Subject ID ____ ____ -____ ____ - ____ ____ ____

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

Subject ID ____ ____ -____ ____ - ____ ____ ____

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

- ◯ Never
- ◯ 1 time
- ◯ 2 times
- ◯ 3 times
- ◯ 4 times
- ◯ 5 times
- ◯ 6 times
- ◯ 7 times
- ◯ 8 times
- ◯ 9 times
- ◯ 10 times
- ◯ 11 times
- ◯ 12 times or more

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

Subject ID ____ ____ -____ ____ - ____ ____ ____

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. ○ click to copy date

a. Date of draw __ __ / __ __ __ / __ __ __ __ *(dd/mmm/yyyy)* 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 eCRF

Enter data from the deceased donor's records

1. Donor Scandia transplant number [open text box]

2. Donor's Date of Birth [_ _ / _ _ _ /_ _ _ _] *(dd/mmm/yyyy)*

3. Donor's Gender O Female O Male

4. Donor's Weight [X X X . X] kg

5. Donor's Height [X X X . X] cm

6. Body Mass Index [X X. X] kg/m^2

7. Donors Blood Type O A O B O AB O O

8. Donor CMV status: O Positive O Negative O Not Available

9. Donor EBV status: O Positive O Negative O Not Available

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	O Molecular O Serologic	i.___ HLA-A (1st allele) ii.___HLA-A (2nd allele)
b. HLA-B	O Molecular O Serologic	i.___ HLA-B (1st allele) ii.___HLA-B (2nd allele)
c. HLA-DR	O Molecular O Serologic	i.___ HLA-DR (1st allele) ii.___HLA-DR (2nd allele)

11. Cause of Death

O Anoxia

O CVA/Cerebrovascular/Stroke

O Head Trauma

O CNS Tumor

O Other: Specify text box

12. Donor HbA1c %: __._%(If Swedish X 0.923 + 1.345=HbA1c DCCT

O Not Available

13. Comments: text box

A. CHEST X-RAY (Visit 1 and 2)

	No	Yes	
1.	○	○	Was a chest X-Ray performed?

a. Date chest X-Ray was performed: ___ ___ / ___ ___ ___ / ___ ___ ___ ___
(dd/mmm/yyyy)

b. Chest X-Ray interpreted as: (select one)

○ Normal

○ Abnormal; clinically significant

_____ i.) Please specify abnormality:

○ Abnormal: not clinically significant

_____ ii.) Please specify abnormality:

c) Reason:

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:

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/mmm/yyyy)

   b. Reason:

2.

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

3. Temperature threshold (Celsius)

	Heat	Cold	Difference
a. hand (thenar)	i. ☐	ii. ☐	iii. ☐
b. foot (dorsum)	i. ☐	ii. ☐	iii. ☐

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

5. SSR

	Latency (s)	Amplitude (mV)
a. hand	i. ☐	ii. ☐
b. foot	i. ☐	ii. ☐

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)

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^2 ☐ 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.
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.

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: _____

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

27. Vital sign measurements at time of infusion

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

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

____

Date of Visit _____ *(dd/mmm/yyyy)*

A. COAGULATION STATUS (Visits1, 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 _____ $x10^9$/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 _____ $x10^{12}$/L ☐ Not Available
3. Hemoglobin _____ ○ mg/dL or ○ g/L ☐ Not Available
4. Hematocrit _____ % ☐ Not Available
5. White blood cell count _____ $x10^9$/L ☐ Not Available
6. Lymphocyte _____ $x10^9$/L ☐ Not Available
7. Neutrophils [total] _____ $x10^9$/L ☐ Not Available
8. Eosinophils _____ $x10^9$/L ☐ Not Available
9. Monocytes _____ $x10^9$/L ☐ Not Available
10. Basophils _____ $x10^9$/L ☐ Not Available

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

1.	Date of Draw	☐	☐ *Click to copy Date of Visit*
2.	Sodium	☐ mmol/L	☐ Not Available
3.	Potassium	☐ mmol/L	☐ Not Available
4.	Creatinine	☐ µmol/L	☐ Not Available
5.	Glucose	☐ mmol/L	☐ Not Available
6.	Albumin	☐ g/L	☐ Not Available
7.	Alk Phosphorous	☐ ○ µkat/L or ○ U/L	☐ Not Available
8.	ALT (SGPT)	☐ ○ µkat/L or ○ U/L	☐ Not Available
9.	AST (SGOT)	☐ ○ µkat/L or ○ U/L	☐ Not Available
10.	LDH	☐ ○ µkat/L or ○ U/L	☐ Not Available
11.	Total Bilirubin	☐ µmol/L	☐ Not Available
12.	CRP (C-reactive protein)	☐ ○ mg/dL or ○ mg/L	☐ Not Available

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

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	O	O	
2.	Head, Eyes, Ears, Nose, Throat	O	O	
3.	Respiratory	O	O	
4.	Cardiovascular	O	O	
5.	Gastrointestinal	O	O	
6.	Endocrine/Metabolic (except Diabetes)	O	O	
7.	Genitourinary/Reproductive	O	O	
8.	Neurological	O	O	
9.	Blood/Lymphatic	O	O	
10.	Musculoskeletal	O	O	
11.	Hepatic/Biliary	O	O	
12.	Allergies/Immunologic	O	O	
13.	Psychological/Psychiatric	O	O	
14.	Other		O	

E. COMMENTS (optional)

Subject ID ____ ____ -____ ____ - ____ ____ ____

A. PRA

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

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

No **Yes**

1. ○ ○ 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

No **Yes**

1. ○ ○ Has the subject experienced any Serious Adverse Events?

   a. **If yes, then complete the Adverse Event form.**

No **Yes**

2. ○ ○ Were QOL questionnaires mailed to the subject?

   a. Date questionnaires mailed: __ __ / __ __ __ / __ __ __ __
   (dd/mmm/yyyy)

   b. Reason:

	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)

Subject ID ____ ____ -____ ____ - ____ ____ ____

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 ≥0.1 nmol/L (≥0.3 ng/mL) **and** 75 +/- 5 day visit metabolic assessments have been completed.
1.b	○	○	Graft Failure: the subject has confirmed graft failure evidenced by c-peptide < 0.1 nmol/L (<0.3 ng/mL) **and** has received CITSteering Committee (if before Day 75) approval or Nordic Network Steering Committee (if after Day 75) approval for a second infusion.
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.

Date of SC approval: __ __/__ __ __/__ __ __ __

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)	_ _ /_ _ _ /_ _ _ _	○	○	○
2.	Cytomegalovirus IgM antibody (CMV IgM)	_ _ /_ _ _ /_ _ _ _ ○ click to copy above date	○	○	○
3.	Epstein-Barr Virus IgG antibody (EBV IgG)	_ _ /_ _ _ /_ _ _ _ ○ click to copy above date	○	○	○
4.	HIV	_ _ /_ _ _ /_ _ _ _ ○ click to copy above date	○	○	○
5.	Hepatitis C antibody (HCV Ab)	_ _ /_ _ _ /_ _ _ _ ○ click to copy above date	○	○	○
6.	Hepatitis B surface antigen (HBsAg)	_ _ /_ _ _ /_ _ _ _ ○ click to copy above date	○	○	○
7.	Hepatitis B surface antibody (HBsAb)	_ _ /_ _ _ /_ _ _ _ ○ click to copy above date	○	○	○
8.	Hepatitis B Core antibody (HBcAb)	_ _ /_ _ _ /_ _ _ _ ○ click to copy above date	○	○	○
9.	CMV by PCR	_ _ /_ _ _ /_ _ _ _ ○ click to copy above date	○	○	○
10.	EBV by PCR	○ click to copy above date	○	○	○

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 ____ ____ -____ ____ - ____ ____ ____

A. INDUCTION MEDICATIONS

Drug	Date	Total Dose on this Date (mg)
○ ATG ○ Other	(dd/mmm/yyyy)	

Add new Entry

B. CELL PROLIFERATION INHIBITOR

Drug	Dose (mg) per 24 hours	Start Date	Stop Date
○ MMF ○ Sirolimus		(dd/mmm/yyyy)	(dd/mmm/yyyy)

Add new Entry

C. MAINTENANCE IMMUNOSUPPRESSION MEDICATIONS

Drug	Dose (mg) per 24 hours	Start Date	Stop Date
○ Tacrolimus ○ Cyclosporine		(dd/mmm/yyyy)	(dd/mmm/yyyy)

Add new Entry

D. TROUGH LEVELS

Drug	Date of blood draw	Trough Level (ng/mL)
○ Tacrolimus ○ Sirolimus ○ Cyclosporine	(dd/mmm/yyyy)	☐ undetectable

Add new Entry

E. MONOCLONAL ANTIBODY IL-2 RECPTOR BLOCKER

Drug	Dose (mg) per 24 hours	Date
○ Basiliximab		(dd/mmm/yyyy)

Add new Entry

F. List <u>other immunosuppressive</u>, <u>anti-coagulant</u>, <u>infection prophylaxis</u> 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
				(dd/mmm/yyyy)	(dd/mmm/yyyy)

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

G. COMMENTS

Subject ID ____ ____ -____ ____ - ____ ____ ____

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 ____ ____ -____ ____ - ____ ____ ____

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 ≥ 5 years at the time of enrollment, and a sum of patient age and insulin dependent diabetes duration of ≥ 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 $mmol/L^2/hr \cdot wk^{-1}$) 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^2 .
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^2 . The absolute (raw) GFR value will be used for subjects with body surface areas >1.73m^2.
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.	○	○	Homocygotic 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 ≤ 5mg 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

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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.
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B. EXCLUSION CRITERIA

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	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^2 .
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^2 . The absolute (raw) GFR value will be used for subjects with body surface areas >1.73m^2.
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.
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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).
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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.
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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 ≤ 5mg 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.

