

conduct of xenotransplantation clinical trials. Also, the collection of information will help ensure that the sponsor maintains important information in a cross-referenced system that links the relevant records of the xenotransplantation product recipient, xenotransplantation product, source animal(s), animal procurement center, and significant nosocomial exposures. The PHS guideline describes an occupational health service program for the protection of health care workers involved in xenotransplantation procedures, caring for xenotransplantation product recipients, and performing associated laboratory testing. The guideline also describes public health needs for: (1) A national xenotransplantation database, which is currently under development by the PHS; (2) a central PHS biologic specimen archive, also under consideration; and (3) the Secretary's Advisory Committee on Xenotransplantation, which was developed and has been implemented by the Department of Health and Human Services (DHHS). These public health programs and the PHS guideline are intended to protect the public health and to help ensure the safety of using xenotransplantation products in humans by preventing the introduction, transmission, and spread of infectious diseases associated with xenotransplantation.

The PHS guideline also recommends that certain specimens and records be maintained for 50 years beyond the date of the xenotransplantation. These include: (1) Records linking each xenotransplantation product recipient with relevant health records of the source animal, herd or colony, and the specific organ, tissue, or cell type included in or used in the manufacture of the product (3.2.7.1); (2) aliquots of serum samples from randomly selected animal and specific disease investigations (3.4.3.1); (3) source animal biological specimens designated for PHS use (3.7.1); animal health records (3.7.2), including necropsy results (3.6.4); and (4) recipients' biological specimens (4.1.2).

The retention period is intended to assist health care practitioners and officials in surveillance and in tracking the source of an infection, disease, or illness that might emerge in the recipient, the source animal, or the animal herd or colony after a xenotransplantation.

The recommendation for maintaining records for 50 years is based on clinical experience with several human viruses that have presented problems in human to human transplantation and are

therefore thought to share certain characteristics with viruses that may pose potential risks in xenotransplantation. These characteristics include long latency periods and the ability to establish persistent infections. Several also share the possibility of transmission among individuals through intimate contact with human body fluids. Human immunodeficiency virus (HIV) and Human T-lymphotropic virus are human retroviruses. Retroviruses contain ribonucleic acid that is reverse-transcribed into deoxyribonucleic acid (DNA) using an enzyme provided by the virus and the human cell machinery. That viral DNA can then be integrated into the human cellular DNA. Both viruses establish persistent infections and have long latency periods before the onset of disease, 10 years and 40 to 60 years, respectively. The human hepatitis viruses are not retroviruses, but several share with HIV the characteristic that they can be transmitted through body fluids, can establish persistent infections, and have long latency periods, e.g., approximately 30 years for Hepatitis C.

In addition, the PHS guideline recommends that a record system be developed that allows easy, accurate, and rapid linkage of information among the specimen archive, the recipient's medical records, and the records of the source animal for 50 years. The development of such a record system is a one-time burden. Such a system is intended to cross-reference and locate relevant records of recipients, products, source animals, animal procurement centers, and nosocomial exposures.

Respondents to this collection of information are the sponsors of clinical studies of investigational xenotransplantation products under investigational new drug applications (INDs) and xenotransplantation product procurement centers, referred to as source animal facilities. Currently, there are 12 respondents who are sponsors of INDs that include protocols for xenotransplantation in humans. Other respondents for this collection of information are 18 source animal facilities which provide source xenotransplantation product material to sponsors for use in human xenotransplantation procedures. These 18 source animal facilities keep medical records of the herds/colonies as well as the medical records of the individual source animal(s). The total annual reporting and recordkeeping burden is estimated to be approximately 156 hours. The burden estimates are based on FDA's records of xenotransplantation-related INDs and

estimates of time required to complete the various reporting and recordkeeping tasks described in the guideline. FDA does not expect the level of clinical studies using xenotransplantation to increase significantly in the next few years.

FDA is requesting an extension of OMB approval for the following reporting and recordkeeping recommendations in the PHS guideline:

TABLE 1.—REPORTING RECOMMENDATIONS

PHS Guideline Section	Description
3.2.7.2	Notify sponsor or FDA of new archive site when the source animal facility or sponsor ceases operations.
3.4	Standard operating procedures (SOPs) of source animal facility should be available to review bodies.
3.5.1	Include increased infectious risk in informed consent if source animal quarantine period of 3 weeks is shortened.
3.5.4	Sponsor to make linked records described in section 3.2.7 available for review.
3.5.5	Source animal facility to notify clinical center when infectious agent is identified in source animal or herd after xenotransplantation product procurement.

TABLE 2.—RECORDKEEPING RECOMMENDATIONS

PHS Guideline Section	Description
3.2.7	Establish records linking each xenotransplantation product recipient with relevant records.
4.3	Sponsor to maintain cross-referenced system that links all relevant records (recipient, product, source animal, animal procurement center, and nosocomial exposures).
3.4.2	Document results of monitoring program used to detect introduction of infectious agents which may not be apparent clinically.