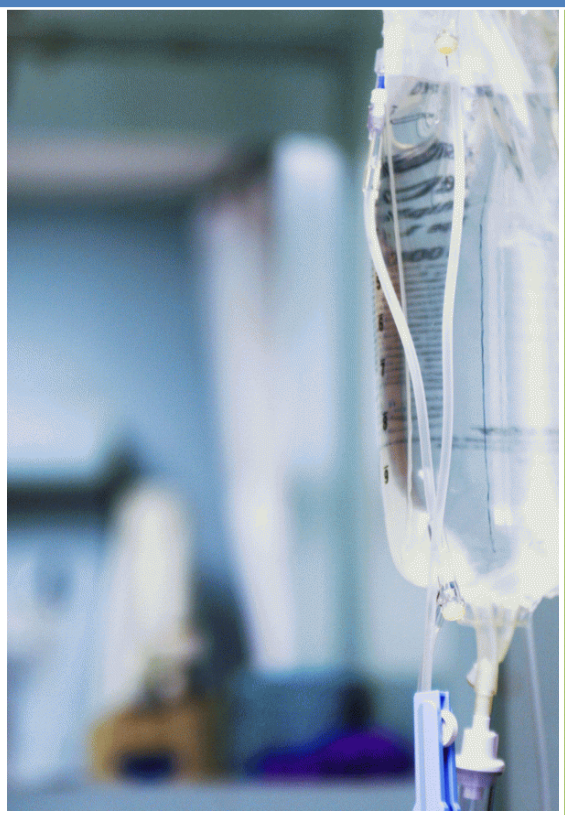
2014

CLINICAL GUIDELINES FOR PANCREATIC ISLET TRANSPLANTATION



BC TRANSPLANT
An agency of the Provincial Health Services Authority

Vancouver Coastal Health
Promoting wellness. Ensuring care.

Revised on July 31, 2014

AMB.03.005 Rev02 Eff Date: 01-Sept-2014

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1 Pre-Transplant

1.1 Introduction

Whole Pancreas Transplantation

In the early years of the BC Pancreas Transplant Program, simultaneous whole pancreas with kidney transplantation was the sole operation performed (both organs from the same deceased donor) in the treatment of diabetic patients with renal failure. In 2000, the Pancreas Transplant Program was expanded to include an option for patients to first undergo a living donor kidney transplant, followed by a pancreas transplant (pancreas-after-kidney). The pancreas-after-kidney program has both expanded the available number of kidneys from deceased donors for transplant by fostering live donor kidney transplant and reduced the necessity for renal dialysis (the consequence of waiting for a combined kidney and pancreas from a deceased donor to become available). The subsequent pancreas transplant was effective at eliminating the patient's need for insulin and provided protection for the transplanted kidney from damage from the diabetic state.

Islet Transplantation

In 2003, the BC Pancreatic Islet Transplant Program performed the first pancreatic islet transplants in British Columbia. The goal of the program was to provide an opportunity for diabetic patients to receive a pancreatic islet transplant, and to contribute to the research and advancement of the islet transplant field.

In the initial phase of the Islet Transplant Program, patients considered for islet transplantation were restricted to type I diabetes with little or no evidence of diabetes-associated renal disease. In this group of patients, successful islet transplantation was shown to have a protective effect on native kidney function.

On occasion, diabetic patients who have undergone a prior living donor kidney transplant and were desirous of whole pancreas transplantation, were found to have an unacceptably high risk for complications or were technically unsuitable to undergo a subsequent pancreas transplant. They therefore would miss out on the advantages a pancreas transplant would offer.

In several centres where islet transplant is performed, successful islet transplantation can be achieved in diabetic patients who have already undergone a kidney transplant. Such islet transplants are being undertaken with minor additional immunosuppression at the time of islet transplantation, and resume what is required for maintaining the kidney transplant. Islet-after kidney transplant allows the patient to benefit from the advantages of improved blood glucose control and protection of the transplanted kidney from the diabetic state without significant additional immunosuppression risk.

The original goal of the Islet Transplant Program was to study the impact (positive or negative) of islet transplantation in individuals with little or no target organ damage, such as established kidney disease or retinopathy. Based on the initial success of the Program, the BC Pancreatic Islet Transplant Program at Vancouver General Hospital (VGH) will expand to consider selected diabetic patients who have undergone a previous kidney transplant for an islet transplant. The aim of the program is to provide type I diabetic patients, who have undergone a successful kidney transplant but are not suitable for whole pancreas transplant, a pancreatic islet transplant.

Expected Benefits of an Islet after Kidney Transplant

- *a successful islet transplant will provide the diabetic kidney transplant recipient with improved blood control with a reduction or elimination of the need for exogenous insulin;*
- *a reduction (or elimination) of the cumulative effects of diabetes on the transplanted kidney;*
- *a favourable impact on the other organs and body systems which are typically affected by the secondary complications of diabetes.*

1.2 Referral (All Patients)

Referrals (for either islet with no previous kidney transplant; or islet after kidney transplant) to the BC Pancreatic Islet Transplant Program may come through either the '*Best Care*' Diabetes Program at Vancouver General Hospital, from a referring endocrinologist or from the Renal Transplant program (See Figure 1).

The referring program completes the Islet Transplant Referral Form (Appendix A) and sends the form and all the requested information to the Pancreatic Islet Program Clinical Coordinator at the VGH address below.

Contact information:
Clinical Coordinator
Pancreatic Islet Program
Gordon and Leslie Diamond Health Care Center
Solid Organ Transplant Clinic
5th Floor, 2775 Laurel Street
Vancouver, B.C. V5Z 1M9
Telephone: 604-875-5182
Fax: 604-875-5236

