

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

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Date: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
(dd/mmm/yyyy)

**INSTRUCTIONS:** Please ask the subject the appropriate question (A, B, or C) according to their current visit. **If their answer is “no” do not fill out the remainder of the survey. If their answer is “yes” proceed to question #1 and complete the survey.**

- A. Screening Visit: “Have you experienced any hypoglycemia in the past 12 months?”  Yes  No
- B. Wait List: “Have you experienced any hypoglycemia in the past 12 months?”  Yes  No
- C. Post Transplant: “Have you experienced any hypoglycemia since your last visit?”  Yes  No

1. Check the category that best describes you: (check only one)
  - I always have symptoms when my blood sugar is low
  - I sometimes have symptoms when my blood sugar is low
  - I no longer have symptoms when my blood sugar is low
  
2. Have you lost some of the symptoms that used to occur when your blood sugar was low?
  - Yes
  - No
  
3. In the past six months how often have you had hypoglycemia episodes where you felt confused, disoriented, or lethargic and were unable to treat yourself?
  - Never
  - Once or twice
  - Every other month
  - Once a month
  - More than once a month

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4. In the past twelve months, how often have you had hypoglycemia episodes where you were unconscious or had a seizure and needed glucagon or intravenous glucose?

- |                               |  |
|-------------------------------|--|
| <input type="radio"/> Never   | <input type="radio"/> 7 times          |
| <input type="radio"/> 1 time  | <input type="radio"/> 8 times          |
| <input type="radio"/> 2 times | <input type="radio"/> 9 times          |
| <input type="radio"/> 3 times | <input type="radio"/> 10 times         |
| <input type="radio"/> 4 times | <input type="radio"/> 11 times         |
| <input type="radio"/> 5 times | <input type="radio"/> 12 times or more |
| <input type="radio"/> 6 times |  |

5. How often in the last month have you had readings less than 70 mg/dl (3.9 mmol/L) with symptoms?

- Never
- 1-3 times
- 1 time/week
- 2-3 times/week
- 4-5 times/week
- Almost daily

6. How often in the last month have you had readings less than 70 mg/dl (3.9 mmol/L) without symptoms?

- Never
- 1-3 times
- 1 time/week
- 2-3 times/week
- 4-5 times/week
- Almost daily

7. How low does your blood sugar go before you feel symptoms?

- 60-69mg/dl (3.3-3.8 mmol/L)
- 50-59mg/dl (2.8-3.2 mmol/L)
- 40-49mg/dl (2.2-2.7 mmol/L)
- < 40 mg/dl (2.2 mmol/L)

8. To what extent can you tell by your symptoms that your blood sugar is low?

- Never
- Rarely
- Sometimes
- Often
- Always

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**A. FASTING, POSTPRANDIAL C-PEPTIDE AND PLASMA GLUCOSE**

Not Done

1. a. Date of draw   
(dd/mmm/yyyy) Time of draw   
(24-hour clock)
- b. Fasting c-peptide  nmol/L  undetectable  not available
- c. Fasting glucose  mmol/L  not available

Not Done

2. a. Date of draw   
(dd/mmm/yyyy)  click to copy date Time of draw   
(24-hour clock)
- b. Was insulin administered prior to post-prandial blood draw?  
No Yes
- c. Post-prandial c-peptide  nmol/L  undetectable  
 not available
- d. Post-prandial glucose  mmol/L  not available

**B. COMMENTS (optional)**

# CIT01 DONOR CRF

Lot Number xx-xxx, Recipient Number xx-xx-xxx

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## CIT01 DONOR ECRF

*Enter data from the deceased donor's records*

1. Donor Scandia transplant number
2. Donor's Date of Birth  (dd/mmm/yyyy)
3. Donor's Gender  Female  Male
4. Donor's Weight  kg
5. Donor's Height  cm
6. Body Mass Index  kg/m<sup>2</sup>
7. Donors Blood Type  A  B  AB  O
8. Donor CMV status:  Positive  Negative  Not Available
9. Donor EBV status:  Positive  Negative  Not Available

# CIT01 DONOR CRF

Lot Number xx-xxx, Recipient Number xx-xx-xxx

## 10. Donor HLA Type

HLA Antigen	Test Method (Select one)	Results (at least one of i or ii must be filled in for)
a. HLA-A	<input type="radio"/> Molecular <input type="radio"/> Serologic	i. ___ HLA-A (1 <sup>st</sup> allele) ii. ___ HLA-A (2 <sup>nd</sup> allele)
b. HLA-B	<input type="radio"/> Molecular <input type="radio"/> Serologic	i. ___ HLA-B (1 <sup>st</sup> allele) ii. ___ HLA-B (2 <sup>nd</sup> allele)
c. HLA-DR	<input type="radio"/> Molecular <input type="radio"/> Serologic	i. ___ HLA-DR (1 <sup>st</sup> allele) ii. ___ HLA-DR (2 <sup>nd</sup> allele)

## 11. Cause of Death

- Anoxia  
 CVA/Cerebrovascular/Stroke  
 Head Trauma  
 CNS Tumor  
 Other: Specify

12. Donor HbA1c %:

Not Available

13. Comments:



**B. CARDIAC FUNCTION: ECG (Visit 1 and 2)**

**No    Yes**

1.  Was an ECG performed?

a. Date ECG was performed: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
(dd/mmm/yyyy)

b. ECG interpreted as: (select one)

Normal

Abnormal; clinically significant

i.) Please specify abnormality:

Abnormal: not clinically significant

ii.) Please specify abnormality:

c. Reason:

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**C. MYOCARDIAL SCINTIGRAM (Visit 1)****No Yes**1.   Was a myocardial scintigram performed?a. Date myocardial scintigram performed: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
(dd/mmm/yyyy)

b. Myocardial scintigram interpreted as:

 Normal Abnormal; clinically significant i.) Please specify abnormality: Abnormal: not clinically significant ii.) Please specify abnormality:

c. Reason:



**D. NEUROPHYSIOLOGY** (Visit 1, 12, and Y1)

No Yes

1.   Was a neurophysiology exam performed?

a. Date neurophysiology exam performed: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
 (dd/mm/yyyy)

b. Reason: \_\_\_\_\_

2.

ENeG	DL (ms)	MCV (m/s)	CMAP (mV)	F-latency (ms)	SCV (m/s)	SNAP (uV)
median nerve	a.i. <input type="text"/>	a.ii. <input type="text"/>	a.iii. <input type="text"/>	a.iv. <input type="text"/>	a.v. <input type="text"/>	a.vi. <input type="text"/>
radial nerve					b.i. <input type="text"/>	b.ii. <input type="text"/>
peroneal nerve	c.i. <input type="text"/>	c.ii. <input type="text"/>	c.iii. <input type="text"/>			
tibial nerve	d.i. <input type="text"/>		d.ii. <input type="text"/>	d.iii. <input type="text"/>		
sural nerve					e.i. <input type="text"/>	e.ii. <input type="text"/>

**3 Temperature threshold (Celsius)**

	Heat	Cold	Difference
a. hand (thenar)	i. <input type="text"/>	ii. <input type="text"/>	iii. <input type="text"/>
b. foot (dorsum)	i. <input type="text"/>	ii. <input type="text"/>	iii. <input type="text"/>

4. **RR-Variation:** a. At Rest %  b. Deep breathing %

**5. SSR**                      **Latency (s)**      **Amplitude (mV)**

a. hand	i. <input type="text"/>	ii. <input type="text"/>
b. foot	i. <input type="text"/>	ii. <input type="text"/>

**E. ABDOMINAL ULTRASOUND** (Visit 1, 3 and 4)

**No Yes**

1.   Was an abdominal ultrasound performed?

a. Date abdominal ultrasound performed: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
(dd/mmm/yyyy)

b. Abdominal ultrasound interpreted as:

Normal

Abnormal; clinically significant

i.) Please specify abnormality:

\_\_\_\_\_

Abnormal: not clinically significant

ii.) Please specify abnormality:

\_\_\_\_\_

c. Reason:

\_\_\_\_\_

**F. COMMENTS (optional)**

\_\_\_\_\_

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**GFR**

1. Date of specimen collection   
(dd/mmm/yyyy)

2. GFR measured using  Iohexol  51Cr-EDTA  99technetium-DPTA

a.  Raw Clearance  mL/min  Not Available

or

Std Clearance  mL/min/1.73m<sup>2</sup>  Not Available

**COMMENTS (optional)**

Screening/Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

**A. INFORMED CONSENT (each consent signed will add to a growing list)**

1. a. Version number of consent document:   N/A

b. Version date:   N/A  
(dd/mmm/yyyy)

2. Date informed consent signed:  **ADD NEW ENTRY**  
(dd/mmm/yyyy)

**YES NO**  
3.   The subject agreed to permit the collection and storage of blood samples for future research studies.

**YES NO**  
4.   The subject agreed to permit the collection and storage of blood samples for future genetic testing (i.e. DNA) for other diseases related to diabetes.

