fungal cultures taken prior to exposure to antibiotics, disinfection during processing or terminal sterilization, and final packaging cultures prior to release. The Eye Bank Association of America Medical Standards include procurement procedures that use aseptic technique, microbiologic culture at the time of corneal preservation in tissue culture medium containing antibiotics (no longer recommended) or at the time of surgery, and reporting of adverse reactions. Ocular and other tissue released for transplantation is not necessarily purported to be sterile, unless labeled so.

Discussion

This topic is being presented to inform the members about the recent reported cases of bacterial transmission to recipients of human musculoskeletal tissue, resulting in significant morbidity and mortality. In its presentation, CDC will make recommendations that may prevent such occurrences. The Center for Biologics Evaluation and Research, FDA will summarize the current regulations that attempt to safeguard human tissue intended for transplantation from communicable disease contamination and cross-contamination, and will explain the proposed good tissue practice (GTP) regulations that would further strengthen FDA's ability to help ensure a safe tissue supply. In addition, members of the tissue-banking and eye-banking communities will inform the committee about the steps that they have taken to address their concerns about this problem.

Charge

Committee members will be asked to provide a general discussion on the mechanisms for preventing bacterial and fungal contamination and infectious disease transmission by human tissue intended for transplantation.