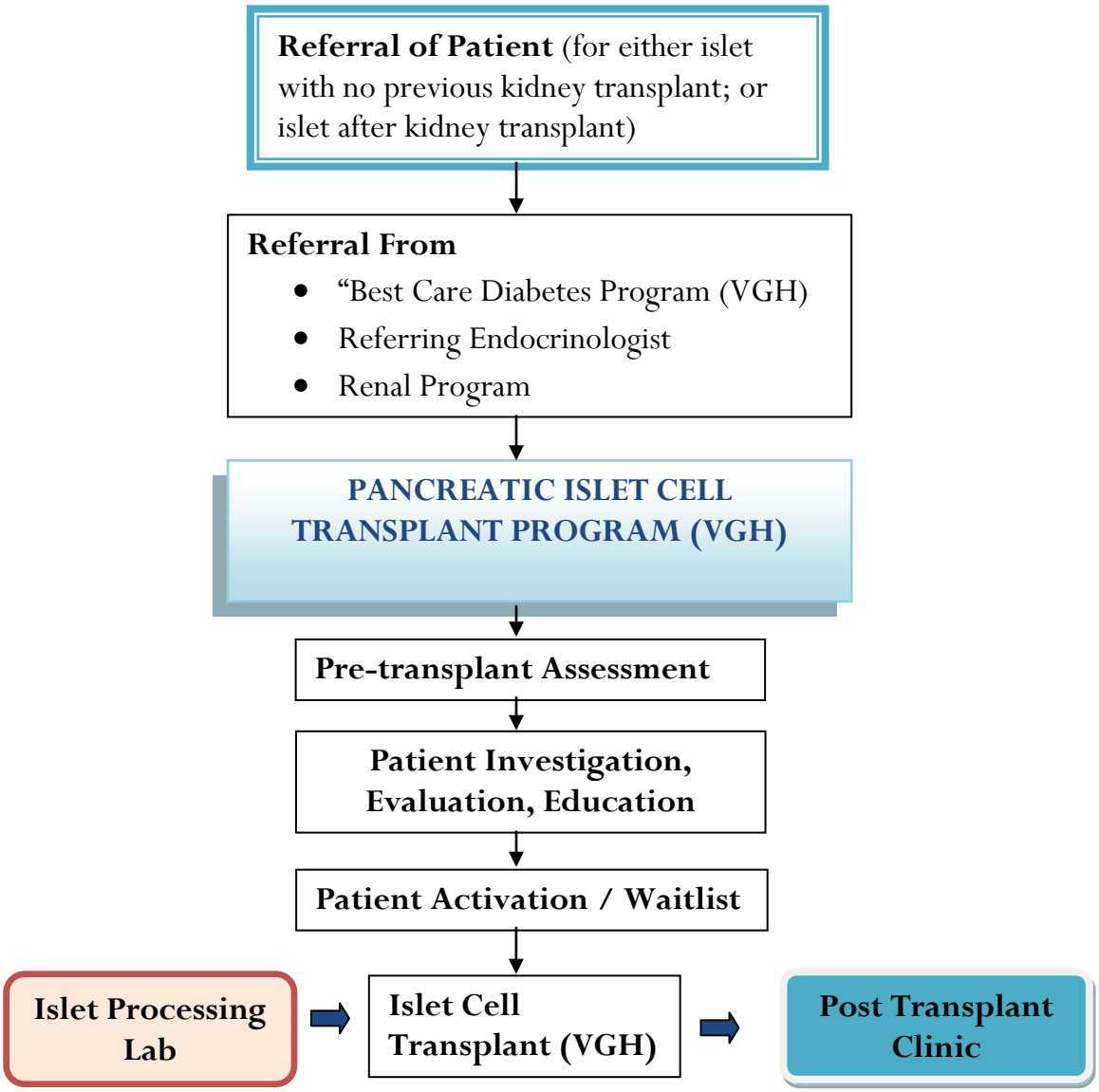


Figure 1. Overview of the BC Pancreatic Islet Transplant Program (for either islet with no previous kidney transplant; or islet after kidney transplant).

1.3 Who May Be Considered?

1.3.1 Inclusion and Exclusion Criteria *(For Potential Islet Recipients with No Previous Kidney Transplant)*

FOR ISLET AFTER KIDNEY TRANSPLANT CRITERIA SEE SECTION 5.1.3.2

INCLUSION CRITERIA (No Previous Kidney Transplant)

- Type 1 Diabetes for greater than 5 years
  - Negative / negligible C-peptide (fasting and/or stimulated)
- Age greater than 20 years
- Retinopathy - all stages
- Renal Status:
  A) little or no evidence of significant diabetes related renal disease.
  - creatinine clearance greater than 70 mL/min/1.73m^2 (GFR or Nuclear)
  - documented history of albumin/creatinine ratio greater than 1.8 mg/mmol in men and 2.5 mg/mmol in women

  B) severe hypoglycemic unawareness

EXCLUSION CRITERIA* (No Previous Kidney Transplant)

- BMI greater than 30 (will consider BMI greater than 30 on individual basis)
- Current or recent smokers (more than zero cigarettes at any time in previous 6 months)
- Planned pregnancy
- Malignant hypertension causing end stage organ damage (retinopathy, stroke, acute coronary syndrome)
- Severe concurrent illness likely to limit life or require extensive systemic treatment
- Active infection or evidence of ongoing or recurrent viral disease
- Inadequate understanding, compliance, or unwillingness to participate with clinical requirements of the Islet transplant program

(*May vary depending on individual patient and physician assessment)

1.3.2 Inclusion and Exclusion Criteria *(For Potential Islet Recipients after Kidney Transplant)*

INCLUSION CRITERIA (AFTER KIDNEY TRANSPLANT)

The BCT Islet Transplant Program will consider type I diabetic patients for an islet-after-kidney transplant who:

- have type 1 diabetes
- are between the age of 18 to 65 years of age, **and**
- have complicated diabetes management characterized by erratic glucose control, significantly elevated HbA1c and/or hypoglycemic unawareness, **and**
- have been assessed for whole pancreas (after kidney) transplantation but were found unsuitable for reasons of an unacceptable peri-operative risk (i.e. cardiac disease) or technical issues (i.e. extensive atherosclerotic disease of iliac vessels), **and**
- are at least one year following successful kidney transplant with stable renal function and without a prior episode of significant acute graft rejection which required an anti-lymphocyte antibody treatment, **and**
- are presently managed on standard immunosuppression drug dosages (with or without steroids), **and**
- have not had a episode of a significant immunosuppression-related infection or neoplasm (which may increase the risks associated with the use of induction agents)

EXCLUSION CRITERIA* (AFTER KIDNEY TRANSPLANT)

Patients will be excluded from consideration for islet-after- kidney transplantation who:

- fail to meet inclusion criteria
- demonstrate presence of measurable C-peptide
- have a PRA (panel reactive antibody) percentage greater than 40
- are current or recent smokers (more than zero cigarettes at any time in previous 6 months)
- weigh more than 90 kilograms or have a body mass index of greater than 32
- have high daily insulin requirements (more than 1 unit of insulin/kg body weight
- have documented hepatic disease or chronic pancreatitis
- have clinically significant anemia or a hematological condition which increases the risks associated with anticoagulation use
- have other health concerns where use of induction therapy or continued immunosuppression may be contra-indicated (i.e. malignancy or unresolved infection)

(*May vary depending on individual patient and physician assessment)

1.4 Patient Assessment & Laboratory Testing *(All patients: for either islet with no previous kidney transplant; or islet after kidney transplant)*

Upon referral the patient will:

- Be seen in consultation with transplant team including:
  - Transplant Surgeon
  - Transplant Nephrologist
  - Transplant Endocrinologist
  - Clinical coordinator (nurse) for Pancreatic Islet Transplant Program

- Receive information which outlines:
  - Deceased donation and the source of islet tissues including risks of transfer of disease
  - Wait list issues, including how potential recipients are selected
  - Induction immunosuppression and possible side effects
  - Procedure including potential complications
  - Post transplant follow-up
  - Expected outcomes
  - Expected need for two or more procedures to complete the transplant process

The following results are to be forwarded to the Pancreatic Islet Transplant Program **at the time of referral** (See Appendix A):

Laboratory Testing

- Referring physician consult letter to include a complete history and physical
- **Chemistry**: Na, K, Cl, bicarbonate, albumin, total protein, Ca, Mg, PO4, uric acid, creatine kinase, creatinine, creatinine clearance, urea, HbA1C, GGT, AST, ALT, alk phos, amylase, total bilirubin, direct bilirubin, LDH, fasting blood glucose, serum protein electrophoresis.
- **Hematology**: CBC and differential;
- **Coagulation**: INR, PTT, platelets;
- **Iron studies**: total iron, TIBC, iron saturation, ferritin;
- **Urine Studies**: urine for microalbuminuria, total protein, routine and microscopy;
- **Lipid Studies**: Total cholesterol, LDL, HDL, triglycerides;
- **C-peptide** (fasting);
- **TSH;**
- Mammography, PAP (females); prostate exam (males);
- Complete eye assessment including fungus photography by transplant ophthalmologist (may be ordered upon request of physician);

1.4 Patient Assessment & Laboratory Testing (Cont.)

The Pancreatic Islet Transplant Program (for either islet with no previous kidney transplant; or islet after kidney transplant) completes (or updates) the following investigations after receiving referral, and once patient is deemed a transplant candidate:

- Chest X-ray
- Abdominal Ultrasound
- Serology: CMV IgG, EBV IgG, HIV, HbsAg, HbsAb, HbcAb, anti-HCV, HSV, VZV
- Blood group and screen

Additional testing as deemed necessary by the transplant team.

1.5 Patient Activation *(All patients: for either islet with no previous kidney transplant; or islet after kidney transplant)*

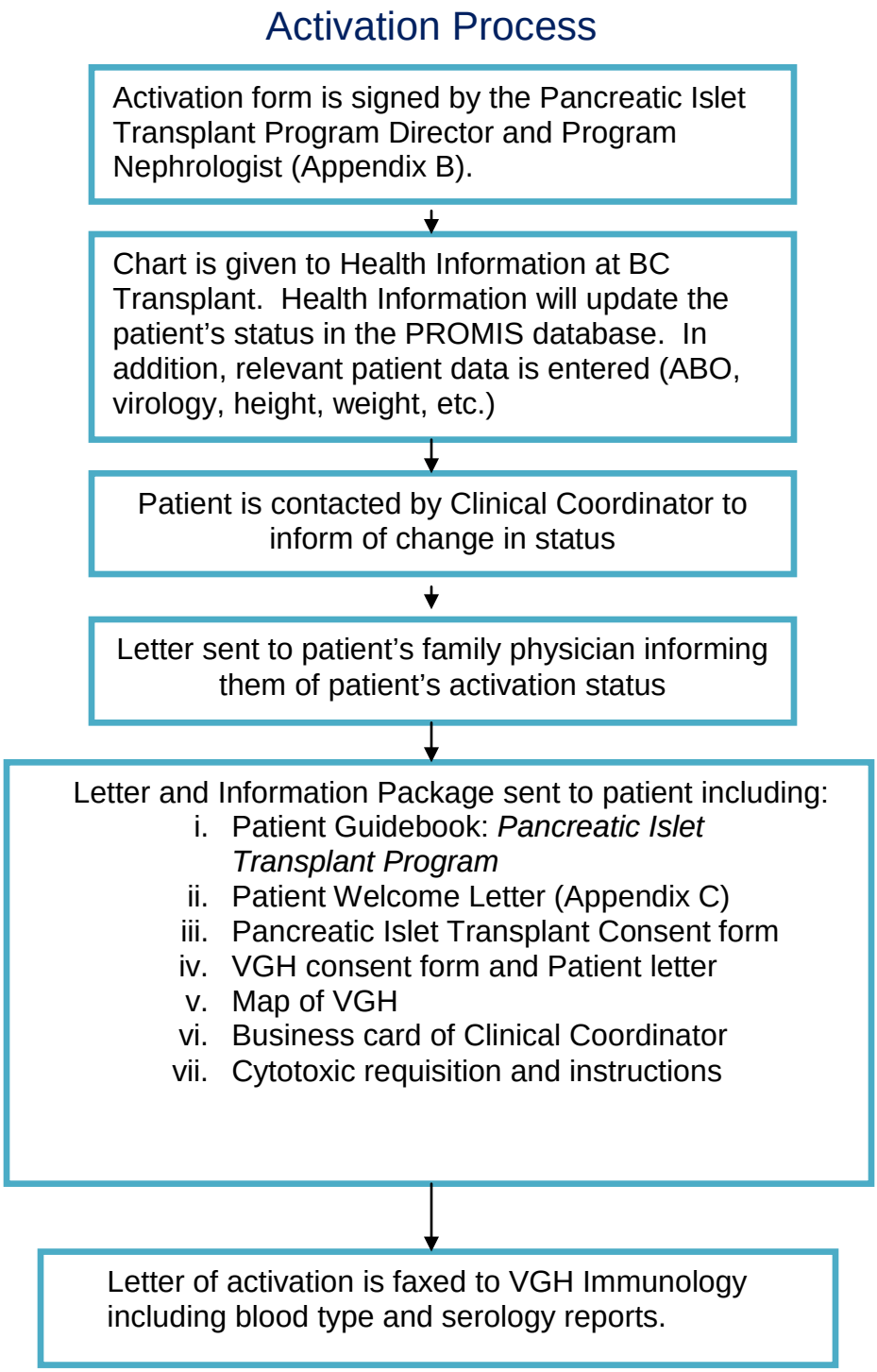
When the assessment process is complete, the candidate is reviewed by the Pancreatic Islet transplant team (Pancreatic Islet Program Director, Transplant Nephrologist, Transplant Endocrinologist, and Clinical Coordinator). Patients that meet eligibility criteria are approved as candidates for transplantation. Refer to Figure 2 for Activation process.

Whether the patient is found suitable or unsuitable (or patient does not wish to proceed with pancreatic islet transplantation), the primary care of the patient remains with the "Best- Care Diabetes Program (VGH)", or their own endocrinologist, nephrologist, and their family physician.

On-Going Suitability

- Patients in the Pancreatic Islet Transplant Program are to maintain regular contact with the program nurse clinician including weekly phone calls and six monthly clinic visits;
- All patients will provide monthly blood work, including sample for immunology lab;
- Patients will be informed to contact the Pancreatic Islet Program clinical coordinator regarding wait list issues, change in information, etc.
- Yearly review by the Pancreatic Islet Transplant Program.

Figure 2. Flowchart of Activation Process.



1.6 Recipient and Donor Selection

Islet cells are obtained from the pancreas of a deceased donor (see 5.1.7 Preparation of Islet Cells, below).

Allocation of isolated islets is determined by several factors (including but not limited to):

- ABO, crossmatch
- Size and weight, BMI, insulin demands of recipient
- Requirement for second or completion islet transplant
- Number of islets obtained from isolation process
- Clinical necessity
- Duration of time on waitlist

1.7 Preparation of Islet Cells

Islet cells for transplant are prepared by the Ike Barber Human Islet Laboratory, Vancouver, B.C., a registered facility with Health Canada. Cells are processed from a whole pancreas following specific Standard Operating Procedures (Figure 3).

An islet isolation will be considered suitable for transplant where:

- there are greater than 400,000 Islet Equivalents (I.E.) on final count, and
- there is a minimum of 5000 I.E. per kilogram of body weight of the intended recipient

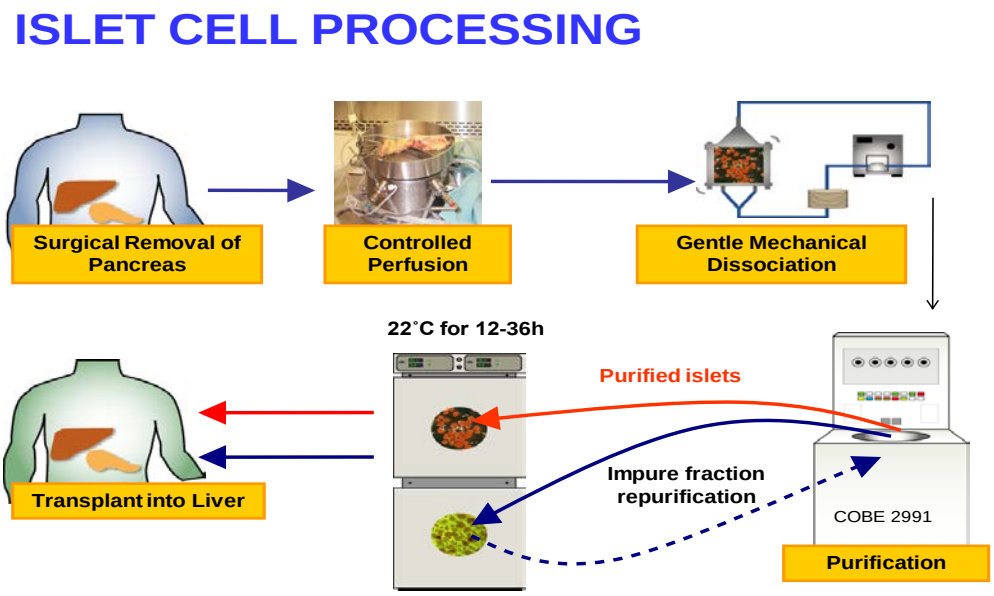


Figure 3. Schematic diagram of islet cell processing.

2 Transplant

2.1 Admission *(All patients: for either islet with no previous kidney transplant; or islet after kidney transplant)*

When pancreatic islets suitable for transplantation become available, the selected patient is admitted to the Transplant Ward at Vancouver General Hospital, either the day before the transplant, or same day; at the discretion of the Transplant Team. The patient will be asked to have nothing by mouth (NPO) at midnight the night before the procedure except medications with sips of water. Participating medical, surgical, nursing, and pharmacy members of the Transplant Team, along with the support services and laboratories are notified as soon as possible pre-procedure. Refer to most current physician orders.

Patient Investigations (Refer to current VGH pre-printed orders):

Stat investigations performed upon admission include:

- Blood group type and screen
- Electrolytes, urea, creatinine, glucose
- CBC and manual diff, INR, PTT
- Urinalysis;
- Calcium, phosphate, magnesium, albumin, total protein, amylase
- AST, ALT, alkaline phosphatase, total bilirubin, direct bilirubin, GGT
- 1 red-top tube and 1 green-top tube for immunology
- C-peptide level
- Beta-HCG for all females of child-bearing age
- EKG
- Chest X-Ray

Preparation:

- For first transplants, PICC or CVC inserted in radiology as soon as patient is admitted;
- NPO at midnight before procedure except medications with sips of water;
- Insertion of peripheral IV with D5 ½ NS started at 100 mL/hr;
- Glucose monitoring / insulin orders as written by endocrinology or the transplant team;
- Consultation with endocrinology;
- Administration of prophylactic antibiotics: cefazolin 2 grams IV on call to Radiology. If allergic to penicillin, administer clindamycin 600 mg IV on call to Radiology.
- Preparation of insulin infusion (50 units insulin R in 500 ml NS);
- Patient sent to Radiology with heparin 2,000 units syringe, to be administered subcutaneously;

Immunosuppression Pre-Transplant (Pre-Islet Infusion)

For First Transplant Procedure:

- Anti-thymocyte globulin (ATG, Thymoglobulin®) (1mg/kg/day) IV over twelve hours. Pre-medication for anti-thymocyte globulin to be given ½ hour before start of infusion:
  - Methylprednisolone 125 mg IV
  - Acetaminophen 650 mg PO
  - Diphenhydramine 50 mg IV
- Tacrolimus and mycophenolate mofetil are started post-op

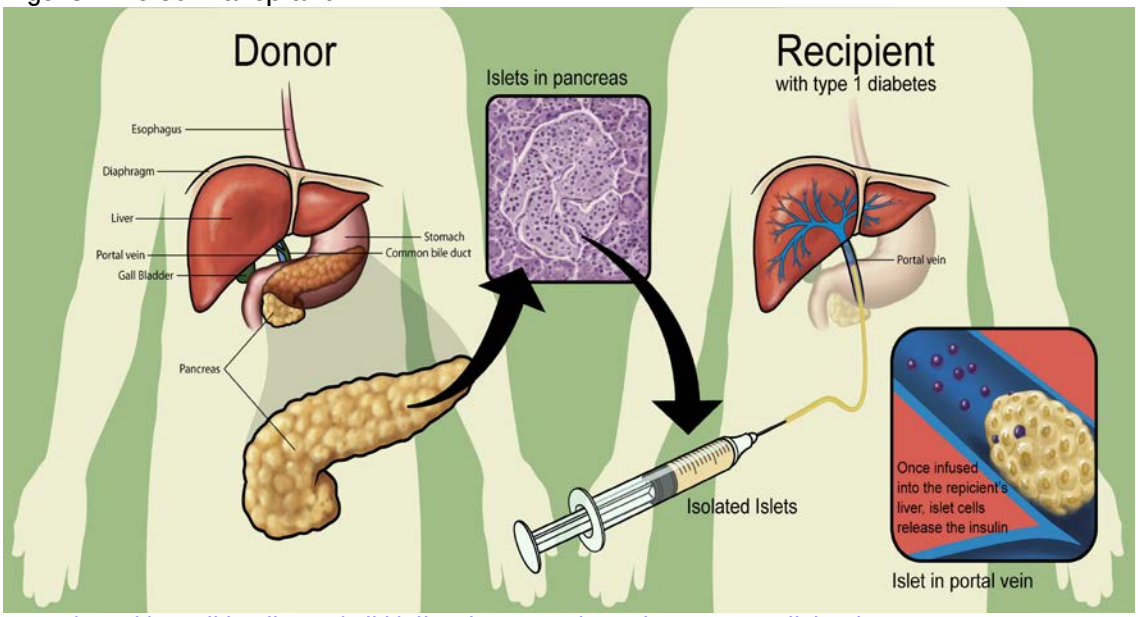
For Second or Greater Transplant Protocol:

- Maintenance of current mycophenolate and tacrolimus

2.2 Islet Transplant *(All patients: for either islet with no previous kidney transplant; or islet after kidney transplant)*

The Pancreatic Islet transplant procedure takes place in the Radiology department in the ~~a~~ Angiography Suite. A percutaneous transhepatic portal vein catheter is placed (under local anesthetic) under fluoroscopic control by the radiologist. Once the catheter is suitably located in the portal vein, portal pressures are determined and the islets are infused. This procedure is usually performed over 30 minutes. Portal pressures are monitored throughout the procedure. Once the infusion is complete, the catheter track is occluded and the catheter is removed. The patient is observed for one hour in the Angiography Suite before returning to the Transplant Unit.

Figure 4. Islet Transplant.



From: http://en.wikipedia.org/wiki/File:Islet_transplantation_PLoS_Medicine.jpg

2.3 Post-Transplant Immunosuppression (Post Islet Transfusion)

2.3.1 Islet Recipients with No Previous Kidney Transplant

At the time of the first transplant, Pancreatic Islet transplant recipients receive induction immunosuppression with anti-thymocyte globulin (ATG, Thymoglobulin®), followed by maintenance immunosuppression with mycophenolate mofetil and tacrolimus. For a second or greater transplant, basiliximab is used as the induction agent. This approach is subject to review and per practice results from international studies and may be modified as new information is acquired.

Also refer to current BCT Clinical Guidelines for Transplant Medications

First Transplant Protocol:

- Anti-thymocyte globulin at 1 mg/kg/day IV (over 12 hours for the first dose and then over 6 to 8 hours for subsequent doses as tolerated) via central line for 4 days (A total of 5 daily doses). This is started as soon as possible once patient arrives on the Transplant Unit after islet transfusion.
- Pre-medication for anti-thymocyte globulin to be given ½ hour before start of the anti-thymocyte infusion for first post transplant dose only (subsequent premedication will be given only if deemed necessary by Transplant Physicians):
  - Methylprednisolone 125 mg IV
  - Acetaminophen 650 mg PO
  - Diphenhydramine 50 mg IV
- Tacrolimus at 0.05 mg/kg/dose PO every 12 hours (at 0800 and 2000 hours)
- Mycophenolate Mofetil 1 gram PO every 12 hours (at 0800 and 2000 hours)

Second or Greater Transplant Protocol:

- Basiliximab 20 mg IV to be given stat on return to transplant unit after islet cell transfusion. Second basiliximab 20 mg dose to be given on post transplant day 4
- Tacrolimus (dose is based on previous dose patient was on mg PO every 12 hours (at 0800 and 2000 hours)
- Mycophenolate mofetil 1 gram PO every 12 hours (at 0800 and 2000 hours)

CMV Prophylaxis

For CMV positive patients receiving anti-thymocyte globulin:

- Valganciclovir 900 mg PO daily for 2 months. Adjust valganciclovir dose based on renal function.
- CMV PCR with each bloodwork for 6 months

For CMV mismatch patients (regardless of induction therapy):

- Valganciclovir 900mg PO daily for 4 months. Adjust valganciclovir dose based on renal function.
- CMV PCR with each bloodwork for 8 months.

Other Medications

- Dalteparin 5,000 units subcutaneously daily for 7 days
- EC ASA 80 mg PO daily for 14 days
- Co-trimoxazole single strength one tablet PO daily for 6 months
- Dextran 40 10% Solution in Normal Saline (NS) 500ml IV over 8 to 12 hours on alternative days for 3 doses.

Glucose Monitoring

- The endocrinology service and/or transplant team will be responsible for the management of the patient's glucose / insulin post-transplant.

Routine Post-operative Regimen

During the early post-op period, the patient remains under close observation:

- NPO for 4 hours post transplant, then diabetic diet
- Bed rest for 4 hours, then activity as tolerated
- Vital signs: Every 15 mins for 4 hrs, every hour for 4 hrs, then 4 times daily
- Check catheter site for bleeding every hour for 4 hours
- IV D5 ½ NS at 100 mL/hr; discontinue when taking PO.

Investigations:

Bloodwork to be done at 1800 hours on day of transplant and then daily at 7 am:

- CBC and manual diff, INR, PTT
- Electrolytes, creatinine, urea, glucose
- AST, ALT, alkaline phosphatase, total bilirubin , direct bilirubin, GGT
- C-peptide level

Additional daily bloodwork:

- Calcium, phosphate, magnesium, albumin, total protein, amylase

Anti-thymocyte globulin (ATG, Thymoglobulin®) monitoring:

- T-cell subset count on post-transplant day 2

Tacrolimus monitoring:

- Tacrolimus trough level daily starting day 2: target 5 to 8 ng/mL for first month, then target 3 to 5 ng/mL after first month.
- Tacrolimus levels will be measured using Tandem Mass Spectrometry.

Ultrasound:

- Obtain ultrasound with Doppler of portal vein early am post transplant day 1.

2.3.2 Islet Recipients AFTER Kidney Transplant

Post-Transplant Immunosuppression

For First Transplant Procedure:

- A total of 5 daily doses of anti-thymocyte globulin (ATG, Thymoglobulin®) will be administered IV via a PICC line or CVC
- For the first dose, ATG 1.5 mg/kg/day IV will be given over eight to twelve hours, and started as soon as the patient returns to the Transplant Unit. For subsequent doses, ATG will be given over 6 to 8 hours as tolerated.
- Pre-medication for ATG (below) will be given ½ hour before start of infusion for the first two doses of ATG only; subsequent premedication will be given only if deemed necessary by the transplant physicians:
  - Methylprednisolone 125 mg IV
  - Acetaminophen 650 mg PO
  - Diphenhydramine 50 mg IV

- Mycophenolate mofetil doses are reduced by half (500 mg PO BID at 8 am and 8 pm) while on ATG, and resumed at full doses on completion of the ATG treatment
- Hold tacrolimus until the last day of ATG and then resumed at doses equivalent to 0.075 mg/kg/dose to achieve target tacrolimus trough levels of 8 to 10 ng/mL.
- If the patient has been receiving prednisone pre-islet transplant, this is continued as previously (except in the first two days post transplant where IV methylprednisolone (Solumedrol®) will be the corticosteroid)

For Second or Greater Transplant Protocol:

- Patients who receive a subsequent islet transplant will be given basiliximab 20 mg IV day 0 and day 4 instead of the ATG.
- Maintenance immunosuppression will consist of tacrolimus, with dose increased to 0.075 mg/kg/dose to achieve target drug levels of 8 to 10 ng/mL; mycophenolate mofetil 1 gram PO BID as tolerated; prednisone PO if the patient was on this drug prior to islet transplantation.
- If patient is on mycophenolate mofetil, tacrolimus, and prednisone for kidney transplant immunosuppression, during islet after kidney transplant, hold prednisone while on methylprednisolone. Once methylprednisolone is discontinued, restart prednisone as per islet transplant protocol.

Etanercept (Islet after Kidney)

The anti-TNF agent, Etanercept, will be given to all islet transplant recipients during the induction period, whether for initial or subsequent transplants.

- 50 mg IV one hour prior to transplant and 25 mg SC on days 3, 7 and 10 post-transplant.

2.3.2 Islet Recipients AFTER Kidney Transplant (Cont)

CMV Prophylaxis (Islet after Kidney)

Refer to current CMV orders

For CMV positive patients receiving anti-thymocyte globulin:

- Valganciclovir 900 mg PO daily for 2 months. Adjust valganciclovir dose based on renal function.
- CMV PCR will be performed with each bloodwork for 6 months.

For CMV mismatch patients (regardless of induction therapy):

- Valganciclovir 900mg PO daily for 4 months. Adjust valganciclovir dose based on renal function.
- CMV PCR with each bloodwork for 8 months.

Other Medications (Islet after Kidney)

Refer to current Physician Orders

- Dalteparin 5000 IU subcutaneously daily until hospital discharge
- EC ASA 80 mg PO daily
- Co-trimoxazole single strength one tablet PO daily for 6 months
- Dextran 40 10% Solution in Normal Saline (NS) 500ml IV over 8 to 12 hours on alternative days for 3 doses.

Glucose Monitoring (Islet after Kidney)

- The Transplant Team will be responsible for the management of the patient's glucose / insulin post-transplant via preprinted protocol.

Routine Post-operative Regimen (Islet after Kidney)

During the early post-op period, the patient remains under close observation:

- NPO for 4 hours post transplant, then diabetic diet
- Bed rest for 4 hours, then activity as tolerated
- Vital signs: Every 15 mins for 4 hrs, every hour for 4 hrs, then 4 times a day.
- Check catheter site for bleeding every hour x 4 hours
- IV D5 ½ NS at 100 mL/hr; discontinue when taking PO.

Investigations:

Bloodwork to be done at 1800 hours on day of transplant and then daily at 7 am:

- CBC and manual diff, INR, PTT
- Electrolytes, creatinine, urea, glucose
- AST, ALT, alkaline phosphatase, total bilirubin, direct bilirubin, GGT
- C-peptide level

2.3.2 Islet Recipients AFTER Kidney Transplant (Cont)

Additional daily bloodwork:

- Calcium, phosphate, magnesium, albumin, total protein, amylase

Tacrolimus monitoring:

- Tacrolimus trough level starting day 7 and continued daily until target 8 to 10 ng/mL is achieved for the first month, then target 6 to 8 ng/mL for months 2 and 3, and 4 to 6 ng/mL thereafter.

Ultrasound:

- Obtain ultrasound with Doppler of portal vein early am post transplant day 1

2.4 Expected Length of Stay *(All patients: for either islet with no previous kidney transplant; or islet after kidney transplant)*

Patients will remain in hospital overnight on the day of transplant. Discharge is at the discretion of the medical team physician(s).

The remainder of the therapy and monitoring will continue on an out-patient basis.

3 Post-Transplant

3.1 Ambulatory Care Phase *(All patients: for either islet with no previous kidney transplant; or islet after kidney transplant)*

All patients will be followed in the Post Transplant Clinic at Vancouver General Hospital. The following summarizes the care provided following discharge from hospital.

For first 30 days following discharge:
Patients will return to clinic twice weekly (or as required) for:

- Assessment by Transplant Team
- Monitoring immunosuppression drugs, CMV antigenemia
- Administration of IV medications (as required)
- Monitoring of glucose control and adjustment of Insulin or oral hyper-glycemic agents (as required)

From 30 to 60 days following discharge:
Patients will return to clinic every 2 weeks (or as required**).**

After 60 days following discharge:
The interval between clinic visits will be increased at the discretion of the Medical Team.

3.2 Long Term Care

Long-term follow-up is decided by the Transplant Team and is based on patient condition.

3.3 Rejection

At present for pancreatic islet transplantation there is no strategy as yet to monitor for rejection. If rejection occurs it is usually recognized too late to intervene. Pancreatic ǂ islet transplant patients are therefore put on a higher level of immunosuppression initially to decrease the risk of rejection. Signs of rejection would most likely be an increase in blood glucose readings. This underscores the rationale for close blood glucose monitoring post transplant.

3.4 Infection

A possible side effect of immunosuppression is an increase in infections. Early diagnosis and appropriate treatment are essential. Patients are counseled on the signs of infection and how to prevent them. Common infections and the medications that prevent/treat them are:

- *Candida*, oral thrush - treated with nystatin or fluconazole (anti-fungals)
- *Herpes simplex* virus - treated with acyclovir (anti-viral)
- *Cytomegalovirus*, CMV - treated with ganciclovir and valganciclovir
- *Pneumocystis carinii* pneumonia, PCP - treated with cotrimoxazole or pentamidine (anti-bacterial)

3.5 Prophylactic Dental Coverage

Refer to current BCT Clinical Guidelines for Transplant Medications and Clinical Guidelines for Kidney Transplantation

3.6 Immunizations

The use of live vaccines is contraindicated in immunosuppressed patients. These include:

- Oral polio
- Measles
- Rubella
- BCG
- Smallpox
- Yellow fever

Flu vaccine is not contraindicated in transplant patients. However, patients may not obtain any benefit because immunosuppression may prevent the production of sufficient antibodies. Patients requesting the flu vaccine should be referred to their family physician.

Refer to current version of: BCCDC Communicable Disease Control, Immunization Program, Section III - Immunization of Special Populations

3.7 Exceptional Distribution – Follow-up of Recipients

Human cells, tissues and organs that are to be used in transplantation are regulated under Health Canada's Safety of Human Cells, Tissues and Organs For Transplantation Regulations (CTO Regulations), Dec 2007. The CTO Regulations apply to all individuals and establishments in Canada that handle, process, distribute or import human organs or minimally manipulated cells and tissues for homologous use in transplantation in another individual.

The purpose of the CTO Regulations is to minimize the potential health risks to Canadian recipients of human CTO by addressing the safety in the processing and handling of these products. Source establishments must determine that donors are not unsuitable to donate on the basis of the contraindications or exclusion criteria set out in the Regulations.

However, it is recognized that in exceptional circumstances and compassionate reasons, islets may be transplanted even when there may be a contraindication during donor assessment (e.g., incomplete donor screening). The process is documented on an Exceptional Distribution Form (Appendix D) by the BC Transplant Organ Donation Coordinator. The transplanting physician must authorize the exceptional distribution including obtaining informed consent of the recipient. Copies of the exceptional distribution form are to be included in the recipient chart.

It is important that in all cases, appropriate follow-up of recipients is performed by the post-transplant medical care team. Each exceptional distribution is to be reviewed and assessed by the team for any follow-up treatment and diagnosis.

Risk for Viral Mediated Disease Transmission

In Exceptional Distribution cases involving risk for viral mediated disease transmission, the following will be faxed from BC Transplant Quality Assurance to the transplant hospital or outpatient location:

1) *Fax Coversheet - Required Medical Follow-up for Transplant Recipient(s) (See Appendix D)*
2) *Copy of the Exceptional Distribution Form*
3) *Reference - Recommended Follow-up Testing for Recipients Transplanted under Risk for Viral Mediated Disease Transmission*

The Post Transplant Coordinator at VGH will ensure the above documents are reviewed by the post-transplant medical care team and the recommended follow-up is performed at the required intervals.

APPENDICES

List of Appendices	
Appendix A.	**Islet Transplant Referral Form & Checklist for Accompanying Information**
Appendix B.	**Pancreatic Islet Transplant Activation Form**
Appendix C.	**Welcome to the Pancreatic Islet Transplant Program**
Appendix D.	**Notice of Exceptional Distribution and Required Follow-up** **1) Fax Coversheet** **2) Exceptional Distribution Form** **3) Recommended Follow-up Testing for Recipients Transplanted under Risk for Viral Mediated Disease Transmission**

**Forms/orders may be revised periodically. Ensure you are using the most current version available.

Appendix A
ISLET TRANSPLANT REFERRAL FORM

BC TRANSPLANT — Vancouver Coastal Health — Promoting wellness. Ensuring care.

ISLET TRANSPLANT REFERRAL FORM

PCIS LABEL

Referral Date: _____

Last name: _____ First name: _____

Sex: ☐ male ☐ female Race: _____

PHN: _____ DOB _____

Address: _____ Postal Code: _____

Home phone: _____ Cell phone: _____

Contact name: _____ Relationship: _____ Phone: _____

Referring Endocrinologist: _____ Phone: _____ Fax: _____

General Practitioner: _____ Phone: _____ Fax: _____

Address: _____

Other Specialists involved with care: _____

Age Diabetes Diagnosed _____ Insulin Type & Doses _____

Previous Kidney Transplant? ☐ No ☐ Yes Date: _____ Donor-Living _____ Deceased _____

Height: _____ Weight: _____ ABO: _____

Does the patient speak English? ☐ Yes ☐ No, if no what language? _____

Special needs? _____

Please Mail to: (✓ check one)

Clinical Coordinator, Islet Cell Program
Pre-Assessment Transplant Clinic
Gordon and Leslie Diamond Health Centre
5th Floor, 2775 Laurel Street
Vancouver, BC V5Z 1M9
Tel: 604-875-5182
Fax: 604-875-5236

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Please complete other side

BC TRANSPLANT Vancouver Coastal Health

Promoting wellness. Ensuring care.

CHECKLIST FOR ACCOMPANYING INFORMATION

Patient Name: _____ **DOB:** _____

A) Please include:
(Patient Investigation to be completed by the referring doctor prior to referral to BC Transplant)

☐ **Information regarding medical history**

☐ **Consult notes (ophthalmology, neurology, etc.)**

☐ **Lab work including:**

- **Chemistry:** Na, K. Cl, bicarb, Albumin, Total protein, Ca, MG, PO4, Uric acid, CK, Creatinine, Urea, HbA1C, GGT, AST, ALT, Alk phos, Amylase, Total Bili, Direct Bili, LDH, fasting blood glucose, homocysteine.
- **Hematology:** CBC and Differential, Platelets, INR, PTT
- **Iron Studies:** total iron, ferritin, TIBC, iron saturation
- **Urine Studies:** 2 X 24 hour urine for creatinine clearance and microalbuminuria and ratio, urine R&M
- **Lipid Studies:** Total Cholesterol, LDL, HDL, and Triglycerides
- **C-Peptide**
- **TSH**

B)

☐ **Blood GFR**

☐ **Regular Mammogram/PAP/Prostate/Testicular exam?**

☐ **Dental information; i.e. regular exams? concerns?**

☐ **Psychosocial concerns and notes**

☐ **Other relevant test results such as cardiac studies**

Appendix B

Pancreatic Islet Transplant Activation Form

BC TRANSPLANT | Vancouver Coastal Health

Promoting wellness. Ensuring care.

PANCREATIC ISLET TRANSPLANT ACTIVATION

PCIS LABEL

Patient Name: _____

DOB: _____

PHN: _____

Blood Group: _____

CMV Status: _____

Date of activation: _____

Considerations: _____

_____

_____

_____

Signatures:

_____

Dr. M. Meloche

_____

Dr. R. J. Shapiro

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Appendix C

WELCOME TO THE PANCREATIC ISLET TRANSPLANT PROGRAM

Date

Dear <patient>,

You have been approved and activated to the Pancreatic Islet Transplant Program waiting list. As you are aware, the waiting list is randomized and we therefore cannot indicate how long you will be waiting for your Pancreatic Islet Transplant, but we estimate it to be between 3 weeks and 3 years.

While you are waiting, it is important to keep me up-to-date on address changes, additional phone numbers where I can reach you, and any changes in your health.

If you are going to be away from home on vacation etc, please let me know how I can contact you. *This is very important because if we are unable to reach you within a few hours we will need to consider someone else for the transplant.* You will have approximately 12 hours to get to Vancouver General Hospital (VGH). If you are unable to make it within that time, you will just be placed "on hold" until you arrive back home from vacation.

We require monthly blood-work. The accompanying requisition and instruction sheet needs to be taken to your laboratory to be maintained as a standing order. This specimen will be used for cross matching with potential donors during the month. If we do not have a specimen, we cannot test you and therefore you will not be eligible for transplant that month.

When you receive the call for transplant

A member of the transplant team will contact you. Please inform them of any medical problems and general state of health. It is a good idea to have all your travel plans and other family arrangements made before this call.

You will be informed of when you need to arrive at VGH admitting, Jim Pattison Pavillion the entrance is located on 12th Avenue. For your first islet transplant, you may be admitted the day before the procedure. For second or greater transplants, your admission will be at 06:30 at Emergency admitting (in the emergency department), VGH; the entrance is located on 10th Avenue. A map is included in this package.

Also included in this package are your consent for the procedure of Pancreatic Islet Transplant and a form for your contact information. Please sign these forms and return them to me in the envelope included.

A contact sheet is also included; please complete it and send it back with your consent.

If you have any questions, please do not hesitate to call me.

Sincerely,

Clinical Coordinator
Pancreatic Islet Transplant Program

Appendix D

BC Transplant (BCT)
3rd Floor, West Tower, 555 West 12th Ave.
Vancouver, BC
CANADA V5Z 3X7

Telephone (604) 877-2240
Toll Free 1-800-663-6189
FAX (604) 604-877-2111

FAX COVERSHEET
Required Medical Follow-Up
FOR TRANSPLANT RECIPIENT(S)

FROM:_____ Date:_____

Number of Pages _____ [Attach copy of Exceptional Distribution]
(including this one)

☐	SPH Heart Clinic	Fax: 604-806-8763	Attention:
☐	SPH Kidney Clinic	Fax: 604-806-8076	Attention:
☐	BCCH	Fax: 604-875-2943	Attention:
☐	VGH SOT Clinic	Fax: 604-875-4088	Attention:
☐	OTHER	Fax:	Attention:

Please note that the organ recipient listed below requires Medical follow-up as a result of Exceptional Distribution of Organs:

Date of Transplant:_____

Name of Recipient: _____Organ transplanted:_____

A copy of the Exceptional Distribution is attached.

PLEASE INFORM THE RECIPIENT'S MEDICAL PHYSICIAN IMMEDIATELY. If further information is required, please do not hesitate to contact our department.

BC Transplant Exceptional Distribution Form

PART A

Source Establishment: ❑ BC Transplant ❑ Other (Provide Name)_____

Donor ID No.: _____ Date of Distribution of Organ: _____

Receiving Program or Transplant Centre: ❑ VGH ❑ SPH ❑ BCCH ❑ Ike Barber Lab ❑ Other_____

Name of Organ:
❑ Heart ❑ Lung (Dbl) ❑ Lung (Rt) ❑ Lung (Lt) ❑ Liver ❑ Pancreas ❑ Pancreas for Islets
❑ Kidney (Rt) ❑ Kidney (Lt) ❑ Adjunct Vessels Other Describe (e.g. small bowel):_____

Reason for Exceptional Distribution (include all tests not completed or conditions not met and risk of disease transmission). Refer to back of form:
(Check if applicable) ❑ RPR not available
Completed by: Date:

PART B

TRANSPLANTING PHYSICIAN / SURGEON

The justification for acceptance is for compassionate reasons related to the interests of the recipient, including medical emergency and an organ determined safe is not immediately available.

I (or my authorized designate) have had a conversation with the recipient and/or next of kin/substitute decision maker in which I explained the reason(s) for Exceptional Distribution as defined above, and the risks associated with this reason(s). I have obtained informed consent from the recipient and/or next of kin/substitute decision maker and I authorize the acceptance of the organ(s) described above for transplant.

Name	Signature	Date	Time

THIS MUST BE FULLY COMPLETED WITH DATE AND TIME

Return completed signed copy to BCT Quality Assurance. FAX 604-877-2111

Doc.: RQA.04.016 Rev: 03 Eff Date: 15-Feb-2013 Ref Doc: RQA.02.018 CO#: 2013-344 Page 1 of 1

Copy 1 (white) - BCT Donor Chart Copy 2 (yellow) - QA Copy 3 (pink) - Sign and Return with Cooler Copy 4 (goldenrod) - Recipient Chart

Recommended Follow-up Testing for Recipients Transplanted under Risk for Viral Mediated Disease Transmission

NOTICE TO TRANSPLANT RECIPIENT MEDICAL TEAM:

The following protocol has been approved by the BC Transplant Medical Advisory Committee (MAC) as a course of action for follow-up of recipients transplanted at risk for HIV and/or Hepatitis:

IT IS RECOMMENDED THAT RECIPIENTS ARE RETESTED FOR HIV, HEPATITIS B AND HEPATITIS C at:

- 4 weeks
- 8 weeks
- 6 months
- 1 year

Recommended Test Methods**:
HIV - Conventional antibody testing
HBV - HBsAg and HBcIgM
HCV - Conventional antibody testing

***NOTE: If there is clinical or epidemiological evidence to suggest a patient may have become infected with any of these viruses and antibody tests are negative, then PCR testing should be discussed with the medical team.*