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1. Scandinavia Donor ID Number: \_\_\_\_\_
2. Islets lot Number: \_\_\_\_\_
3. LMW-DS lot Number: \_\_\_\_\_  Not Applicable (Study Arm II)
4. LMW-DS expiration date \_\_\_\_\_  Not Applicable  
(dd/mmm/yyyy) (Study Arm II)
5. Admission date: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
(dd/mmm/yyyy)
6. Has this subject been selected to participate in the PET sub-study?  Yes  No
7. Time of skin puncture: \_\_\_\_\_  
(0000-2359)
8. Time of confirmed good position of the catheter in portal: \_\_\_\_\_  
(automated calculated time used for placement of the catheter) (0000-2359)
9. Number of punctures through the liver capsule needed for placement: \_\_\_\_\_
10. Date and time islet infusion started: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_ \_\_\_\_\_  
(dd/mmm/yyyy) (0000-2359)
11. Date and time islet infusion stopped: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_ \_\_\_\_\_  
(dd/mmm/yyyy) (0000-2359)
12. Total packed cell volume infused: \_\_\_\_\_ (x x . x mL)
13. Total volume infused (including rinse): \_\_\_\_\_ (mL)
14. Total IEQ infused: \_\_\_\_\_

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15. Subject's weight at time of transplant: \_\_\_\_\_ (xxx.x kg)

16. Total IEQ/kg infused: \_\_\_\_\_ (x x x x x . x IEQ/kg) [Will autocalculate on the web]

17. Total intraportal heparin dose delivered: \_\_\_\_\_ (U/kg)  Not Applicable (Study Arm I)

18. Total LMW-DS:

a. Amount administered intraportally (bolus + with islets): \_\_\_\_\_ (xxx . x mg)  Not Applicable  
(Study Arm II)b. Amount administered intraportally after islet transplantation: \_\_\_\_\_ (xxxx. x mg)  Not Applicable  
(Study Arm II)c. Date and time LMW-DS infusion started: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
 Not Applicable (Study Arm II) (dd/mmm/yyyy) (0000-2359)d. Date and time LMW-DS infusion stopped: \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
 Not Applicable (Study Arm II) (dd/mmm/yyyy) (0000-2359)

19. Type, brand and size of the catheter: \_\_\_\_\_

20. Catheter introduction method: (select one)

 Percutaneous transhepatic Open surgical method Other, specify: \_\_\_\_\_

21. Ablation method: (select one)

 None Gel foam Cautery Gel foam and coils Laser Other, specify: \_\_\_\_\_

22. Infusion method: (select one)

Gravity-fed bag set

Infusion pump

Other, specify:

23. Portal Pressure

a. Portal Pressure before infusion.   mmHg  cmH20

b. Portal Pressure 15 minutes after total infusion.   mmHg  cmH20

24. Central Venous Pressure (CVP)

a. CVP before placement of portal catheter.   mmHg  cmH20

b. CVP after placement of portal catheter.   mmHg  cmH20

25. Hemoglobin:

a. Immediately prior to infusion  (g/L)  (0000-2359)

b. Immediately after end of infusion:  (g/L)  (0000-2359)

c. Four hours after start of infusion:  (g/L)  (0000-2359)

d. 2 hours after removal of portal catheter.:  (g/L)  (0000-2359)

26. Instructions:

Enter APTT timepoints during the first 5 hours. Time begins at the start of islet infusion.

**Required timepoints include: 0min, 20min, 22min, 50min, 90min, 130min, 190min, 250min, and 310min.** If necessary, additional timepoints may also be entered.

After 5 hours, enter APTT timepoints every hour. until APTT < 75sec.

Timepoint (min)

APTT

ADD Entry

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27. Vital sign measurements at time of infusion

	Time (0000-2359)	Pulse (xxx beats/min.)	O <sup>2</sup> saturation (xxx.xx %)	Systolic BP (xxx mmHg)	Diastolic BP (xxx mmHg)
a. Immediately Pre-Infusion/Baseline	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
b. 15 Minutes after start of infusion	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
c. 30 Minutes after start of infusion	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
d. 60 Minutes after start of infusion	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
e. 120 Minutes after start of infusion	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
f. 180 Minutes after start of infusion	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
g. 240 Minutes after start of infusion	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
h. 300 Minutes after start of infusion	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

No Yes

28.   Was the infusion prematurely terminated?

a. Reason? (Select one)

Increase in portal pressure

Other, specify:

No Yes

29.   Was there evidence of an adverse event during infusion?

Complete an Adverse Event form

30. COMMENTS



Subject ID

Date of Visit  (dd/mmm/yyyy)

**A. COAGULATION STATUS** (Visits 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, and Y1)

- 1. Date of blood draw   *Click to copy Date of Visit*
- 2. APTT  seconds
- 3. PK  INR
- 4. Fibrinogen   mg/dL or  g/L
- 5. Platelet Count  x10<sup>9</sup>/L

**B. HEMATOLOGY** (Visits 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 and Y1;  
Note: Items 6 - 10 collected at visits 1, 2, 6, 9 - 12, and Y1)

- 1. Date of draw   *Click to copy Date of Visit*
- 2. Red blood cell count  x10<sup>12</sup>/L  Not Available
- 3. Hemoglobin   mg/dL or  g/L  Not Available
- 4. Hematocrit  %  Not Available
- 5. White blood cell count  x10<sup>9</sup>/L  Not Available
- 6. Lymphocyte  x10<sup>9</sup>/L  Not Available
- 7. Neutrophils [total]  x10<sup>9</sup>/L  Not Available
- 8. Eosinophils  x10<sup>9</sup>/L  Not Available
- 9. Monocytes  x10<sup>9</sup>/L  Not Available
- 10. Basophils  x10<sup>9</sup>/L  Not Available

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**C. SERUM CHEMISTRY** (Visits: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, and Y1)

- |     |                          |   |                          |                                    |
|-----|--------------------------|---|--------------------------|------------------------------------|
| 1.  | Date of Draw             | <input type="text"/>                                    | <input type="checkbox"/> | <i>Click to copy Date of Visit</i> |
| 2.  | Sodium                   | <input type="text"/> mmol/L                             | <input type="checkbox"/> | Not Available                      |
| 3.  | Potassium                | <input type="text"/> mmol/L                             | <input type="checkbox"/> | Not Available                      |
| 4.  | Creatinine               | <input type="text"/> $\mu$ mol/L                        | <input type="checkbox"/> | Not Available                      |
| 5.  | Glucose                  | <input type="text"/> mmol/L                             | <input type="checkbox"/> | Not Available                      |
| 6.  | Albumin                  | <input type="text"/> g/L                                | <input type="checkbox"/> | Not Available                      |
| 7.  | Alk Phosphorous          | <input type="text"/> $\circ$ $\mu$ kat/L or $\circ$ U/L | <input type="checkbox"/> | Not Available                      |
| 8.  | ALT (SGPT)               | <input type="text"/> $\circ$ $\mu$ kat/L or $\circ$ U/L | <input type="checkbox"/> | Not Available                      |
| 9.  | AST (SGOT)               | <input type="text"/> $\circ$ $\mu$ kat/L or $\circ$ U/L | <input type="checkbox"/> | Not Available                      |
| 10. | LDH                      | <input type="text"/> $\circ$ $\mu$ kat/L or $\circ$ U/L | <input type="checkbox"/> | Not Available                      |
| 11. | Total Bilirubin          | <input type="text"/> $\mu$ mol/L                        | <input type="checkbox"/> | Not Available                      |
| 12. | CRP (C-reactive protein) | <input type="text"/> $\circ$ mg/dL or $\circ$ mg/L      | <input type="checkbox"/> | Not Available                      |

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**D. FASTING LIPID PANEL:** (Visit 1, 3, 9, 10, 11, 12 and Y1)

1. Date of Draw   *Click to copy Date of Visit*  
(dd/mmm/yyyy)
2. Total Cholesterol  mmol/L
3. LDL  mmol/L
4. HDL  mmol/L
5. Triglycerides  mmol/L

**E. URINE STUDIES** (Visit 1, 10, 12, and Y1)

1. Date of specimen collection   *Click to copy Date of Visit*  
(dd/mmm/yyyy)
2. Urine albumin  mg/mmol

**F. COMMENTS**

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

**A. DIABETES HISTORY**

1. Year diagnosed with diabetes:   
(yyyy)

2. Year insulin therapy began:   
(yyyy)

**B. DIABETES KETOACIDOSIS (DKA):**

1. Has the subject experienced DKA within the last 12 months? (select one)

- Yes
- No
- Unknown

2. Has the subject been hospitalized for DKA within the last 12 months? (select one)

Yes

a. Specify number of hospitalizations in the last 12 months

No

Unknown

**C. CIPROFLOXACIN ALLERGY**

1. **No Yes** Is the subject allergic to ciprofloxacin?