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 ○ mmol/L OR ○ Low ○ High *(if glucometer does not register a numerical value for a 'Low' or 'High' reading)*

   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 ○ 2 = 2 hours post-meal ○ 3 = bedtime

   ADD NEW ENTRY

   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

C. COMMENTS

Subject ID ____ ____ -____ ____ - ____ ____ ____

A. Blood Type

1. Date of blood typing: __ __ / __ __ __ / __ __ __ __ *(dd/mmm/yyyy)* ☐ Not Done

2. Blood type: ○ A ○ B ○ AB ○ O

B. HLA typing

1. Date of HLA typing : __ __/__ __ __/__ __ __ __ *(dd/mmm/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	o Molecular o Serologic	i.___ HLA-A (1st allele) ii.___ HLA-A (2nd allele)
b. HLA-B	o Molecular o Serologic	i.___ HLA-B (1st allele) ii.___ HLA-B (2nd allele)
c. HLA-DR	o Serologic	i.___ HLA-DR (1st allele) ii.___ HLA-DR (2nd allele)

C. COMMENTS (optional)

Subject ID ____ ____ -____ ____ - ____ ____ ____

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 ____ ____ -____ ____ - ____ ____ ____

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)

	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

B. Suspect Medication(s)

	Suspect Medication 1	Suspect Medication 2	Suspect Medication 3
1. Name	Low Molecular Weight Sulfated Dextran	Islet Transplantation ☐ Islet Product (check if ever received islets) ☐ 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. ○ No ○ Yes ○ Doesn't apply	ii. ○ No ○ Yes ○ Doesn't apply	iii. ○ No ○ Yes ○ Doesn't apply
6. Event reappeared after reintroduction?	i. ○ No ○ Yes ○ Doesn't apply	ii. ○ No ○ Yes ○ Doesn't apply	iii. ○ No ○ Yes ○ 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
	__ __ / __ __ __ / __ __ __ __ (dd/mmm/yyyy)	__ __ / __ __ __ / __ __ __ __ (dd/mmm/yyyy)

Save

Cancel

Delete

D. Comment:

Enable Delete

(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)*

.

No Yes

2a. ⬭ ⬭ 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.

No Yes

3. ⬭ ⬭ 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.

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

	Cross-match	Results (Select one)	Method (Select one)
a.	Donor T Cell	○ Negative ○ Positive	○ NIH CDC ○ NIH ext CDC ○ Amos CDC ○ AHG CDC ○ ELISA ○ Flow Cytometry
b.	Donor B Cell	○ Negative ○ Positive	○ NIH CDC ○ NIH ext CDC ○ Amos CDC ○ AHG CDC ○ ELISA ○ Flow Cytometry
c.	Auto T Cell	○ Negative ○ Positive ○ Not Done	○ NIH CDC ○ NIH ext CDC ○ Amos CDC ○ AHG CDC ○ ELISA ○ Flow Cytometry
d.	Auto B Cell	○ Negative ○ Positive ○ Not Done	○ NIH CDC ○ NIH ext CDC ○ Amos CDC ○ AHG CDC ○ ELISA ○ 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/mmm/yyyy)*
2. Temperature ____ (°C)
3. Pulse ____ (beats/min)
4. Blood Pressure ___ ___ ___ / ___ ___ ___ (mm Hg)
5. Weight ____ (kg)
6. Height ____ (cm)
7. BMI _____ (kg/m^2) [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	○	○	○	
2. Head, eyes, ears, nose, throat	○	○	○	
3. Respiratory	○	○	○	
4. Cardiovascular	○	○	○	
5. Abdominal	○	○	○	
6. Genitourinary/ reproductive	○	○	○	
7. Neurological	○	○	○	
8. Lymph nodes	○	○	○	
9. Musculoskeletal	○	○	○	
10. Psychological/ psychiatric	○	○	○	
11. Other (specify)____	○	○	○	

Subject ID ____ ____ -____ ____ - ____ ____ ____

C. PHYSICAL EXAMINATION

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

D. COMMENTS (optional)

Subject ID ____ ____ -____ ____ - ____ ____ ____

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 ____ ____ -____ ____ - ____ ____ ____

A. RETINOPATHY

No Yes

1. ○ ○ Was an eye exam completed?

   a. What was the stage of diabetic retinopathy?
   - ○ Not present
   - ○ Mild nonproliferative
   - ○ Moderate nonproliferative
   - ○ Severe nonproliferative
   - ○ Proliferative

No Yes

2. ○ ○ Was a photo of the retina completed?

   a. Was the retinopathy photo sent to the Central Laboratory?

   ○ **Yes** - Date Sent: __ __ /__ __ __ / __ __ __ __
   (dd/mmm/yyyy)

   ○ **No** - Please Comment Below

   b. Reason

B. COMMENTS (optional)

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: