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Document Title:

Purified Human Pancreatic Islets, Deceased Donor Pancreas Qualification

1.0 Document Approvals:

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2.0 Purpose

This document establishes the requirements for the qualification of the deceased donor of the pancreas used in the production of the Purified Human Pancreatic Islets product.

3.0 Scope

This document applies only to the qualification of the deceased donor of the pancreas used in the production of Purified Human Pancreatic Islets product utilized in clinical trials sponsored by DAIT.

4.0 Background

Deceased donor pancreas is the main raw material for the manufacture of the Purified Human Pancreatic Islets product. Donors of pancreata for manufacture of allogeneic islets are subjected to rigorous and stringent evaluations; donor suitability must conform to the standards established in the U.S guidances (cGTP and HCT/P) and regulations (69 FR 29786, May 25, 2004 and 21 CFR 1271). Donor eligibility determination is based on results of donor screening as well as testing.

This document describes the organ (pancreas) donor selection criteria that will be used in the manufacture of the Purified Human Pancreatic Islet product for transplant in the NIH-sponsored CIT clinical studies. The organ donor selection criteria are designed to provide an optimal cell or tissue recovery with minimal risk to the recipient and processing personnel.

5.0 Definitions

None

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6.0 Procedure

6.1 Deceased Donor Acceptance Process

Pancreata are harvested from deceased donors who are 15-65 years of age by the United Network for Organ Sharing (UNOS) Organ Procurement Organizations (OPO). Screening for infectious diseases is performed by the Organ Procurement Organization offering the organ. All testing is performed by Clinical Laboratory Improvement Amendments of 1988 (CLIA) certified laboratories.

A donor is accepted by the manufacturing facility only if he/she: (i) has a favorable medical and social history, (ii) passes the physical examination requirements, and (iii) passes all standard laboratory tests required for multi-organ donor testing for evaluation of the risk of transmissible infectious diseases. The history and physical examination data obtained by the OPO must indicate that the inclusion/exclusion criteria listed below are met.

After donor acceptance, the pancreas is shipped to the manufacturing facility following procurement and preservation in one of the following:

(i) UW Solution (University of Wisconsin solution, DuPont Pharma, Wilmington, Delaware),
(ii) PF/UW Solution [Oxeginated Perfluorodecalin (FluoroMed, LP, Round Rock, Texas)/UW Two Layer Solutions)],
(iii) HTK Solution [Histidine-Tryptophan-Ketoglutarate (FluoroMed, L.P.)]
(iv) PF/HTK Solution.

Upon arrival, a copy of the results of the donor screening tests is attached to the batch record and the container label and medical records are reviewed to verify the presence of the following information:

- UNOS (or DDD in Canada) identification number
- Donor Blood Type
- Donor chart and identification
- Collection Center unique identifier
- Product proper name
- Date and time of collection
- Name of collection center and location

6.2 Deceased Donor Acceptance Requirements:

TEST	METHOD	REQUIREMENT
Identity	Visual Inspection	Container Label must specify Human Pancreas, and a UNOS or DDD number must be present.
Supplier	Visual Inspection	The Organ Procurement Organization (OPO) must be identified.
Review of Supplier's Records	Visual Inspection	**A. Donor Acceptance – Inclusion Criteria** 1. Preservation in (i) UW, (ii) PF/UW, (iii) HTK, or (iv) PF/HTK Solution(s) 2. Maximum 12 hr cold ischemia time 3. Donor age 15-65 years 4. Cause and circumstances of death acceptable to the transplant team

TEST	METHOD	REQUIREMENT
Review of Supplier's Records	Visual Inspection	**B. Donor Acceptance – Exclusion Criteria** Any of the following criteria is grounds for rejection of a potential donor: 1. History or biochemical evidence of Diabetes Mellitus Type 1 or 2 (Transplant teams may consider donor HbA1C > 6.1% in the absence of transfusions in the week prior to death as an indication for exclusion, with discretion for donors who have received transfusions.) 2. Non-heart-beating cardiac death 3. Malignancies as the cause of death, other than resected basal or squamous cell carcinoma or intracranial tumor. 4. Suspected or confirmed sepsis 5. Evidence of clinical or active viral Hepatitis (A, B, HBcAg, or C) (HBsAb+ is acceptable, if there is a history of vaccination) 6. Acquired Immunodeficiency Syndrome (AIDS) 7. HIV seropositivity (HIV-I or HIV-II), or HIV status unknown 8. HTLV-I or HTLV-II (optional) 9. Syphilis (RPR or VDRL positive)* 10. Active viral encephalitis or encephalitis of unknown origin 11. TSE or Creutzfeldt-Jacob Disease 12. Suspected rabies diagnosis 13. Treated or active tuberculosis 14. Individuals who have received pit-hGH (pituitary growth hormone) 15. Any medical condition that, in the opinion of the transplant team, precludes a reasonable possibility of a favorable outcome of the islet transplant procedure. 16. Clinical history and/or laboratory testing suggestive of West Nile Virus, vaccinia, or SARS The following behavioral profiles will also be considered as grounds for rejection of a potential donor: 17. High-risk sexual behavior within 5 years prior to time of death: Men who have had sex with men, individuals who have engaged in prostitution, and individuals whose sexual partners have engaged in high-risk sexual behavior 18. Non-medical intravenous, intramuscular, or subcutaneous drug use within the past five years 19. Persons with hemophilia or related clotting disorders who have received human derived clotting factor concentrates 20. Findings on history or physical examination consistent with an increased risk of HIV exposure. 21. Current inmates of correctional systems and individuals who have been incarcerated for more than 72 consecutive hours during the previous 12 months

In the USA tests for transmissible disease indications must be performed by CLIA-certified laboratories.
*Test results required by FDA regulation

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6.3 Donor Organ Disposition

Participating centers will accept donor pancreata for CIT study participants only with the approval of the PI or designee. The OPO will be notified of the decision to accept or reject the organ.

7.0 Responsibilities

7.1 DAIT Regulatory Affairs is responsible for controlling the pancreata used in the production of the Purified Human Pancreatic Islets product through this SOP.

7.2 The Principal Investigator at each site producing the Purified Human Pancreatic Islets product in DAIT sponsored clinical trials is responsible for:

- reviewing and approving this Deceased Donor Pancreas Acceptance document, and changes proposed thereto.
- training their staff in its proper use.
- assuring its proper use.
- assuring that only pancreata meeting the requirements defined in this Deceased Donor Pancreas Acceptance document are used in the production of the Purified Human Pancreatic Islets product in clinical trials sponsored by DAIT.
- preserving approval records for each pancreas used in the production of the Purified Human Pancreatic Islets product used in clinical trials sponsored by DAIT.

8.0 Equipment & Materials

NA

9.0 Safety Precautions

NA

10.0 Related Document

SOP 3101, Purified Human Pancreatic Islets, Master Production Batch Records

11.0 References

NA

12.0 Appendices

NA

13.0 Attachments

NA