



# *Guidance Document*

## *Effective Quality Assurance of the Donor Risk Assessment Interview*

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# ***AATB/AOPO/EBAA GUIDANCE DOCUMENT EFFECTIVE QUALITY ASSURANCE OF THE DRAI***

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## ***I. INTRODUCTION***

An essential safety element of *tissue* donor screening and ultimately the determination of a deceased *donor's eligibility* is the administration and completion of the *donor risk assessment interview* (DRAI). This guidance document describes components and considerations for developing and implementing an effective *quality assurance program (QA Program)* process for the DRAI.

The DRAI *record* is considered a *relevant medical record* used to determine initial and final *donor eligibility*. Two methods exist to obtain information required to complete the DRAI and each generates a concurrent *record* of the information gathered. Interviews may be conducted face to face, often in a hospital setting for a potential organ/tissue donor, but, more often, the interview is conducted by telephone for a potential tissue donor. For each method, the expectation is that a knowledgeable person regarding the donor's relevant medical history and social behavior is identified and interviewed for the DRAI. In all cases, the interview is conducted according to *standard operating procedures (SOPs)* and concurrently documented using a standardized form to ensure all requirements of the SOP are addressed.

Note: For the purposes of this guidance, the term "*tissue bank*" includes an eye bank, an organ procurement organization, or a tissue bank (but not a tissue bank that handles reproductive tissue only). When used for the first time in the body of this document, a term is italicized if a definition for it appears in section "B. Definitions and Acronyms."

### ***A. Executive Summary***

This guidance document provides expectations and describes best practice for managing an effective QA Program that provides a high level of assurance the DRAI process is being performed consistently as intended.

The QA Program must include all of the following:

- comprehensive SOPs;
- staff qualification, training, and *competency assessment and verification*;
- *quality control* of the documented *record* of the interview;
- an internal *audit* program which includes the performance of periodic assessment of the effectiveness of the SOP and compliance with the SOP; and
- corrective and preventive action as warranted.

Recommendations included in this consensus document represent the collective expertise of many procurement professionals. The definitions, regulatory expectations, components of a QA Program, and reference documents are provided for use by all professionals performing these functions, or entities for which these functions are performed. An effective QA Program as described in this guidance document is expected to be in place.

## **B. Definitions and Acronyms**

These definitions originate from current standards of the AATB and the EBAA, except where noted:

*AUDIT* – A documented review of procedures, records, personnel functions, equipment, materials, facilities, and/or suppliers to evaluate adherence to the written *SOPM*, standards, applicable laws and regulations.

*COMPETENCY* – The ability of an employee to acceptably perform tasks for which he/she has been trained.

*COMPETENCY ASSESSMENT* – The evaluation of the ability of an employee to acceptably perform tasks for which he/she has been trained.

*DEVIATION* – An event that is a departure from a procedure or normal practice.

*DONOR ELIGIBILITY*— Determination made based on donor screening and testing for relevant communicable disease agents and diseases (This definition is derived from § 1271.45(b)).

*DONOR RISK ASSESSMENT INTERVIEW* (aka Medical History Interview, Medical/Social History Questionnaire, or Uniform Donor History Questionnaire/UDHQ) – A documented dialogue in person or by telephone with an individual or individuals who would be knowledgeable of the donor’s relevant medical history and social behavior. For example, this may be: the donor, if living; the next of kin; the nearest available relative; a member of the donor’s household; other individual with an affinity relationship (e.g., caretaker, friend, significant life partner); and/or the primary treating physician. Alternatively, a living donor may complete a written questionnaire. The relevant social history is elicited by questions regarding certain activities or behaviors that are considered to place such an individual at increased risk for a relevant communicable disease agent or disease (RCDAD).

*PROCEDURE* – A series of steps which, when followed, are designed to result in a specific outcome.

*QUALIFIED* - Deemed competent by a recognized authority.

*QUALITY* – The conformance of tissue or a process with pre-established specifications or standards.

*QUALITY ASSURANCE (QA) PROGRAM* – The policies and environment required to meet standards of quality and safety, and provide confidence that the processes and tissue consistently

conform to quality requirements.

*QUALITY CONTROL (QC)* – Specific tests or activities defined by the *QA Program* to be performed to monitor authorization/informed consent, donor screening, recovery, processing, preservation and storage, tissue quality, and test accuracy. These may include but are not limited to, performance evaluations, inspection, testing, and controls used to determine the accuracy and reliability of the tissue bank’s equipment and operational procedures, as well as the monitoring of supplies, reagents, equipment, and facilities.

*RECALL* – An action taken by a tissue bank to locate and retrieve tissue from distribution and dispensary inventories. This includes withdrawals; see

<http://www.fda.gov/Safety/Recalls/ucm165546.htm>

*RECORD* - Information that is inscribed on a tangible medium or that is stored in an electronic or other medium and is retrievable in perceivable form.

*RECOVERY* —Tissue surgically removed from a donor that is intended for use in human transplantation, therapy, research or education.

*RELEVANT MEDICAL RECORDS* – a collection of documents including a current *Donor Risk Assessment Interview*, a physical assessment/physical examination of the donor, laboratory test results (in addition to results of testing for required relevant communicable disease agents), relevant donor records, existing coroner and autopsy reports, as well as information obtained from any source or records which may pertain to donor eligibility regarding high risk behaviors, and clinical signs and symptoms for any relevant communicable disease agent or disease (RCDAD), and/or treatments related to medical conditions suggestive of such risk.

*RESOLUTION* – Adjustment, clarification, and/or correction of practices and/or procedures that results in compliance with the *SOPM* and/or standards.

*STANDARD OPERATING PROCEDURES MANUAL (SOPM)* – A group of standard operating procedures (SOPs) detailing the specific policies of a tissue bank and the procedures used by the staff/personnel. This includes, but is not limited to, procedures to: assess donor eligibility; recovery; processing; quarantine; release to inventory; labeling; storage; distribution; and recalling tissue.

*TISSUE* (aka human cell, tissue and cellular and tissue based products (HCT/Ps)) – A functional group of cells. The term is used collectively to indicate both cells and tissue, and includes ocular tissue.

*TISSUE BANK* (aka Tissue Establishment) – An entity that provides or engages in one or more services involving donated ocular and/or conventional tissue from living or deceased individuals for transplantation purposes. These services include assessing donor eligibility, recovery, processing, storage, labeling, and distribution of tissue.

*VERIFICATION* – The confirmation by examination and provision of objective evidence that

specified requirements have been fulfilled.

Acronyms:

AATB – American Association of Tissue Banks  
aka – also known as  
AOPO – Association of Organ Procurement Organizations  
AST – American Society of Transplantation  
ASTS - American Society of Transplant Surgeons  
CDC – Centers for Disease Prevention and Control  
CFR – Code of Federal Regulations  
DRAI – donor risk assessment interview  
EBAA – Eye Bank Association of America  
FDA – United States Food and Drug Administration  
HCT/Ps – human cell, tissue and cellular and tissue-based products  
HBV – hepatitis B virus  
HCV - hepatitis C virus  
HIV - human immunodeficiency virus  
HRSA – Health Resources and Services Administration  
NATCO – The Organization for Transplant Professionals  
NCHS – National Center for Health Statistics  
QA – quality assurance  
OPTN – Organ Procurement and Transplantation Network  
QC – quality control  
RCDAD - relevant communicable disease agent or disease  
SOP - standard operating procedure  
SOPM – standard operating procedures manual  
TSEs - Transmissible Spongiform Encephalopathy(ies)  
UDHQ - Uniform Donor History Questionnaire  
UNOS – United Network for Organ Sharing  
vCJD – variant Creutzfeldt-Jakob disease  
WNV – West Nile virus

## ***II. Regulatory Expectations***

### **A. Federal**

An evaluation of applicable FDA regulations at 21 CFR Part 1271 and related guidance for human cell, tissue, and cellular and tissue-based products (HCT/Ps) reveals relevant headings that can be applied to functions when performing the DRAI (aka FDA’s “donor medical history interview,” a donor screening function). A list of relevant requirements and a summary of expectations are provided in Appendix A.

#### **1. Recommendations**

- Develop your SOPM to reflect the following:



- the documented record of the interview is made concurrently by the interviewer performing the steps;
  - the documented *record* is the *relevant medical record* and is retained and/or shared; and
  - if made, the audio recording of the DRAI is used for *quality* review purposes only, and is not intended to be the documented record that's retained and/or shared.
- The interview must be conducted in accordance with the SOP.
  - Staff members who administer the DRAI must be *qualified*, be provided with appropriate training, and designated as “authorized” to perform the task.
  - Regularly scheduled assessments of all personnel shall be performed to verify compliance with the SOP.
  - The documented record is expected to accurately reflect the DRAI event.
  - A QA program must include sampling plans that verify the process used, whether the DRAI is recorded or not.
  - When an audio recording is made, an adequate QA sampling policy and *procedure* for reviewing and comparing the written or electronic record to the audio recording of the DRAI must be developed.
  - After sampling has occurred, changes made to any records already shared must be communicated in a timely manner.
  - The decision to retain the audio recording on file and the retention timeframe must be determined by each tissue establishment based on the tissue establishment's use of the recording in determining donor eligibility.

If the audio recording is not used for donor eligibility determination:

- Time periods selected should be reasonable for your operations and tied to quality control measures (e.g., see C. Quality Control, 1. Sampling Plan). The SOPM should include a description that when the record is produced concurrently with the voice recording, and a robust sampling plan is used after recordings are made, there is no need to retain the audio recording for an extended period of time.

If the audio recording is used for donor eligibility determination:

- The retention time period selected must be 10 years from the time of creation.

- The written agreement/contract between a tissue bank receiving donor tissue and the establishment that performs the DRAI on their behalf should ensure that responsibilities are clearly described and understood in regard to activities performed.

### **III. Components of a Quality Assurance Program**

#### **A. Standard Operating Procedures**

Development of an effective, practical SOP is critical. The DRAI takes place when the interviewee may be distraught due to the recent death of the potential donor. This situation presents particular challenges to the interviewer if the SOP is written in a restrictive manner (e.g., requiring that the interview material be read verbatim).

While it is critical to gather all the relevant information required in the DRAI, a well-designed SOP and questionnaire can greatly assist both parties in the interview process. The DRAI is intended to be an interactive conversation (dialogue) designed to collect pertinent information. The use of ‘capture’ questions limits repetitious questioning and can quickly elicit required information. A capture question asks a broad question leading to more specific questioning only if needed.

Note: A group of donation and transplantation professionals representing AOPO, EBAA, NATCO, HRSA, OPTN/UNOS, AST, ASTS, NCHS, CDC, FDA and AATB have developed a uniform donor history questionnaire structured to address challenges when conducting the DRAI. The capture question approach described above is used and is preferred. It is recommended that all agencies performing DRAI activities evaluate this questionnaire for adoption into their processes and, as appropriate, adjust SOPs and staff training accordingly.

#### **B. Staff Qualification, Training and Competency**

The DRAI shall be performed by staff members who have sufficient qualifications, which equates to completion of a formal training program and documented *competency assessments*. To remain *qualified*, interviewer knowledge must be updated when new or revised policies and procedures are implemented.

Effective training of personnel performing DRAI activities is another area of opportunity for assuring the *quality* of the information gathered during the DRAI process. Interviewers are faced with many challenges during this process and should be trained to be sensitive to a number of factors. These include the:

- need to provide empathy to the donor family member(s) or other person interviewed;
- sensitive nature of many questions;
- criticality in obtaining the best information possible to facilitate donor eligibility determination;

- accuracy in completion of the documented record of the interview; and
- management of the interview process when an interviewee desires to limit the questions or the length of time spent on the DRAI.

A varied and challenging number of ‘priorities’ are present in the DRAI process; therefore, it is important to include in training programs for staff, not only the SOP content but also the perspective of the stakeholders in this process. Of particular importance is providing information related to the reason for, and intent of, each question as this may not be intuitive to the interviewer. In the absence of this understanding, interviewers might rephrase the question and miss the intent of a question’s assessment of risk. For example, this can include intent behind questions related to geography and travel during certain periods of time (i.e., related to risk associated with vCJD). As part of their training, personnel shall be made aware of the consequences of the improper performance of their specific jobs.

Discussion of ‘lessons learned’ is effective in maintaining the learning culture. Material for these discussions can be gathered from inside the organization, from reports of problems encountered by other agencies, as well as from audit findings where interviews may not have been completed as required or planned.

Competency assessments shall be conducted by organizations to ensure that the behavior, knowledge, skill, and ability of personnel performing the DRAI align with expectations including criteria of regulations, standards, and SOPs. Competency *verification* shall be done prior to personnel performing the DRAI role independently and should be performed on a recurring basis (such as annually). Recommendations include the use of tools and methods such as:

- observation and assessment of on-site or recorded performance of the DRAI personnel. These reviews can include mock DRAI scenarios and actual DRAIs (recorded or live);
- use of a competency assessment checklist to include all expectations required to complete a comprehensive DRAI. Such expectations should include that the interviewer:
  - provides proper instruction to the interviewee at the start;
  - asks all required questions;
  - executes the intent of the questions;
  - appropriately probes and follows up on responses during the DRAI, as needed; and
  - documents relevant responses accurately.
- clearly defined thresholds for competency. Data should be collected for error tracking and performance trends;
- improvement plans for personnel that have not achieved or retained an acceptable level of competence;
- competency exams to demonstrate knowledge and understanding for the questions and

their intended purpose; and

- inclusion of competency *verification* documentation in the individual's training record.

### C. Quality Control

Quality Control activities shall be described in the SOPM and consist of a timely review of documented records soon after interviews are conducted. This may include direct observation of the administration of the DRAI, listening to audio recordings, and review of the documentation of the DRAI. The intent of quality control measures is to determine if the documented record:

- complies with the established SOP;
- accurately reflects information obtained from the interviewee; and
- is complete and legible.

Note: An audio recording of the dialogue that takes place for the DRAI is not mentioned in, or required by, FDA regulations or guidance, and is not required by standards of the AATB [1], AOPO [2] or EBAA [3]. Because some *tissue banks* record DRAIs in addition to concurrently completing a record, these practices need to be managed using appropriate quality assurance concepts.

Quality Control activities are usually structured and planned based on a confidence level for the process. Therefore, a number of variables should be considered in order to provide confidence in the documented record created concurrently during the course of the interview. Variables that should be taken into account include:

- experience with the current DRAI form and associated SOP;
- interviewer training;
- past results of quality control measures; and
- other quality assurance activities where *deviations* from *procedure* versus desired outcome have been identified.

In the event the DRAI is not completed in accordance with the SOP, the timely performance of corrective measures is essential. Any need to re-contact the interviewee to clarify responses or to obtain missing information should be done as soon as possible.

### 1. **Sampling Plan**

A sampling plan must be used to conduct the quality control program. An effective sampling plan takes into account certain variables (e.g., number of donors, assurance level) that determine an adequate sample size. Sampling plans should be applied to ensure that the sample includes multiple interviewers, that each interviewer is sampled periodically, and if there have been changes in the SOP or the DRAI, sampling may need to be increased. Routine reviews of this

activity should not be used as a substitute for competency assessment. All Quality Control activities must be documented including identification of which records were sampled, whether the activity was acceptable or, if deviations are noted, what immediate corrections were made. If applicable, a description of any long-term corrective actions should be included.

Considerations for **internal** process sampling include:

- select a short period of time, such as within 30 (thirty) days from date of performance, to prevent recurrence of any identified deviation;
- identify a satisfactory, representative number from all interviews done during this time period. See [http://guidebook.dcmam.mil/226/tools\\_links\\_file/stat-sample.htm](http://guidebook.dcmam.mil/226/tools_links_file/stat-sample.htm) where this type of sampling plan is provided:

Total # of Donor Records	# of Donor Records to Review
2 – 150	13
151 – 280	20
281 – 500	29

An additional reference for developing an acceptance sampling system is the American National Standards Sampling Procedures and Tables for Inspection by Attributes (ANSI/ASQ Z1.4-2008).

- the number of interviews each interviewer has completed during this established time and sample each person;
- frequency and sample size may need to be increased when there have been any changes in the SOP or DRAI form, or when a deviation has been identified; and
- interviewers that are newly authorized may require more frequent sampling at onset of performing these activities.

Determination of a sampling plan (schedule) must be documented and the rationale justified. The sampling plan should be robust and as data and experience is gathered, a step-wise adjustment in the sampling frequency may be justified.

Note: An audio recording of the DRAI is not required. . When an audio recording is used as a quality assurance tool, its retention status should be defined in policy and in your written agreement/contract. If an audio recording is utilized to make the donor eligibility determination, it is considered to be a relevant medical record and retained accordingly.

Considerations for **external** process sampling may include the components described above for an internal process. For example, the frequency of the audit and sample size may be modified to reflect the length of time since last audit, availability of recordings, as well as previous audit findings (this includes deviations).

## **D. Audit**

A robust audit program should be designed to periodically assess the ongoing effectiveness of several areas of activity related to the DRAI process. Audit results will provide information on the adequacy of SOPs from the perspective of meeting external requirements (regulations or accrediting body standards). Audits also check internal processes such as compliance with SOPs, quality control, training activities, and competency assessments.

Audits are performed on a planned basis and their frequency is usually determined as part of an overall, internal audit program. Audits include all aspects of the DRAI process. They are typically performed at least once per year by someone not directly involved in the process. The results of past audits as well as the current state of compliance should be considered in determining the need to increase the frequency of audits to ensure the stability of the program.

Audits may include random observations of actual conducted interviews and/or the review of audio recordings of interviews in comparison with the concurrent record. See ‘III. C. 1. Sampling Plan’ above. Consideration should also be given to ensure that the audit program ensures that each interviewer is included. Findings from these audit activities, indicating evidence of compliance or the need for correction, must be documented to demonstrate adequate review and reflect the scope of the audit activity. The quality assurance audit process is not intended to replace quality control activities.

### **1. Examples**

- Upon reviewing an audio recording of the DRAI, it is determined that the interviewer failed to ask the interviewee, “In the past 5 years has the donor had sex in exchange for money or drugs?” The interviewer documented a “no” response to this question on the written DRAI and the tissue was ultimately distributed for transplantation.
  - In this instance, in the absence of other information addressing such high risk behavior, the donor determination was incomplete. The tissue bank that released the tissue would submit an HCT/P Deviation Report to FDA, providing a synopsis of the occurrence, detailing the root cause, and delineating corrective actions to be performed. Corrective actions could include: contacting the interviewee again to ask the question, *recall* of the tissue, -re-training the interviewer, and an audit of other past interviews performed by the interviewer. Reporting to state agencies and accrediting bodies may also need to occur, as applicable.
- Upon reviewing an audio recording of the DRAI, it is determined that the interviewer inappropriately paraphrased a question. For example, the tissue bank’s DRAI includes the question, “Was the donor or any of his/her blood relatives diagnosed with or been told they were at risk for Creutzfeldt-Jakob Disease or variant Creutzfeldt-Jakob Disease?” The interviewer actually asked the interviewee, “Did the donor ever have mad cow disease?” The interviewer documented a “no” response to this question on the DRAI and the tissue was ultimately distributed for transplantation.
  - FDA guidance states that if the person interviewed “is not familiar with the term “Creutzfeldt-Jakob Disease” or “variant Creutzfeldt-Jakob Disease,” you may try

to describe those in layman's terms. If the person being interviewed is still not familiar with those terms, you may consider the lack of familiarity with those terms as a negative response to questions using those terms." In this instance, the interviewer did not first ask about "Creutzfeldt-Jakob Disease" or "variant Creutzfeldt-Jakob Disease" and did not ask about the donor's blood relatives, so this risk was not assessed as required. The tissue bank that released the tissue would submit an HCT/P Deviation Report to FDA, providing a synopsis of the occurrence, detailing the root cause, and delineating corrective actions to be performed. Corrective actions could include: contacting the interviewee again to ask the question, *recall* of the tissue, re-training the interviewer, and an audit of other past interviews performed by the interviewer. Reporting to state agencies and accrediting bodies may also need to occur, as applicable.

- While observing the interview process in real time, it is determined that the interviewer omitted part of a question. For example, the tissue bank's DRAI includes the question, "Has the donor ever used a needle to inject drugs into his/her veins, muscles, or under the skin for non-medical use?" The interviewer actually asked the question, "Has the donor ever used a needle to inject drugs?" The interviewer documented a "no" response to this question on the DRAI and the tissue was ultimately distributed for transplantation.
  - In this instance, the essence of the question was actually asked. It can be argued that the question that was asked was actually more inclusive than the question on the DRAI. For example, if the donor ever injected drugs for a medical purpose, that would be captured in this question. Moreover, the question asked simply queries if the donor ever used a needle to inject drugs, so a negative response would rule out needing to determine the route. If the interviewee provided a "yes" response, then further clarification would be needed. The interviewer provided a "no" response" so no reporting to any regulatory agency or accrediting body would be necessary. For this example, documentation justifying this decision should be maintained in donor records and shared if applicable. Corrective action necessitates re-training the interviewer and possibly performing an audit of other past interviews performed by the interviewer.
- Upon reviewing an audio recording of the DRAI and comparing it to the DRAI record, it is determined that the interviewer failed to accurately document the interviewee's actual response. For example, the tissue bank's DRAI includes the question, "Did the donor drink alcohol?" The interviewee reported that the donor drank 4 beers each night, but the interviewer documented the response as "no." The tissue was ultimately distributed for transplantation.
  - In this instance, given that the additional medical information does not indicate an increased risk for a relevant communicable disease agent or disease, no HCT/P Deviation Report need be submitted. However, the tissue bank releasing the tissue should document justification why the error is not relevant to disease transmission. The tissue bank would still need to document its findings in their QA report and treat it as a deviation, along with any corrective action(s) it deems necessary, such as re-training the interviewer and possibly performing an audit of other past interviews performed by the interviewer.

**Note: Corrected DRAI records need to be shared appropriately, and without delay, with all tissue banks involved with recovery of tissue, or receipt of tissue, from the donor.**

#### **E. Corrective and Preventive Action**

Quality assurance should also include documented investigations, corrective actions and effectiveness checks when deviations from SOP, regulations, or standards related to the DRAI process are identified. Deviations can be identified:

- during quality control activities;
- as the result of audits or inspections; and
- via feedback from entities with whom the documented record has been shared.

An effective corrective action plan should address immediate action to be taken to rectify the deviation and consider process improvement to prevent recurrence. Effectiveness checks should be performed to confirm that corrective actions have been effective in eliminating the root cause of the deviation. In addition, if a deviation is seen during routine quality control sampling or audit, the sample size may be increased until the corrective action is deemed effective.

The scale and scope of a corrective action plan will depend on factors such as severity and extent of deviation. Severity is best considered from the perspective of the use of the DRAI information in determining final donor eligibility. Extent may be a factor of multiple interviewers and/or length of time the deviations have been identified as occurring.

If quality control activities are performed in a timely manner as described above, the length of time and extent of the deviation is likely to be limited. It may be necessary to prioritize aspects of the investigation based on the risk posed. Risks include inappropriate donor eligibility determination, potential for communicable disease transmission, and/or *recall* of tissue grafts. If the deviation is determined to be extensive, additional resources may be necessary to complete the plan in a timely manner.

Examples of corrective action activities (*resolutions*) may include:

- Notifying without delay all tissue banks that have received the DRAI and reaching agreement on any necessary follow-up actions (e.g., providing frequent updates as action plans are implemented, sharing additional or corrected information, etc.).
- Identifying the need to re-contact interviewees if the intent of the DRAI was not met, or if information provided by the interviewee appears to have been misunderstood or incorrectly recorded by the interviewer.
- Development of a plan to re-contact the interviewee(s) or obtain missing information. Plans should include actions to be taken if there is difficulty locating the person or if she/he is unable or unwilling to assist in clarifying or providing information. If initial attempts to correct or clarify information are unsuccessful, other viable options include:



an inquiry with the primary care physician of the donor; locating another knowledgeable person; or, the use of a private investigator to locate the original interviewee.

- Evaluating existing processes to identify the root cause of a deviation. Training and retraining is often identified as a root cause and/or corrective action and care should be taken to assure that if retraining is determined to be the appropriate corrective action, effectiveness checks are performed and confirm that this was root cause rather than the underlying SOP or process.
- While every effort should be made to obtain information required from the DRAI, in the event it is not possible, a risk assessment should be performed for each case. This risk assessment should be completed in collaboration with the tissue processor(s) that determines donor eligibility. A careful review of additional records may provide missing, or clarify questionable, information.
- When a deviation is discovered, an investigation must be performed to determine the scope of the problem. Depending on the circumstances/results of the investigation, a planned audit of other interviews performed by that interviewer may be indicated.

## **1. Timely Notification**

Timely notification is critical. When tissue associated with a deviation related to the DRAI have been distributed for transplant, the tissue processor has a time frame of no more than 45 (forty-five) days to report the incident to FDA under HCT/P Biological Product Deviation reporting requirements. Actions required prior to submission of this report include obtaining additional information and performing a health hazard (risk) assessment. If it is not possible to resolve or address the deviation and the associated risks, further actions may be necessary (e.g., disposition of the tissue remaining in quarantine or inventory, a recall may be indicated for tissues that were already distributed for transplant).

## ***IV. Appendix***

### **A. Federal Expectations [4, 5, 6, 7] and Summary**

#### **Subpart C - Donor Eligibility Final Rule**

§ 1271.3 How does FDA define important terms in this part?

(n) *Donor medical history interview*

(s) *Relevant medical records*

§ 1271.50 How do I determine whether a donor is eligible?

(a) *Determination based on screening and testing.*

(b) *Eligible donor.*

§ 1271.55 What records must accompany an HCT/P after the donor-eligibility determination is complete; and what records must I retain?

(a) *Accompanying records.*

(b) *Summary of records.*

- (d) *Record retention requirements*
- § 1271.75 How do I screen a donor?
  - (a) *All donors.*
  - (d) *Ineligible donors.*

#### HCT/P Donor Eligibility Final Guidance

#### IV. DONOR SCREENING (§ 1271.75)

- C. What sources of information do I review?
- E. What risk factors or conditions do I look for when screening a donor?

#### Subpart D – Current Good Tissue Practice Final Rule

#### § 1271.150 Current good tissue practice requirements.

- (a) *General.*
- (b) *Core CGTP requirements.*
- (c) *Compliance with applicable requirements*
  - (1) *Manufacturing arrangements*

#### § 1271.160 Establishment and maintenance of a quality program.

- (a) *General.*
- (b) *Audits.*

#### § 1271.170 Personnel.

- (a) *General.*
- (b) *Competent performance of functions.*
- (c) *Training.*

#### § 1271.180 Procedures.

- (a) *General.*
- (b) *Review and approval.*
- (c) *Availability.*
- (d) *Standard procedures.*

#### § 1271.270 Records.

- (a) *General.*
- (b) *Records management system.*
- (c) *Methods of retention.*
- (d) *Length of retention.*
- (e) *Contracts and agreements.*

#### Current Good Tissue Practice Final Guidance

#### III. CGTP REQUIREMENTS (§ 1271.150)

- C. How Do I Ensure that Another Establishment with Which I Have a Contract, Agreement or Other Arrangement Complies with CGTP Requirements?
- D. What Steps Should I Take if I Become Aware and Then Determine that the Establishment Performing Any Step in Manufacture for Me is No Longer in Compliance with Part 1271?

#### V. ESTABLISHMENT AND MAINTENANCE OF A QUALITY PROGRAM (§ 1271.160)

- A. What is a Quality Program?
- B. Which Establishments Must Establish and Maintain a Quality Program?

- C. What is the Role of the Quality Program Regarding Procedures?
- D. What Must I Do When Information is Received From Sources Outside the Establishment, and What Must I Do with this Information?
- E. With Whom Must an Establishment Share Information Pertaining to the Possible Contamination of or Potential for Transmission of Communicable Disease by an HCT/P?
- F. How Can a Quality Program Ensure that Appropriate Corrective Actions Related to Core CGTP Requirements Are Taken, When Necessary?
- G. What Must the Quality Program Ensure Regarding Personnel?
- H. How Does the Quality Program Ensure that Appropriate Monitoring Systems Are in Place?
- I. When HCT/P Deviations Occur, What is the Role of the Quality Program?
- J. What Are the Requirements for Performing Quality Audits of Your Establishment?
- K. Will FDA Review the Quality Audit During Inspection of the Establishment?

#### VI. PERSONNEL (§ 1271.170)

- A. What Are the Specific Requirements for Personnel at HCT/P Establishments?
- B. How Would I Ensure that Personnel Have the Necessary Education, Experience and Training to Perform Their Job?

#### VII. PROCEDURES (§ 1271.180)

- C. May I Use Procedures From Established Industry Standards?

#### XII. RECOVERY (§ 1271.215)

- B. What Are Some Ways that a Recovery Establishment Could Ensure that HCT/Ps Are Recovered in a Way That Does Not Cause Contamination or Cross-Contamination During Recovery, or Otherwise Increase the Risk of the Introduction, Transmission, or Spread of Communicable Disease?
- D. What Are Ways in Which a Processor Receiving HCT/Ps From a Recovery Establishment Under Contract with the Processor Could Verify the Identity of the Donor and Could Ensure That the Donor Records Are From the Same Donor as the HCT/Ps?

#### XIX. RECORDS (§ 1271.270)

- A. What are the General Requirements for Records?
- B. What Kind of Records Management System Must I Have?
- C. What Are Acceptable Methods of Record Retention?
- D. For How Long Must I Retain my HCT/P Manufacturing Records?
- E. What Records of Contracts and Agreements Must I Maintain?

In summary, regulatory requirements include:

- Tissue donors must be screened for relevant communicable disease and disease agents (RCDADs) and a donor must be determined ineligible who is identified as having a risk factor for, or clinical evidence of, any RCDAD (HIV types 1 & 2, HBV, HCV, human TSEs, *T. pallidum* (syphilis), WNV, vaccinia, sepsis, and risk associated with xenotransplantation).
- Donor eligibility determinations, including donor screening, are considered “core CGTP” requirements and includes contracts, agreements or other arrangements with parties that

perform these functions on behalf of a tissue establishment.

- A quality program must be in place that addresses all core CGTP requirements. Expected functions that must be covered:
  - Establishing and maintaining appropriate procedures relating to core CGTP requirements, and ensuring compliance with respect to such procedures, including review, approval, and revision;
  - Ensuring that procedures exist for documenting information related to core CGTP requirements;
  - Ensuring that appropriate corrective actions relating to core CGTP requirements, including re-audits of activities where deviations have been identified, are taken and documented.
  - Verifying corrective actions to ensure actions taken have been effective and are in compliance with CGTP. Where appropriate, corrective actions must include both short-term action to address the immediate problem and long-term action to prevent the problem's recurrence.
  - Ensuring proper training and education of personnel involved in activities related to core CGTP requirements;
  - Establishing and maintaining appropriate monitoring systems as necessary to comply with requirements;
  - Investigating and documenting deviations (and trends) relating to core CGTP requirements. Each investigation must include a review and evaluation of the deviation, efforts made to determine the cause, and the implementation of corrective action(s) to prevent recurrence.
  
- A quality audit of activities related to core CGTP requirements must be periodically performed for review by management.
  
- An establishment that performs functions on your behalf must have a quality program that addresses these operations, and it's expected that periodic compliance audits of the establishment are performed. During the audit, you should consider reviewing a representative sample of the donor medical history interview records that were previously provided by the recovery establishment to confirm their accuracy by checking with the source of the information.
  
- A recommendation is that contracts, agreements or other arrangements describe the responsibilities of all parties. When donor eligibility is determined following a review of records obtained by another establishment, the contract, agreement or other arrangement should specifically identify what records will be obtained, in what format they will be provided, responsibilities for record retention and access, and if the reviewing firm will convey donor eligibility conclusions back to the firm that collected the information.
  
- Regarding personnel, a sufficient number to ensure compliance with requirements is expected; they must have the necessary education, experience, and training to ensure competent performance of their assigned functions; they can perform only those activities for which they are *qualified* and authorized; and all personnel must be trained, and

retrained as necessary, so they perform their assigned responsibilities adequately.

- Procedures must be established and maintained to meet core CGTP requirements for related steps that the tissue establishment personnel perform. You must design these procedures to prevent circumstances that increase the risk of the introduction, transmission, or spread of communicable disease.
- Before implementation of procedures, a responsible person must review and approve them, and procedures must be readily accessible to personnel in the area where the operations to which they relate are performed.
- A “donor medical history interview” must be obtained and it is considered a “relevant medical record.”
- A review of “relevant medical records” must occur. When review of the donor medical history interview is performed you should make inquiries when circumstances indicate that follow-up information might be relevant.
- SOPs must be established and maintained to assure review of relevant medical records is properly conducted.
- SOPs must ensure records, such as the donor medical history interview, are current, complete and reliable as well as accurate, indelible, and legible.
- Records must be maintained concurrently with the performance of each required step and must be as detailed as necessary to provide a complete history of the work performed. Any requirement where an action can be documented involves the creation of a record, which is subject to the requirements for records.
- If other records are “available” and they can include information pertaining to risk factors for relevant communicable disease (e.g., social behavior, treatments), you should make inquiries to obtain all relevant information.
- “Available” means that a record or information exists, or is pending, and can be obtained through due diligence, within a reasonable amount of time. A “reasonable” amount of time is a period of time that would allow for the collection of important information without compromising the utility of the tissue.
- The initial tissue establishment that performed the donor medical history interview should document the findings. The establishment that makes the HCT/P available for distribution should review the records of the findings to make sure that all release criteria (including donor eligibility) were met, and would retain the documented findings.
- You must establish and maintain a records management system. Records must be maintained in such a way as to facilitate review of the HCT/Ps history before making tissue allografts available for distribution. The regulations do not specify the details of a

records management system, but you should organize your records in a useful manner in accordance with the requirements in this section. The recovery establishment must maintain copies of all transferred records and organize them in its records management system.

- You may retain required records as original paper records, or as true copies such as photocopies, microfiche, or microfilm. Equipment that is necessary to make the records available and legible, such as computer and reader equipment, must be readily available. Records stored in electronic systems must be backed up.
- Records must be retained for 10 years after their creation, or at least 10 years after the date of administration of an HCT/P, or if the date of administration is not known, then at least 10 years after the date of the HCT/P's distribution, disposition, or expiration, whichever is latest.
- A list of the responsibilities of any establishment that performs a manufacturing step for you should be maintained and this should ensure that responsibilities are understood. For-cause and random comparisons of documentation should be performed.
- If non-compliance by a contractor is discovered, you must take reasonable steps to ensure the establishment develops a corrective action plan and you should review the plan and verify that corrective actions have been taken under the establishment's quality program.

## *V. References*

1. *Standards for Tissue Banking*, AATB, McLean, VA, current edition
2. *Standards and Interpretive Guidelines*, AOPO, Vienna, VA, current edition
3. *Medical Standards*, EBAA, Washington, DC, current edition
4. U.S. Department of Health and Human Services, Food and Drug Administration, Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products; Final Rule (69 FR 29785, May 25, 2004).
5. U.S. Department of Health and Human Services, Food and Drug Administration, Final Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/PS), August 8, 2007.
6. U.S. Department of Health and Human Services, Food and Drug Administration, Current Good Tissue Practice for Human Cell, Tissue, and Cellular and Tissue-Based Product Establishments; Inspection and Enforcement; Final Rule (69 FR 68612, November 24, 2004).
7. U.S. Department of Health and Human Services, Food and Drug Administration, Final Guidance for Industry, Current Good Tissue Practice (CGTP) and Additional

Requirements for Manufacturers of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps), December 2011.