Supporting Statement A for

Tissue and Organ Donor Epidemiology Study (TODES)

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ATTACHMENTS

Attachment 1: List of Participating Organizations
Attachment 2: Organ and Tissue Participants Data Variables Requested
Attachment 3: Eye Bank Participants Data Variables Requested
Attachment 4: TODES Working Group

A.1 Circumstances Making the Collection of Information Necessary

HHS and its Operating Divisions (e.g., FDA) regulates human cells, tissues, and cellular and tissue-based products (HCT/Ps)—defined as articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. Examples of HCT/Ps include bone, ligament, skin, dura mater, heart valves, cornea, tendon, oocytes, semen, and hematopoietic progenitor cells (HPCs) derived from peripheral and umbilical cord blood (UCB). All HCT/Ps are regulated under Section 361 of the Public Health Service Act to prevent the introduction, transmission, and spread of communicable disease; some HCT/Ps are also regulated as biologic, device, or combination products. In order to minimize the risk of infectious disease transmission, donors must be screened (including a donor medical history interview and medical records review) and tested to evaluate for either the risk or presence of communicable diseases. The proposed study, Tissue and Organ Donor Epidemiology Study (TODES), fits within the HHS public health research agenda as described here and in the other supporting documents.

A workshop in June 2005 ("Preventing Organ and Tissue Allograft-Transmitted Infection: Priorities for Public Health Intervention") identified gaps in organ and tissue safety in the United States.[1] Participants developed a series of allograft safety initiatives, assessed progress, and identified priorities for future interventions. Despite progress, improved recognition and prevention of donor-derived transmission events is needed. It was concluded that this requires systems integration across the organ and tissue transplantation communities including organ procurement organizations, eye and tissue banks, and transplant infectious disease experts. Commitment of resources and improved coordination of efforts are required to develop essential tools to enhance safety for transplant recipients.

In May 2010, the U.S. Food and Drug Administration (FDA) held a workshop entitled Emerging Infectious Diseases: Evaluation to Implementation for Transfusion and Transplantation Safety. The goal of this meeting was to identify a research agenda to characterize the risk for transmission of donor-derived infections and to inform the development of guidelines for emerging infectious diseases.[2] With respect to the evaluation of donors, the participants discussed knowledge gaps in current evaluation practices (i.e., screening and testing donors for infectious agents). The sensitivity and specificity of current approaches are largely unknown. Serologic assays detect chronic or persistent infections but are less useful for diagnosing more recent infections. Some cases of donor-derived infection in organ transplantation occur due to the limitations of serologic testing (e.g., window-period cases before seroconversion). Nucleic acid testing (NAT) is useful for detecting infection only in blood samples of viremic donors and is not available for every potential organism. Variability in performance and practice limits the ability to compare and interpret existing testing data derived from donor populations that could, in turn, inform decisions regarding optimal assay selection. For example, almost all organ-procurement organizations use assays indicated for donor screening, but a few may use diagnostic tests. Programs use antibody assays from different manufacturers (resulting in differing performance characteristics), and while all tissue banks and many OPOs use NAT routinely, some OPOs only perform NAT in special

circumstances (e.g., on the basis of donor characteristics). There are few data regarding the clinical performance of these assays in donor populations.

Because of the lack of standardization of donor evaluation procedures and data collection, pathogen characteristics, and recipient surveillance, recognizing emerging infectious diseases in organ and tissue transplantation remains challenging. Gaps in systematic identification and characterization of the scope and magnitude of donor-derived infectious disease transmissions through organ and tissue transplantation remain a challenge to improvements in assessing risk and in developing more effective donor screening and testing strategies. Studies of blood and organ donors suggest that the probability of viremia for HIV, HCV, HBV, and human T-cell lymphotropic virus in the United States is higher in tissue and organ donors than in first-time blood donors.[3] However, prospective data collection is needed to define baseline seroprevalence in different donor populations, particularly since the more recent implementation of NAT; these data could be used to develop enhanced strategies for donor screening and testing to prevent disease transmission.

TODES is being conducted in order to better understand the impact of donor screening and selection procedures, and to determine the extent of donor-donation level data that are collected for organ and tissue (including ocular) donors. The data that are obtained from Organ Procurement Organizations (OPOs) and Eye Banks will provide a better characterization of the deceased donor pool; information regarding data management and storage practices; and a measure of the degree of standardization of data collected by various organizations across the U.S. TODES may provide better estimates of the risk of HIV, HBV and HCV infections associated with organ and tissue transplantation and the potential for disease transmission; illustrate differences in laboratory screening methods and the impact of protocol variations; and serve as a pilot for future studies. This retrospective study will provide a framework for future, prospective studies of organ and tissue donors that could inform policy decisions regarding donor qualification procedures and, potentially, increase the donor pool.

References

1. Organ and Tissue Safety Workshop 2007: Advances and Challenges. Jay A. Fishman, D. Michael Strong and Matthew J. Kuehnert. CELL AND TISSUE BANKING. Volume 10, Number 3 (2009), 271-280.

2. Food and Drug Administration Emerging infectious diseases: evaluation to implementation for transfusion and transplantation safety public workshop [cited 2011 Feb 13]. http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/WorkshopsMeetingsConferences/ucm206773.htm.

3. Zou S, Dodd RY, Stramer SL, Strong DM. Probability of viremia with HBV, HCV, HIV, and HTLV among tissue donors in the United States. NEJM. 2004;351:751–9.

A.2 Purpose and Use of the Information Collection

Currently, infectious disease transmission rates associated with organ and tissue transplants are unknown and are believed to have a high potential for underreporting. The lack of comprehensive data on infectious disease prevalence and incidence in potential donors corresponding to donor demographics, particularly for tissues, limits our ability to create accurate data-driven risk profiles for donors, and impedes improvements to the screening process. As an important first step in addressing this issue, the HHS Office of the Assistant Secretary for Health Office of HIV/AIDS & Infectious Disease Policy awarded a contract to RTI International (RTI) in September 2012 for the design and conduct of a Tissue and Organ Donor Epidemiology Study (TODES).
TODES will capture extant data on infectious disease testing results for HIV, HBV, and HCV, as well as other characterizing information about potential organ and tissue donors, from participating organ procurement organizations and eye banks. RTI will request that these organizations extract specific information on all deceased donors and eligible referrals from their operational databases (for the period 2009-2013) and provide the data extract to RTI for secondary analysis. The results of the analyses, including infectious disease prevalence and incidence estimates and donor characterizations, will be compiled in a TODES final report and submitted to HHS. The report will also provide an assessment of the general availability and quality of the retrospective data requested from the organ and tissue communities, which will inform the design of future organ and tissue safety studies.

This study will engage in secondary analyses of extant data from organ and tissue procurement and processing facilities. The extant data were collected at the time that the deceased organ and/or tissue donor was identified and entered into a tracking database maintained by the organization for this purpose. In order to reduce the burden on the participants, TODES will obtain some of the organ donor/donation data from the United Network for Organ Sharing (UNOS) which operates a centralized national Organ Procurement and Transplantation Network (OPTN) for the purpose of managing the nation's organ transplantation system under contract with the U.S. Department of Health and Human Services (Contract No. HHSP23320095651WC).

A.3 Use of Information Technology and Burden Reduction

The specific data to be obtained from the participating organizations include the following categories of information:

1. Donor demographics and death information;
2. Donor infectious disease test results for HIV, HBV, and HCV; including serological assays and nucleic acid testing when available; and
3. Basic donation and disposition information regarding organs, tissues, and/or eyes.

A list of requested variables in Attachments 2 and 3, from which RTI created a master data dictionary. The participating organizations will extract the relevant data from their existing donor records for calendar years 2009 – 2013; the data will be transmitted

securely to RTI as line data (one record per donor), and RTI will merge all participating organization data into a common TODES database.

RTI will construct this TODES database within the context of all participating organizations operating under their data policies and procedures. Databases are built for specific purposes, and not all participating organizations have built their databases with multi-organization research in mind. One of the goals for TODES is to identify and document such differences and the resulting limitations on analysis and interpretation. This information will be used to design a future prospective study. In an effort to control organizational variation in final TODES database, RTI developed the master data dictionary mentioned earlier as a guide for all participating organizations.

RTI will ask each participating organization to extract the data in the format and structure defined in this master data dictionary. Ideally, the data requested for the TODES project will require a minimum amount of additional processing, mathematical manipulations, or summarization by the submitting organizations. To account for circumstances where the organization's data cannot be easily extracted into the format required by the master data dictionary and is delivered in a format/structure not in agreement with the master data dictionary, RTI will complete a data review of all extracted and delivered data. Since TODES will merge datasets collected from each participating organization with UNOS data, the data review will involve a study of the fidelity between delivered dataset and the UNOS data, as well as a study of the dataset's contents.

First, the data review process will involve reviewing the variables contained in the data and the contents of each variable in comparison with the master data dictionary. This data review will identify variables that do not match the variable names in the master data dictionary, as well as identify variables that contain information not in correspondence with the variable contents required by the master variable dictionary. Second, the dataset will be merged with the UNOS data to assess fidelity between the two datasets. The assessment of fidelity is an attempt to ensure records in UNOS do in fact represent the subjects represented in the participating organization's dataset.

Once RTI assesses the delivered data, RTI will write up a set of data related questions for delivery to the participating organization. The answers to these questions will help RTI understand the data better and enable RTI to incorporate the data into the TODES database with improved accuracy.

Once the participating organization that delivered the data has answered the questions, RTI will incorporate the organization's dataset into the TODES database using an operational data dictionary and SAS programming. Ideally the delivered datasets will be in agreement with the master data dictionary; however, RTI anticipates some delivered datasets to require additional processing to make them compatible with the master data dictionary. Instead of asking the participating organization to redo the delivery, RTI will process the data in a consistent manner utilizing the answers received from the participating organization regarding their data. In order to incorporate data into the TODES database, some variables will simply need copying over, but other variables will need at least a variable name change, while others may need derivation. Each participating organization's operational data dictionary will document all of these decisions and operations. The operational data dictionary will contain information on

TODES variable name, description, length and format, as well as a definition. The variable name and structure of each variable listed in the operational data dictionary will be controlled by the master data dictionary. The definition will contain the information necessary to identify which variables were simply copied over, which variables were renamed, and which variables were derived. For derived variables, the definition column will also contain the instructions to derive the variable from source data. Once RTI has constructed a TODES compliant version of the participating organization's dataset and completed the operational data dictionary, the TODES study team will incorporate the dataset into the overall TODES database.

As noted above, one TODES goal is to inform the design of a prospective study of infection prevalence and incidence within the organ procurement/tissue banking community. Before a prospective study is implemented, many of the unknowns which could contribute to uncontrolled variation in infection measures need to be identified and documented. During the construction of TODES database, the TODES study team will attempt to standardize the data to a certain degree, but some inconsistencies will be unavoidable. The TODES study team will document decisions and observations made about the data that influence accuracy, utility, and generalizability of the TODES database for infection prevalence/incidence estimation. All final analysis interpretations will acknowledge these decisions and observations and the resulting limitations.

A.4 Efforts to Identify Duplication and Use of Similar Information

The research agenda represented by this study's goals includes developing a process of collaboration between government (i.e., regulatory, public health, policy), industry (e.g., tissue manufacturing, supply, test manufacturers), and the allograft transplant provider community (clinicians, hospitals, professional organizations, OPOs, and tissue recovery banks). Through this collaboration, the existing gaps in information about organ and tissue donors and infection rates can begin to be filled in. Without this collaboration; there is currently no other study that seeks to provide prevalence and incidence estimates and correlate them with donor characteristics for these donors.

A.5 Impact on Small Businesses or Other Small Entities

Small businesses or entities are not involved. All respondents are tissue and eye procurement organizations of which some serve several states, one state, partial states, or parts of several states.

A.6 Consequences of Collecting the Information Less Frequently

Each organ procurement and eye bank organization is being asked to provide their data only once.

A.7 Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

The proposed data collection is consistent with 5 CFR 1320.5.

A.8 Comments in Response to the Federal Register Notice and Efforts to Consult Outside Agency

As required by 5 CFR 1320.8(d), the 60-day Federal Register notice was published on August 28, 2014, Vol. 79, pp 51333-4. No comments were received in response to this notice.

A.9 Explanation of Any Payment or Gift to Respondents

The respondents, OPOs and eye banks, will be extracting data for TODES that have already been collected by those organizations. Some of the data requested by RTI were previously extracted and provided to the United Network for Organ Sharing (UNOS), the American Association of Tissue Banks (AATB), or the Eye Bank Association of America (EBAA) for required reporting and transplant matching purposes. RTI has communicated with the respondents and several have reported that their database administrators on staff can more easily extract the requested data while other organizations have estimated that more time will be necessary due to fewer organizational resources and/or the need to extract data from multiple data systems. Our estimated respondent burden hours shown in Table 12-1 reflect our best estimate of the time to extract data as averaged across all of the respondent organizations. For OPOs and eye banks with limited resources that request compensation for their TODES extraction efforts, RTI will offer those organizations $37.06 per hour of staff time required in appreciation of their efforts.

A.10 Assurance of Confidentiality Provided to Respondents

TODES project will not allow RTI or HHS to track information back to individual persons either as donors or recipients of transplanted organs and tissues. The sharing of data for research purposes under TODES will be covered by Data Use Agreements executed between each participating organization and RTI.

A.11 Justification for Sensitive Questions

Based on the protocols for this study, there are no sensitive questions being asked for the purpose of this data collection. Variables extracted by respondent organizations are associated with deceased organ, tissue, and eye donors, with no selection criteria associated with a deceased donor's identity. Furthermore, no contact will be made with any person or organization with contact with any deceased donor eligible for inclusion.

A.12 Estimates of Hours Burden Including Annualized Hourly Costs

Table A.12-1: Estimated Annualized Burden Hours

It is estimated that the OPO respondents will spend on average 85 minutes extracting the requested study data, which Eye Bank respondents will spend on average 55 minutes extracting requested study data. Both sets of respondents are best characterized as database administrators per the U.S. Bureau of Labor Statistics, with average hourly rates of $37.06. The annualized cost to these respondents is estimated at $1133.29 based on that $37.06 per hour with only one data collection cycle in total to occur within a one year timeframe upon OMB approval.

Type of Respondents	Number of Respondents	Number of Responses per Respondent	Average Burden Per Response (in hours)	Total Annual Burden Hours
OPOs	17	1	85/60	24.1
Eye Banks	7	1	55/60	6.4
Total	24	2		30.5

A.12 - 2 ANNUALIZED COST TO RESPONDENTS

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Type of Respondents	Number of Respondents	Frequency of Response	Average Time per Respondents	Hourly Wage Rate*	Respondent Cost
OPOs	17	1	85/60	$37.06	$894.62
Eye Banks	7	1	55/60	$37.06	$238.67
Totals	24	2			$1133.29

*http://www.bls.gov/ooh/computer-and-information-technology/database-administrators.htm

A.13 Estimate of Other Total Annual Cost Burden to Respondents or Record Keepers

There are no capital or start-up costs, and no maintenance or service cost components to

report.

A.14 Annualized Cost to the Federal Government

The annual total cost to the Federal Government for the proposed study is estimated to be approximately $259,512. The costs of planned activities for this study are provided in table 14-1 according to the phase of the project. The total costs in each part of the study includes personnel time (salaries) for the investigators and research staff, and Activity specific items such as provision of the incentive amounts for participants during the Participant Enrollment and Data Collection phase of the study.

Table 14.1 Annualized Costs to the Federal Government

Item	Avg. Salary	Fringe Rate	% Effort	Annualized Cost
OASH Project Manager Officer GS13	$109,000	30%	20%	$28,400
3 contractor staff at RTI	$339,991	included	65% (combined)	$220,994
RTI Contract Consultants	$100/hr	NA	2.8% (combined)	$4918
Operational Costs for Data Collection Activities –Printing, equipment, overhead), non-labor				$5,000
Other Contractual costs for data collection, non-labor				0
Travel costs associated with data collection				0
Other costs, non-labor				$200
Total				

A.15 Explanation for Program Changes or Adjustments

This is a new data collection.

A.16 Plans for Tabulation and Publication and Project Time Schedule

A.16 - 1 Project Time Schedule

Activity	Time Schedule
Receive OMB Approval	March 2015
Execute DUAs with OPOs and other facilities	February 2015 – April 2015

Estimated implementation of data collection	Upon OMB Approval
Data verification and final analysis	April 2015- June 2015
Draft report	April 2015 – June 2015
Final Report	July 2015 – August 2015

A.17 Reason(s) Display of OMB Expiration Date is Inappropriate

The OMB expiration date will be displayed in the upper-right hand corner of the questionnaire."

A.18 Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification statement of OMB Form 83-I.