Subject unable to receive islet transplant with ciprofloxacin added.

**D. MEDICAL HISTORY**

	Assessment	Any significant medical history?		If Yes, please give details.
		No	Yes	
1.	Skin	<input type="radio"/>	<input type="radio"/>	
2.	Head, Eyes, Ears, Nose, Throat	<input type="radio"/>	<input type="radio"/>	
3.	Respiratory	<input type="radio"/>	<input type="radio"/>	
4.	Cardiovascular	<input type="radio"/>	<input type="radio"/>	
5.	Gastrointestinal	<input type="radio"/>	<input type="radio"/>	
6.	Endocrine/Metabolic (except Diabetes)	<input type="radio"/>	<input type="radio"/>	
7.	Genitourinary/Reproductive	<input type="radio"/>	<input type="radio"/>	
8.	Neurological	<input type="radio"/>	<input type="radio"/>	
9.	Blood/Lymphatic	<input type="radio"/>	<input type="radio"/>	
10.	Musculoskeletal	<input type="radio"/>	<input type="radio"/>	
11.	Hepatic/Biliary	<input type="radio"/>	<input type="radio"/>	
12.	Allergies/Immunologic	<input type="radio"/>	<input type="radio"/>	
13.	Psychological/Psychiatric	<input type="radio"/>	<input type="radio"/>	
14.	Other		<input type="radio"/>	

**E. COMMENTS (optional)**

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**A. PRA**

1. Date of test   *Not done*  
(dd/mmm/yyyy)

2. PRA Screen (%)

- Negative
- Positive

\_\_\_\_\_ a. PRA  %

*Answers in b and c will be validated against a list of known A, B and DR antigens. .*

\_\_\_\_\_ b. Anti-Class 1 antibodies present to  
(must make an entry for A , for B, or for both)

1) A antigen:

2) B antigen:

\_\_\_\_\_ c. Anti-Class 2 antibodies present to

1) DR antigen:

3. MICA Antibody Screen

Results (select one)

- Positive
- Negative
- Not Performed

**B. COMMENTS (optional)**

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

**A. REDUCED FOLLOW-UP**

1.  **No**  **Yes** Was follow-up visit (phone or in person) conducted?
- a. Date of contact or visit:   
(dd/mmm/yyyy)
- 1) Which type of visit was conducted? (select one)
- Phone
  - In person
- (If Phone, skip section C; if In person, skip Section B)**
- b. Reason:

**If Q.A1 is answered no, skip sections B and C.**

**B. PHONE FOLLOW-UP**

1.  **No**  **Yes** Has the subject experienced any Serious Adverse Events?
- a.

2.  **No**  **Yes** Were QOL questionnaires mailed to the subject?
- a. Date questionnaires mailed:   
(dd/mmm/yyyy)
- b. Reason:

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

- No**   **Yes**  
3.         Has the subject experienced any hypoglycemic events grade 3-4 as defined in the Toxicity Criteria for Adverse Events?  
    |  
    |   a.   **If yes, then complete the Adverse Event form.**

**C. IN-PERSON FOLLOW-UP**

- No**   **Yes**  
1.         Has the subject experienced any Serious Adverse Events?  
    |  
    |   a.   **If yes, then complete the Adverse Event form.**

- No**   **Yes**  
2.         Has the subject experienced any hypoglycemic events grade 3-4 as defined in the Toxicity Criteria for Adverse Events?  
    |  
    |   a.   **If yes, then complete the Adverse Event form.**

**D. COMMENTS (optional)**



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**A. REQUIREMENTS FOR A SECOND TRANSPLANT**

Question 1.a or 1.b and questions 2-8 must be answered YES in order for the subject to be eligible for a second islet transplant.

No Yes

- 1.a   Partial Graft Function: the subject has either a basal or stimulated c-peptide level  $\geq 0.1$  nmol/L ( $\geq 0.3$  ng/mL) **and** 75 +/- 5 day visit metabolic assessments have been completed.
- 1.b  No  Yes Graft Failure: the subject has confirmed graft failure evidenced by c-peptide  $< 0.1$  nmol/L ( $< 0.3$  ng/mL) **and** has received CIT Steering Committee (if before Day 75) approval or Nordic Network Steering Committee (if after Day 75) approval for a second infusion.
- Date of SC approval:

2.   Subject has been compliant with study monitoring and prescribed immunosuppressive therapy.
3.   No evidence of a serious and life-threatening infection, adverse event, or other condition that precludes attempting an intraportal injection or continuation of the post-transplant treatment regimen.
4.   No evidence of post-transplant lymphoproliferative disorder (PTLD).
5.   No evidence of progressive renal dysfunction, with blood creatinine rising above 2.0 mg/dL (177 umol/L) with calcineurin inhibitor trough levels within maintenance levels.
6.   No evidence of hypersensitization, allergic responses, or other potentially serious drug reactions to medications required by the protocol.
7.   It has been  $< 8$  months since the first islet transplant.
8.   Absence of any medical condition that, in the opinion of the investigator, will interfere with safe and successful second islet transplant.

**B. COMMENTS (optional)**

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

**A. SEROLOGY**

	Infectious Disease	Date Sample Drawn (dd/mmm/yyyy)	Negative	Positive	Not Obtained
1.	Cytomegalovirus IgG antibody (CMV IgG)	<input type="text" value="___/___/___"/> <input type="radio"/> click to copy above date	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2.	Cytomegalovirus IgM antibody (CMV IgM)	<input type="text" value="___/___/___"/> <input type="radio"/> click to copy above date	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3.	Epstein-Barr Virus IgG antibody (EBV IgG)	<input type="text" value="___/___/___"/> <input type="radio"/> click to copy above date	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4.	HIV	<input type="text" value="___/___/___"/> <input type="radio"/> click to copy above date	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5.	Hepatitis C antibody (HCV Ab)	<input type="text" value="___/___/___"/> <input type="radio"/> click to copy above date	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6.	Hepatitis B surface antigen (HBsAg)	<input type="text" value="___/___/___"/> <input type="radio"/> click to copy above date	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7.	Hepatitis B surface antibody (HBsAb)	<input type="text" value="___/___/___"/> <input type="radio"/> click to copy above date	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8.	Hepatitis B Core antibody (HBcAb)	<input type="text" value="___/___/___"/> <input type="radio"/> click to copy above date	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9.	CMV by PCR	<input type="text" value="___/___/___"/> <input type="radio"/> click to copy above date	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10.	EBV by PCR	<input type="text" value="___/___/___"/> <input type="radio"/> click to copy above date	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

**B. COMMENTS (optional):**

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

No Yes  
1.   Is the test applicable to the subject?

a. Results

- Negative
- Positive

b. Date of test : \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_ (dd/mmm/yyyy)

c. If no, specify reason:

- Male
- Sterile
- Post-Menopausal

**If the results of the test are positive, exclude the subject from the study.**

2. Comments (optional)

Subject ID 

Page 1 of 2

**A. INDUCTION MEDICATIONS**

Drug	Date	Total Dose on this Date (mg)
<input type="radio"/> ATG  <input type="radio"/> Other <input type="text"/>	<input type="text"/> (dd/mmm/yyyy)	<input type="text"/>

Add new Entry

**B. CELL PROLIFERATION INHIBITOR**

Drug	Dose (mg) per 24 hours	Start Date	Stop Date
<input type="radio"/> MMF <input type="radio"/> Sirolimus	<input type="text"/>	<input type="text"/> (dd/mmm/yyyy)	<input type="text"/> (dd/mmm/yyyy)

Add new Entry

**C. MAINTENANCE IMMUNOSUPPRESSION MEDICATIONS**

Drug	Dose (mg) per 24 hours	Start Date	Stop Date
<input type="radio"/> Tacrolimus <input type="radio"/> Cyclosporine	<input type="text"/>	<input type="text"/> (dd/mmm/yyyy)	<input type="text"/> (dd/mmm/yyyy)

Add new Entry

**D. TROUGH LEVELS**

Drug	Date of blood draw	Trough Level (ng/mL)
<input type="radio"/> Tacrolimus <input type="radio"/> Sirolimus <input type="radio"/> Cyclosporine	<input type="text"/> (dd/mmm/yyyy)	<input type="text"/> <input type="checkbox"/> undetectable

Add new Entry

Subject ID

**E. MONOCLONAL ANTIBODY IL-2 RECEPTOR BLOCKER**

Drug	Dose (mg) per 24 hours	Date
<input type="radio"/> Basiliximab	<input type="text"/>	<input type="text"/> (dd/mmm/yyyy)

Add new Entry

**F. List other immunosuppressive, anti-coagulant, infection prophylaxis medications taken from time of study entry until completion of the study.**

Add new Entry

Drug	Dose per 24 hours	Unit	Route*	Start Date	Stop Date
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/> (dd/mmm/yyyy)	<input type="text"/> (dd/mmm/yyyy)

\*Route: 1 = oral, 2 = intravenous, 3 = intramuscular, 4 = topical, 5 = inhaled, 6 = subcutaneous, 7 = intradermal, 8 = sublingual, 9 = intra-articular, 10 = ophthalmic, 11 = intralesional, 12 = rectal, 13 = vaginal, 99 = other

**G. COMMENTS**

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

Page 1 of 2

**A. REQUIREMENTS FOR A THIRD TRANSPLANT**

Questions 1-11 must be answered YES in order for the subject to be eligible for a third islet transplant.

**No    Yes**

1.   The subject remains without full islet graft function.
2.   There is evidence of partial graft function [C-peptide > 0.1nmol/L (0.3ng/mL)]
3.   No evidence of post-transplant lymphoproliferative disorder (PTLD)
4.   The CIT Principal Investigator and Site Principal Investigator have determined that there were no relevant protocol deviations at the site.
  - a. Date of SC approval   
(dd/mmm/yyyy)
5.   The subject has been compliant with study monitoring and prescribed immunosuppressive therapy.
6.   No evidence of a serious and life-threatening infection, adverse event or other condition that precludes attempting an intraportal injection or continuation of the post-transplant treatment regimen.
7.   No evidence of progressive renal dysfunction, with blood creatinine rising above 2.0 mg/dL (177 umol/L).
8.   No evidence of hypersensitization, allergic responses or other potentially serious drug reactions to medications required by the protocol.
9.   No evidence of abnormal liver ultrasound and LFTs within 1.5 times the upper limit of the normal range prior to the third transplant.
10.   The 28 day (+ or - 3 days) visit following the second transplant has been completed.
11.   Less than 8 months has passed after the first islet transplantation.

**If any of these questions are answered NO, the user will receive a message saying, “Subject is INELIGIBLE for re-transplant.”**

Subject ID  \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_ Page 2 of 2

**B. COMMENTS (optional)**

**A. INCLUSION CRITERIA**

The site personnel will verify the following eligibility for study randomization using the subject's source documentation (medical records, laboratory records, clinic records):

No Yes

1.   Patients between 18 to 65 years of age.
2.   Subjects who are able to provide written informed consent and comply with the procedures of the study protocol.
3.   Clinical history compatible with type 1 diabetes with onset of disease at < 40 years of age and insulin-dependence for  $\geq 5$  years at the time of enrollment, and a sum of patient age and insulin dependent diabetes duration of  $\geq 28$ .
4.   Absent stimulated C-peptide < 0.3ng/ml [0.099 nmol/L] in response to a mixed meal tolerance test (Boost® 6 ml/kg body weight to a maximum of 360 ml; another product with equivalent caloric and nutrient content may be substituted for Boost®) measured at 60 and 90min after the start of consumption.
5.   Involvement in intensive diabetes management defined as self monitoring of glucose values no less than a mean of three times each day averaged over each week and by the administration of three or more insulin injections each day or insulin pump therapy. Such management must be under the direction of an endocrinologist, diabetologist, or diabetes specialist with at least 3 clinical evaluations during the previous 12 months prior to enrollment.
6.   At least one episode of severe hypoglycemia, defined as an event with one of the following symptoms: memory loss; confusion; uncontrollable behavior; irrational behavior; unusual difficulty in awakening; suspected seizure; seizure; loss of consciousness; or visual symptoms, in which the subject was unable to treat him/herself and which was associated with either a blood glucose level < 54 mg/dL [3.0 mmol/L] or prompt recovery after oral carbohydrate, intravenous glucose, or glucagon administration, in the 12 months prior to study enrollment.
7.   At least one of the following: (check all that apply)
  - a.  Reduced awareness of hypoglycemia as defined by a Clarke score of 4 or more or a HYPO score greater than or equal to the 90th percentile (1047) during the screening period and within the last 12 months prior to randomization;
  - b.  Marked glycemic lability characterized by wide swings in blood glucose despite optimal diabetes therapy and defined by a glycemic lability index (LI) score greater than or equal to the 90th percentile (433 mmol/L<sup>2</sup>/hrwk<sup>-1</sup>) during the screening period and within the last 6 months prior to randomization;
  - c.  A composite of a Clarke score of 3 or more or a HYPO score greater than or equal to the 75th percentile (423) in combination with a LI greater than or equal to the 75th percentile (329) during the screening period and within the last 12 months prior to randomization.



**B. EXCLUSION CRITERIA**

The site personnel will verify eligibility for randomization using the subject's source documentation (medical records, laboratory records, clinic records, etc.), if any of the following are identified, the subject will not be eligible for randomization:

No Yes

1.   Known IgE mediated allergy to antibiotics and antifungal medications (ciprofloxacin, gentamycin, and amfotericin B) used in the culture medium.
2.   Known hypersensitivity to dextran.
3.   A body mass index (BMI) > 30.0 kg/m<sup>2</sup>.
4.   Insulin requirement of > 1.0 U/kg/day.
5.   HbA1c > 10%.
6.   Untreated proliferative diabetic retinopathy.
7.   Blood pressure SBP > 160mmHg or DBP >100mmHg.
8.   Measured glomerular filtration rate (GFR) using 51Cr-EDTA, 99technetium-DPTA, or iohexol < 80ml/min/1.73m<sup>2</sup>. The absolute (raw) GFR value will be used for subjects with body surface areas >1.73m<sup>2</sup>.
9.   Presence or history of macroalbuminuria (>300mg/g of creatinine).
10.   Presence or history of panel-reactive anti-HLA antibodies >80% by flow cytometry. Subjects with panel reactive anti-HLA antibodies above background ≤ 80%, can be included if the antigen specificity of the antibodies can be determined for future avoidance; however, if the antigen specificity of the antibodies cannot be determined they will be excluded.
11.   **For female subjects:** Positive pregnancy test, presently breast-feeding, or unwillingness to use effective contraceptive measures for the duration of the study and 4 months after discontinuation. **For male subjects:** intent to procreate during the duration of the study or within 4 months after discontinuation or unwillingness to use effective measures of contraception. Oral Contraceptives, Norplant, Depo-Provera, and barrier devices with spermicide are acceptable contraceptive methods; condoms used alone are not acceptable.
12.   Active infection including hepatitis B, hepatitis C, or HIV.

**B. EXCLUSION CRITERIA** *(continued)***No Yes**

13.   Negative screen for Epstein - Barr Virus (EBV) by IgG determination.
14.   Any history of malignancy except for completely resected squamous or basal cell carcinoma of the skin.
15.   Known active alcohol or substance abuse.
16.   Baseline Hgb below the lower limits of normal at the local laboratory; lymphopenia (<1,000/uL), neutropenia (<1,500/uL) or thrombocytopenia (platelets <100,000/uL).
17.   Homocytotic Activated Protein C Resistance (APC-R).
18.   History of hypercoagulability disorder or coagulopathy or international normalized ratio (INR) > 1.5.
19.   Known history of severe co-existing cardiac disease, characterized by ***any one*** of the following conditions: (check all that apply)
- a.  Recent myocardial infarction (within past 6 months).
  - b.  Evidence of ischemia on functional cardiac exam within the last year.
  - c.  Left ventricular ejection fraction <30%.
20.   Consistently abnormal liver function tests at the time of study entry. SGOT (AST), SGPT (ALT), Alk Phos or total bilirubin, with values > 1.5 times normal upper limits on two consecutive measurements > 2 weeks apart.
21.   Acute or chronic pancreatitis.
22.   Patients with active peptic ulcer disease, symptomatic gallstones or a history of portal hypertension.
23.   Severe unremitting diarrhea, vomiting or other gastrointestinal disorders potentially interfering with the ability to absorb oral medications.
24.   Receiving treatment for a medical condition requiring chronic use of systemic steroids, except for the use of  $\leq 5$ mg prednisone daily, or an equivalent dose of hydrocortisone, for physiological replacement.

**B. EXCLUSION CRITERIA** *(continued)***No**   **Yes**

25.   Treatment with any anti-diabetic medication, other than insulin, within 4 weeks of enrollment.
26.   Use of any investigational agents within 4 weeks of enrollment.
27.   Administration of live attenuated vaccine(s) within 2 months of enrollment.
28.   Patients with any condition or any circumstance that in the opinion of the investigator would make it unsafe to undergo an islet transplant.
29.   Treatment with any immunosuppressive regimen at the time of enrollment.
30.   A previous islet transplant.
31.   A previous pancreas transplant, unless the graft failed within the first week due to thrombosis, followed by pancreatectomy and the transplant occurred more than 6 months prior to enrollment.

**A. INCLUSION CRITERIA**

The site personnel will verify the following eligibility for study randomization using the subject's source documentation (medical records, laboratory records, clinic records):

No Yes

1.   Patients between 18 to 65 years of age.
2.   Subjects who are able to provide written informed consent and comply with the procedures of the study protocol.
3.   Clinical history compatible with type 1 diabetes with onset of disease at < 40 years of age and insulin-dependence for  $\geq 5$  years at the time of enrollment, and a sum of patient age and insulin dependent diabetes duration of  $\geq 28$ .
4.   Absent stimulated C-peptide <0.3ng/ml [0.099 nmol/L] in response to a mixed meal tolerance test (Boost® 6 ml/kg body weight to a maximum of 360 ml; another product with equivalent caloric and nutrient content may be substituted for Boost®) measured at 60 and 90min after the start of consumption.
5.   Involvement in intensive diabetes management defined as self monitoring of glucose values no less than a mean of three times each day averaged over each week and by the administration of three or more insulin injections each day or insulin pump therapy. Such management must be under the direction of an endocrinologist, diabetologist, or diabetes specialist with at least 3 clinical evaluations during the previous 12 months prior to enrollment.
6.   At least one episode of severe hypoglycemia, defined as an event with one of the following symptoms: memory loss; confusion; uncontrollable behavior; irrational behavior; unusual difficulty in awakening; suspected seizure; seizure; loss of consciousness; or visual symptoms, in which the subject was unable to treat him/herself and which was associated with either a blood glucose level < 54 mg/dL [3.0 mmol/L] or prompt recovery after oral carbohydrate, intravenous glucose, or glucagon administration, in the 12 months prior to study enrollment.
7.   At least one of the following: (check all that apply)
  - a.  Reduced awareness of hypoglycemia as defined by a Clarke score of 4 or more or a HYPO score greater than or equal to the 90th percentile (1047) during the screening period and within the last 12 months prior to randomization;
  - b.  Marked glycemic lability characterized by wide swings in blood glucose despite optimal diabetes therapy and defined by a glycemic lability index (LI) score greater than or equal to the 90th percentile (433 mmol/L<sup>2</sup>/hrwk<sup>-1</sup>) during the screening period and within the last 6 months prior to randomization;
  - c.  A composite of a Clarke score of 3 or more or a HYPO score greater than or equal to the 75th percentile (423) in combination with a LI greater than or equal to the 75th percentile (329) during the screening period and within the last 12 months prior to randomization.

**B. EXCLUSION CRITERIA**

The site personnel will verify eligibility for randomization using the subject's source documentation (medical records, laboratory records, clinic records, etc.), if any of the following are identified, the subject will not be eligible for randomization:

- | No                        | Yes                   |  |
|---------------------------|-----------------------|--|
| 1. <input type="radio"/>  | <input type="radio"/> | Known IgE mediated allergy to antibiotics and antifungal medications (ciprofloxacin, gentamycin, and amfotericin B) used in the culture medium.  |
| 2. <input type="radio"/>  | <input type="radio"/> | Known hypersensitivity to dextran.   |
| 3. <input type="radio"/>  | <input type="radio"/> | A body mass index (BMI) > 30.0 kg/m <sup>2</sup> .   |
| 4. <input type="radio"/>  | <input type="radio"/> | Insulin requirement of > 1.0 U/kg/day.   |
| 5. <input type="radio"/>  | <input type="radio"/> | HbA1c > 10%.   |
| 6. <input type="radio"/>  | <input type="radio"/> | Untreated proliferative diabetic retinopathy.  |
| 7. <input type="radio"/>  | <input type="radio"/> | Blood pressure SBP > 160mmHg or DBP >100mmHg.  |
| 8. <input type="radio"/>  | <input type="radio"/> | Measured glomerular filtration rate (GFR) using 51Cr-EDTA, 99technetium-DPTA, or iohexol < 80ml/min/1.73m <sup>2</sup> . The absolute (raw) GFR value will be used for subjects with body surface areas >1.73m <sup>2</sup> .  |
| 9. <input type="radio"/>  | <input type="radio"/> | Presence or history of macroalbuminuria (>300mg/g of creatinine).  |
| 10. <input type="radio"/> | <input type="radio"/> | Presence or history of panel-reactive anti-HLA antibodies >80% by flow cytometry. Subjects with panel reactive anti-HLA antibodies above background ≤ 80%, can be included if the antigen specificity of the antibodies can be determined for future avoidance; however, if the antigen specificity of the antibodies cannot be determined they will be excluded.  |
| 11. <input type="radio"/> | <input type="radio"/> | <b>For female subjects:</b> Positive pregnancy test, presently breast-feeding, or unwillingness to use effective contraceptive measures for the duration of the study and 4 months after discontinuation. <b>For male subjects:</b> intent to procreate during the duration of the study or within 4 months after discontinuation or unwillingness to use effective measures of contraception. Oral Contraceptives, Norplant, Depo-Provera, and barrier devices with spermicide are acceptable contraceptive methods; condoms used alone are not acceptable. |
| 12. <input type="radio"/> | <input type="radio"/> | Active infection including hepatitis B, hepatitis C, or HIV.   |

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

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**B. EXCLUSION CRITERIA** *(continued)***No Yes**

13.   Negative screen for Epstein - Barr Virus (EBV) by IgG determination.
14.   Any history of malignancy except for completely resected squamous or basal cell carcinoma of the skin.
15.   Known active alcohol or substance abuse.
16.   Baseline Hgb below the lower limits of normal at the local laboratory; lymphopenia (<1,000/uL), neutropenia (<1,500/uL) or thrombocytopenia (platelets <100,000/uL).
17.   Homocytotic Activated Protein C Resistance (APC-R).
18.   History of hypercoagulability disorder or coagulopathy or international normalized ratio (INR) > 1.5.
19.   Known history of severe co-existing cardiac disease, characterized by ***any one*** of the following conditions: (check all that apply)
- a.  Recent myocardial infarction (within past 6 months).
  - b.  Evidence of ischemia on functional cardiac exam within the last year.
  - c.  Left ventricular ejection fraction <30%.
20.   Consistently abnormal liver function tests at the time of study entry. SGOT (AST), SGPT (ALT), Alk Phos or total bilirubin, with values > 1.5 times normal upper limits on two consecutive measurements > 2 weeks apart.
21.   Acute or chronic pancreatitis.
22.   Patients with active peptic ulcer disease, symptomatic gallstones or a history of portal hypertension.
23.   Severe unremitting diarrhea, vomiting or other gastrointestinal disorders potentially interfering with the ability to absorb oral medications.
24.   Receiving treatment for a medical condition requiring chronic use of systemic steroids, except for the use of  $\leq 5$ mg prednisone daily, or an equivalent dose of hydrocortisone, for physiological replacement.

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

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**B. EXCLUSION CRITERIA** *(continued)***No**   **Yes**

25.   Treatment with any anti-diabetic medication, other than insulin, within 4 weeks of enrollment.
26.   Use of any investigational agents within 4 weeks of enrollment.
27.   Administration of live attenuated vaccine(s) within 2 months of enrollment.
28.   Patients with any condition or any circumstance that in the opinion of the investigator would make it unsafe to undergo an islet transplant.
29.   Treatment with any immunosuppressive regimen at the time of enrollment.
30.   A previous islet transplant.
31.   A previous pancreas transplant, unless the graft failed within the first week due to thrombosis, followed by pancreatectomy and the transplant occurred more than 6 months prior to enrollment.

# BLOOD SUGAR RECORD AND HYPOGLYCEMIC EVENTS

CIT CORE

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

Page 1 of 3

**Instructions for completing this eCRF:** In A1, enter the date of the blood sugar/insulin record you wish to enter. Then, in A2, enter the total insulin dose the subject administered on this date. In A3, enter the blood sugar readings taken on this date. After each blood sugar reading, click SAVE.

When you have entered all of the blood sugar readings associated with a date, click START NEW DATE. The database will provide the next calendar date in A1. You will then start at A1 again, and enter the date for the next set of blood sugar and insulin records. If there are no blood sugar records on a date, click START NEW DATE again to go to the next date. You will be prompted to confirm that there were no records for the date you wish to skip.

All data entered will populate two tables (one for blood sugar and one for insulin), below.

## A. BLOOD SUGAR AND INSULIN RECORDS

1. Date:   
(dd/mmm/yyyy)

2. Enter total insulin administered on this date:  units  not available

(Skip Q 1 & 2 after first blood sugar entry until START NEW DATE is clicked on)

3. Enter each blood sugar reading recorded for this date:

Blood sugar reading:   mg/dl      OR       Low (if glucometer does not register a numerical value for a 'Low' or 'High' reading)  
 mmol/L       High

OR

No insulin or blood sugar readings for this date.

Time:    
00-24 hrs.    00-59 mins.\*  
\*prefill mins. with 00

4. If applicable, select 'Meal Code':  1 = pre-meal      ADD NEW ENTRY  
 2 = 2 hours post-meal  
 3 = bedtime      START NEW DATE

**If a Blood sugar reading is under 54 mg/dl, Low, or Blood sugar reading not available, please complete Part B, next page. If not, skip part B.**



**B. HYPOGLYCEMIC EVENTS**

This section will be triggered for each blood sugar reading < 54 mg/dL, Low, or Blood sugar reading not available. Each of these entries will have an associated Hypoglycemic Event record available. All entries will be visible on a growing table. An 'Add Hypo Event' button will also be available below this table to enter any additional events.

1. Hypoglycemia symptoms (select all that apply):

- a.  Autonomic
- b.  Visual
- c.  Behavioral
- d.  Other neuro
- e.  Confusion
- f.  Seizures
- g.  No symptoms [if chosen, all other options should be greyed out]
- h.  No symptoms recorded or recalled [if chosen, all other options should be greyed out]

2. The reaction was recognized by...(please indicate one)

- Yourself
- Routine test on meter
- Someone else
- Unknown

3. Treatment for the reaction needed...(please check all that apply)

- a.  Help from someone else
- b.  Juice/food/glucose tablets
- c.  Injection of glucagon
- d.  Hospital/ambulance
- e.  Unknown
- f.  None

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

**C. COMMENTS**

Subject ID

**A. Blood Type**

1. Date of blood typing:  (dd/mm/yyyy)  Not Done

2. Blood type:  A  B  AB  O

**B. HLA typing**

1. Date of HLA typing :  (dd/mm/yyyy)  Not Done

HLA Antigen	Test Method (Select one)	Results (Choose from pick lists: at least one of i or ii must be filled in for a – c)
a. HLA-A	<input type="radio"/> Molecular <input type="radio"/> Serologic	i. ___ HLA-A (1 <sup>st</sup> allele) ii. ___ HLA-A (2 <sup>nd</sup> allele)
b. HLA-B	<input type="radio"/> Molecular <input type="radio"/> Serologic	i. ___ HLA-B (1 <sup>st</sup> allele) ii. ___ HLA-B (2 <sup>nd</sup> allele)
c. HLA-DR	<input type="radio"/> Serologic	i. ___ HLA-DR (1 <sup>st</sup> allele) ii. ___ HLA-DR (2 <sup>nd</sup> allele)

**C. COMMENTS (optional)**

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

Page 1 of 1

**A. Continuous Glucose Monitoring System (CGMS)****No    Yes**1.   Was CGMS data collected for this subject for this visit?

a. Reason

If No is selected in Item 1, 1a must be completed and items 1b-1d are not required.

If Yes is selected in Item 1, 1a must not be completed and items 1b-1d are required.

b. Monitoring start date and time :

*(dd/mmm/yyyy) (0000-2359)*

c. Monitoring stop date and time:

*(dd/mmm/yyyy) (0000-2359)*d. **Date** file sent to DCC:*(dd/mmm/yyyy) (0000-2359)*

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

Report Number \_\_\_\_\_

**A. ADVERSE EVENT**

1. Date of adverse event \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
(dd/mmm/yyyy)

2. Date site became aware of AE \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
(dd/mmm/yyyy)

3. Adverse Event Term

\_\_\_\_\_

4. Describe event or problem. (Include any details relating to diagnosis.)

\_\_\_\_\_

**No Yes**

5.   Is this an exacerbation of a pre-existing condition (existing prior to enrollment)? .

6. Describe relevant tests/laboratory data, including dates.

\_\_\_\_\_

7. Describe other relevant history, including preexisting medical conditions. (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

\_\_\_\_\_

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

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Report Number \_\_\_\_\_

## 8. Outcomes attributed to adverse event (Check all that apply)

(ALL choices below represent an SAE except "None of the above")

- Death: \_\_\_\_\_/\_\_\_\_\_/\_\_\_\_\_ (dd/mmm/yyyy)
- Life-threatening
- Hospitalization - initial or prolonged
- Disability
- Congenital anomaly
- Required intervention to prevent permanent impairment/damage
- Important medical event as determined by the site PI or designee
- None of the above (non-serious AE)

If outcome changes to an SAE during a postcomplete change, Q8a and 8b pop-up.

8a. Date the Adverse Event became a Serious Adverse Event:

\_\_\_\_/\_\_\_\_/\_\_\_\_ (dd/mmm/yyyy)

8b. Date the site became aware that the Adverse Event became a Serious Adverse Event:

\_\_\_\_/\_\_\_\_/\_\_\_\_ (dd/mmm/yyyy)

## 9. Intensity - Please follow the guidelines in the "TCAE in Trials of Adult Pancreatic Islet Transplantation"

(Select one)

- Mild/Grade I
- Moderate/Grade II
- Severe/Grade III
- Life-threatening/Grade IV
- Death/Grade V

(If question 9 is Death/Grade V, then go to question 10)

## 10. Was/will an autopsy be performed? (select one)

- No
- Yes \_\_\_\_\_ Please provide a de-identified copy to the DCC
- Unknown

## 11. Indicate outcome of the event

- Continuing
- Resolved (or resolved with sequelae) - If resolved, give date of resolution \_\_\_\_\_ (dd/mmm/yyyy)

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

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Report Number \_\_\_\_\_

- No**   **Yes**
12.         Has the subject **ever** received the investigational drug, LMW-DS?  
       \_\_\_\_\_ a. Relationship to LMW-DS  
                Definite  
                Probable  
                Possible  
                Unlikely  
                Unrelated, Explain: \_\_\_\_\_  
               b. Action taken regarding LMW-DS  
                    None  
                    Dose reduced  
                    Interrupted  
                    Discontinued  
                    Dose increased
- No**   **Yes**
13.         Was a study-related islet transplant procedure **ever** initiated for this subject?  
       \_\_\_\_\_ a. Relationship to islet transplant procedure  
                Definite  
                Probable  
                Possible  
                Unlikely  
                Unrelated, Explain: \_\_\_\_\_  
               b. Action taken regarding islet transplant procedure  
                    Infusion not started  
                    None  
                    Interrupted but completed  
                    Prematurely terminated
- No**   **Yes**
14.         Has the subject **ever** received immunosuppression and/or infection prophylaxis?  
       \_\_\_\_\_ a. Relationship to immunosuppression/infection prophylaxis  
                Definite  
                Probable  
                Possible  
                Unlikely  
                Unrelated, Explain: \_\_\_\_\_  
               b. Action taken regarding immunosuppression/infection prophylaxis  
                    None  
                    Dose reduced  
                    Interrupted  
                    Discontinued  
                    Dose increased

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

Report Number \_\_\_\_\_

**B. Suspect Medication(s)**

	Suspect Medication 1	Suspect Medication 2	Suspect Medication 3
1. Name	Low Molecular Weight Sulfated Dextran	Islet Transplantation <input type="checkbox"/> Islet Product (check if ever received islets) <input type="checkbox"/> Transplant Procedure (check if ever had transplant procedure initiated)	Immunosuppression and infection prophylaxis
2. Total Dose	i. _____	ii. _____	
3. Therapy Dates (if unknown, give best estimate)	Introduction Date ____/____/____ Date of last Dose ____/____/____ (dd/mmm/yyyy)	Date of most recent ____/____/____ Islet Transplantation (dd/mmm/yyyy)	
4. Diagnosis for use	Islet Transplant/Immunosuppression	Type I Diabetes Mellitus	Islet Transplant/Immunosuppression
5. Event abated after use stopped or dose reduced?	i. <input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> Doesn't apply	ii. <input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> Doesn't apply	iii. <input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> Doesn't apply
6. Event reappeared after reintroduction?	i. <input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> Doesn't apply	ii. <input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> Doesn't apply	iii. <input type="radio"/> No <input type="radio"/> Yes <input type="radio"/> Doesn't apply
7. Lot Number	i. _____	ii. _____	
8. Expiration date (if known)	i. ____/____/____ (dd/mmm/yyyy)	N/A	



Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

Report Number \_\_\_\_\_

**C. OTHER MEDICATIONS**

What concomitant medications was the subject receiving at the time of the event?  
(Exclude treatment of event)

**INSTRUCTIONS:**

1. Select the buttons below to add data to the Other Medications text box.
  - Select to add data that has been entered into the subject's Concomitant Meds eCRF
  - Select to add data that has been entered into the subject's Study Treatment Regimen eCRF
2. Please review added data carefully for accuracy and modify this form and the Concomitant Meds eCRF and/or the Study Treatment Regimen eCRF as needed.
3. If the subject was on **insulin therapy at the time of the event**, their insulin therapy must be **added to the text box below**.
4. Add any additional medication information, if applicable.

Subject ID

**Enter concomitant medications**

A. Drug	B. Start Date	C. Stop Date
<input type="text"/>	<input type="text" value="___/___/___"/> (dd/mmm/yyyy)	<input type="text" value="___/___/___"/> (dd/mmm/yyyy)
<p>D. Comment:</p> <input type="text"/> <p><input type="button" value="Enable Delete"/></p>		

*(As drugs are saved, a table is created. Each entry can be edited)*

Drug	Start Date	Stop Date	
			Edit

Subject ID

**A. LYMPHOCYTOTOXIC CROSS-MATCH**

1. Recipient Serum Date:  (dd/mmm/yyyy)

2. Date Crossmatch Performed:  (dd/mmm/yyyy)  (click to copy date)

2a.  No  Yes  
Have you completed a major protocol deviation for this crossmatch (since the sample is >60 days old)?  
Please complete the Major Protocol Deviation eCRF.  
Continue to Question 3.

3.  No  Yes  
Has the subject experienced a pregnancy, infection, or received blood products since the date recipient serum was obtained?  
Fresh recipient serum must be obtained for crossmatch. Enter new recipient serum date in Question 1.  
Continue to Question 4.

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

4. Donor Cell Source:  (PBMC) or  (Spleen/lymph node)

	Cross-match	Results (Select one)	Method (Select one)
a.	Donor T Cell	<input type="radio"/> Negative <input type="radio"/> Positive	<input type="radio"/> NIH CDC <input type="radio"/> NIH ext CDC <input type="radio"/> Amos CDC <input type="radio"/> AHG CDC <input type="radio"/> ELISA <input type="radio"/> Flow Cytometry
b.	Donor B Cell	<input type="radio"/> Negative <input type="radio"/> Positive	<input type="radio"/> NIH CDC <input type="radio"/> NIH ext CDC <input type="radio"/> Amos CDC <input type="radio"/> AHG CDC <input type="radio"/> ELISA <input type="radio"/> Flow Cytometry
c.	Auto T Cell	<input type="radio"/> Negative <input type="radio"/> Positive <input type="radio"/> Not Done	<input type="radio"/> NIH CDC <input type="radio"/> NIH ext CDC <input type="radio"/> Amos CDC <input type="radio"/> AHG CDC <input type="radio"/> ELISA <input type="radio"/> Flow Cytometry
d.	Auto B Cell	<input type="radio"/> Negative <input type="radio"/> Positive <input type="radio"/> Not Done	<input type="radio"/> NIH CDC <input type="radio"/> NIH ext CDC <input type="radio"/> Amos CDC <input type="radio"/> AHG CDC <input type="radio"/> ELISA <input type="radio"/> Flow Cytometry

**B. COMMENTS (optional)**

Screening ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

1. Date of birth \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
(dd/mmm/yyyy)

2. Gender  
 Male  
 Female

3. Ethnicity (Select one)  
 Hispanic or Latino  
 Non-Hispanic or Non-Latino Origin  
 Unknown/not reported

4. Race (Check all that apply)  
 American Indian or Alaskan Native  
 Asian  
 Black or African-American  
 Native Hawaiian or other Pacific Islander  
 White  
 Unknown/not reported

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

A. Date of Visit

\_\_\_\_/\_\_\_\_/\_\_\_\_\_  
(dd/mmm/yyyy)

**B. QUESTIONS FOR FULL HYPO SCORE**

- 1. How many hypoglycemic episodes in the past year have you needed help to recognize?
  
- 2. How many hypoglycemic episodes in the past year have you needed help to treat?
  
- 3. How many hypoglycemic episodes in the past year have you treated with glucagon?
  
- 4. How many hypoglycemic episodes in the past year have required an ambulance call?

**C. COMMENTS**

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

**This form must be entered on the CIT website within 24 hours of notification of a major protocol deviation. Major protocol deviations are deviations that impact the inclusion and/or exclusion criteria, consent violations, alteration of study therapy, or administration of prohibited medications.**

1. Date of deviation:   
(dd/mmm/yyyy)

2. Date site became aware of deviation:   
(dd/mmm/yyyy)

3. Who identified the protocol deviation? (select one)
- Principal Investigator
  - Site Coordinator
  - Monitor / Auditor
  - NIH Medical Monitor
  - NIH Project Manager
  - DCC Protocol Coordinator

4. When did the protocol deviation occur? (select one)
- Prior to study treatment
  - After initiation of study treatment
  - After discontinuation of study treatment, while on mandated protocol follow-up

5. Category of deviation: (select one)
- Impacts the Inclusion and/or Exclusion criteria
  - Involves consent violations
  - Alters protocol-specified study therapy
  - Impacts the ability to evaluate the endpoints of the study
  - Involves administration of prohibited medications
  - Other

6. Provide a detailed description of the protocol deviation:

7. Describe the corrective plan to ensure that this deviation does not occur again:

8. Comments (optional)

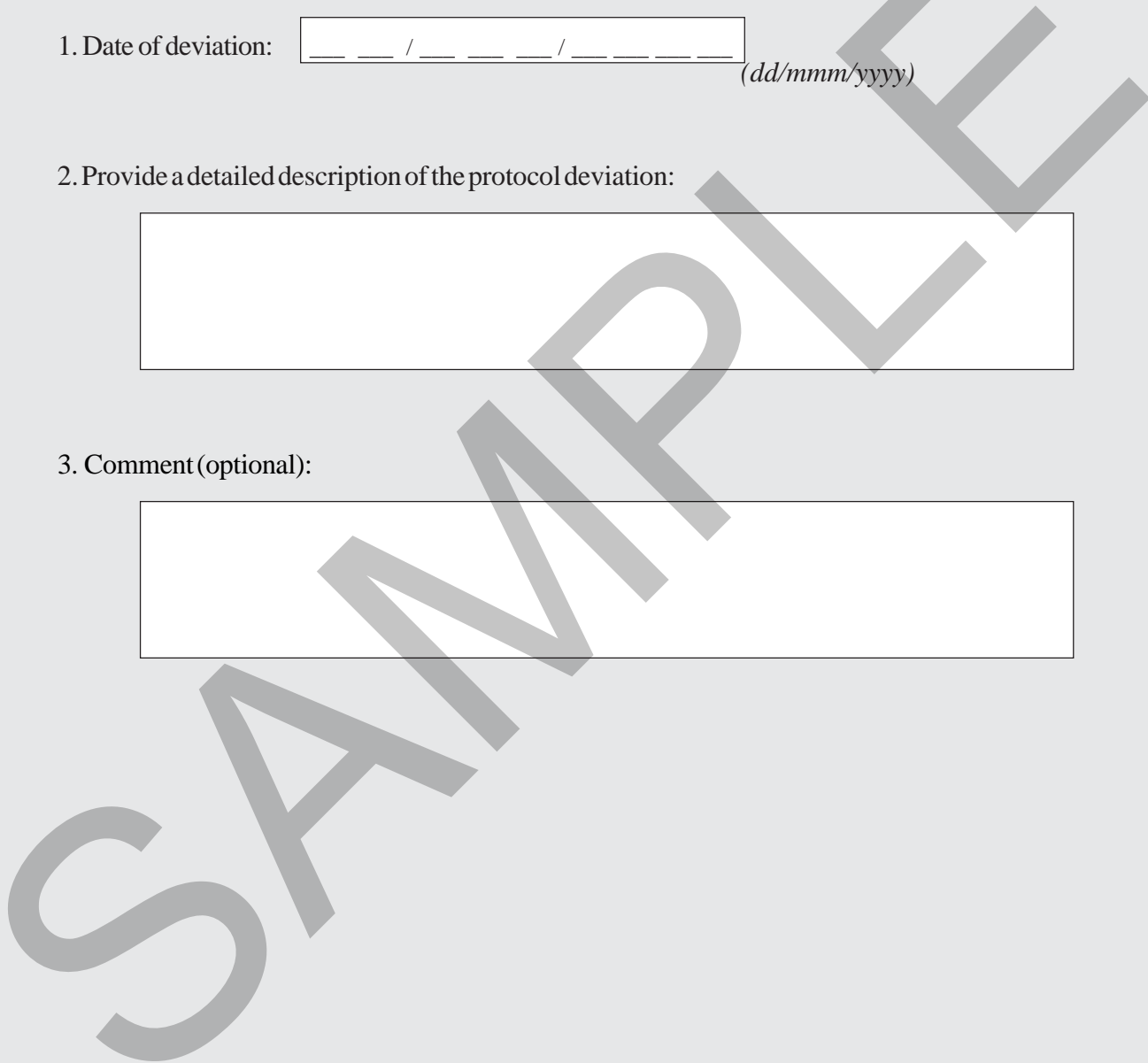
Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

**Minor protocol deviations are those that DO NOT impact the inclusion and/or exclusion criteria, consent violations, alteration of study therapy, or administration of prohibited medications.**

1. Date of deviation:  (dd/mmm/yyyy)

2. Provide a detailed description of the protocol deviation:

3. Comment (optional):





Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

**A. CLINICAL ASSESSMENT**

1. Date of Assessment  (dd/mm/yyyy)
2. Temperature  (°C)
3. Pulse  (beats/min)
4. Blood Pressure  (mm Hg)
5. Weight  (kg)
6. Height  (cm)
7. BMI  (kg/m<sup>2</sup>) [This will be autocalculated on the web.]

**B. PHYSICAL EXAMINATION**  
 (skip part B after initial physical examination)

Assessment	Not Performed	Normal	Abnormal	If abnormality, please describe
1. Skin	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
2. Head, eyes, ears, nose, throat	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
3. Respiratory	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
4. Cardiovascular	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
5. Abdominal	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
6. Genitourinary/reproductive	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
7. Neurological	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
8. Lymph nodes	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
9. Musculoskeletal	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
10. Psychological/psychiatric	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
11. Other (specify) <input type="text"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

**C. PHYSICAL EXAMINATION**

Assessment	Not Performed	Normal	Abnormal but unchanged since last visit	New abnormality	If new abnormality, please describe
1. Skin	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
2. Head, eyes, ears, nose, throat	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
3. Respiratory	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
4. Cardiovascular	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
5. Abdominal	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
6. Genitourinary/reproductive	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
7. Neurological	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
8. Lymph nodes	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
9. Musculoskeletal	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
10. Psychological/psychiatric	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
11. Other (specify) _____ <input type="text"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>

**D. COMMENTS (optional)**

# PREMATURE DISCONTINUATION OF STUDY TREATMENT

CIT CORE

Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

Page 1 of 1

## A. CRITERIA FOR PREMATURE DISCONTINUATION OF STUDY TREATMENT

If one or more of these four criteria is answered YES, begin **Reduced Follow-Up Schedule**.

**No    Yes**

1.          The subject is unwilling or unable to comply with the protocol.
2.          The investigator believes that the study treatment is no longer in the best interest of the subject.
3.          Graft Failure: absence of insulin production by transplanted islets, as evidenced by c-peptide < 0.3 ng/mL. This is determined by (1) c-peptide <0.3 ng/mL on random testing, followed by (2) c-peptide <0.3 ng/mL at baseline, and at 60 and 90 minutes after MMTT. C-peptide levels obtained in the course of the MMTT will be run at the core lab in Seattle, WA.
4.          An unexpected related serious adverse event.

## B. COMMENTS (optional)



Subject ID \_\_\_\_\_ - \_\_\_\_\_ - \_\_\_\_\_

**This form must be entered on the CIT website within 24 hours of study termination.**

1. Date of Study Termination: \_\_\_\_\_/\_\_\_\_\_/\_\_\_\_\_ (dd/mmm/yyyy)

2. Date of last follow up visit: \_\_\_\_\_/\_\_\_\_\_/\_\_\_\_\_ (dd/mmm/yyyy)

3. Indicate the primary reason the subject will no longer be followed: (select one)

- Subject completed study procedures per protocol
- Subject withdrew consent
- Lost to follow-up (Unable/unwilling to travel/moved from area/unable to locate)
- Subject death  
| \_\_\_\_\_ Complete the Adverse Event form
- Screening Eligibility form completed, indicating a “screening success”, but subject did not actually meet eligibility criteria  
| \_\_\_\_\_ Select the eligibility criteria that caused the subject to become ineligible (check all that apply)  
| \_\_\_\_\_ (add list box of eligibility criteria - include instructions for selecting multiple criteria )  
| \_\_\_\_\_ Complete the Major Protocol Deviation form to explain
- Screening Eligibility form completed, indicating a “screening success”, but the subject became ineligible while on wait list  
| \_\_\_\_\_ Select the eligibility criteria that caused the subject to become ineligible (check all that apply)  
| \_\_\_\_\_ (add list box of eligibility criteria - include instructions for selecting multiple criteria)
- Subject randomized but did not actually meet randomization eligibility criteria  
| \_\_\_\_\_ Do NOT complete this Study Termination eCRF if the subject received immunosuppression medications post-randomization in preparation for a CIT Islet Transplant.  
| \_\_\_\_\_ Complete the Major Protocol Deviation form to explain
- Other

| \_\_\_\_\_ Please specify: \_\_\_\_\_

4. Comments (optional):

\_\_\_\_\_

Subject ID

1. Date and time action was taken:

a. Date:  (dd/mmm/yyyy)

b. Time:  (hhmm - 24 hr clock)

2. Action taken on the national transplant waitlist. Check only one (a-e):

a.  Initial Listing

- i  Active status
- ii  Inactive status
- iii  Listed without a status

b.  Status changed to Active

c.  Status changed to Inactive

(select all that apply)

- i  Site PI Unavailable
- ii  Site Study Coordinator Unavailable
- iii  Islet Lab Support Unavailable
- iv  Subject Unavailable
- v  Transient condition while on protocol waitlist
- vi  Institution Closed (i.e. holiday or other closure)
- vii  Other reason:

d.  Removed from the national transplant waitlist

(select all that apply)

- i  Study consent withdrawn AND subject did not receive an islet transplant
- ii  Subject became ineligible AND subject did not receive an islet transplant
- iii  Subject recieved a study islet transplant (do not foresee subsequent islet transplants)

iv  Other Reason:

e.  Other Action Taken: