ADULT TO ADULT LIVING DONOR LIVER TRANSPLANTATION COHORT STUDY

RETROSPECTIVE STUDY MANUAL OF OPERATIONS

Reprinted for the Study Coordinator Refresher Training Course
June 26, 2008 - Ann Arbor, MI

RETRO MANUAL OF OPERATIONS

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The Adult to Adult Living Donor Liver Transplant Cohort Study Group (A2ALL)
Website & Access Instructions/Information

The University of Michigan is the Data Coordinating Center for this project, and we have developed a website at www.nih-a2all.org.

The front page is a public page with basic information about the study. On the left side, there is a log-on section that requires a username and password to access the private site. Your username is the first initial of your first name and your entire last name (example: Mary Smith is msmith). Your temporary password is sent to you in an automatically-generated email. You should change your password after your first logon.

The private site contains:

Study calendar: The calendar is for posting attendance information for the A2ALL Study Groups, Project Executive Committee, Steering Committee and Study Coordinator conference calls and meetings. Clicking on a specific day will provide dial-in information for the call.

Study Directory: The directory contains contact information for all of the study participants (including administrative assistant contact information).

Workgroups and members list: Here you may view workgroup membership by person.

Individual Study Group Links: Each study group has a tab on the website which houses agendas, minutes and meeting documents for upcoming and prior conference calls.

Master Documents section: Contains A2ALL documents being worked on and updated by the various work groups.

Search documents tab: You may type in a keyword to locate a document.

BioDBX: This is where you will log on to enter A2ALL study data.

A2ALL: Adult-to-Adult Living Donor Liver Transplant Cohort Study

Retrospective Study Protocol Number A2ALL-Retro-01

Version 2.0

Approval Date: February 20, 2003
Amended October 11, 2004

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1. Introduction

Adult to adult living donor liver transplantation (LDLT) is a relatively new procedure increasingly used at major transplantation centers. Too few cases are performed at any one center and approaches to the patient and donor are too diverse across centers to provide reliable and generalizable information on donor and recipient outcomes from individual centers. Therefore, the National Institutes of Health has organized a network of nine leading liver transplantation centers and a data coordinating center (DCC) to accrue and follow sufficient numbers of patients being considered for and undergoing LDLT to provide generalizable results from adequately powered studies. This network has established the Adult to Adult Living Donor Liver Transplantation Cohort Study (A2ALL) that will conduct both retrospective and prospective studies of LDLT.

2. Background/Significance

Over the last 20 years liver transplantation has become the standard of care and the only cure for end stage liver disease. Its success has led to over 4,000 transplants performed yearly. But there are at least 17,000 patients on the transplantation list awaiting cadaveric liver donation. As the waiting list has expanded, waiting time has also grown. As a result, patient mortality has increased while awaiting transplantation, and patients are often critically ill by the time of transplantation. Among possible remedies, living donor transplantation has become widely accepted for pediatric transplantation. Adult-to-adult LDLT is a more challenging procedure and may be associated with greater risk to the donor because of the larger portion of liver that is required. Right lobe adult-to-adult LDLT is a recently developed procedure, but nearly a thousand have already been performed in the United States. Although still a small number relative to the several thousand adult cadaveric liver transplants performed annually, LDLT has the potential for changing the face of liver transplantation. Not only does LDLT avoid the lengthening waiting period for a cadaveric transplant, it greatly reduces the ischemic period of the transplanted organ, allows more time for evaluation of the donor, and changes the operation from an emergency into a scheduled procedure. The major disadvantage of LDLT is that it is a difficult and potentially fatal operation for the donor. It also provides the recipient with a smaller portion of liver than would have been received with cadaveric transplantation.

The research objectives of the A2ALL Study concern factors that influence the outcomes of adult-to-adult LDLT. Recruited into this longitudinal cohort study will be adult patients and potential donors being considered for LDLT. Recipients and their donors will be followed for sufficient time to determine outcomes related to LDLT. These outcomes will be compared with those of transplant candidates who are evaluated for but do not receive LDLT. The primary objective concerns comparison of morbidity and mortality of patients who receive LDLT with a group or groups of patients with similar illnesses and prognoses. It is also important to compare the outcomes after LDLT to those after cadaveric transplantation. Transplant physicians need this information on outcomes to advise patients and prospective donors. Therefore, sufficient patient and donor pairs will be recruited to determine whether recipients of LDLT have substantially different survival than non-LDLT recipients. A large number of donors and recipients

from several geographically distributed institutions will be necessary to reliably determine if outcomes are different with the two approaches.

These issues are best addressed through prospective data collection. But, the main outcomes of the A2ALL prospective data collection will not be available for at least 5 years. Therefore, to gain initial insights into outcomes associated with these procedures, a retrospective cohort or look back study has been designed to compare the outcomes of LDLT and cadaveric liver transplants and the outcomes for living liver donors beginning in 1998 at the nine participating transplant centers of the A2ALL study. In order to be conducted rapidly and efficiently, this study will rely exclusively on existing medical records and patient materials.

3. Study Objectives/Specific Aims

3.1. Overall Aim of the Retrospective Cohort Study

The primary study objective is to determine whether the *decision* to undergo LDLT is beneficial for the patients who choose LDLT. The principal hypothesis is that receipt of a living liver allograft leads to better long term outcomes for liver transplant candidates than *pursuit* of cadaveric transplant. This is a study of the decision to perform LDLT. Several different patient outcomes will be considered.

3.2. Comparison of mortality between LDLT and non-LDLT recipients

3.2.1. Primary Aim

To compare the survival distribution from time of identification of a potential living donor between those receiving an LDLT and those not receiving one.

3.2.2. Secondary Aims

To compare the survival of LDLT vs. cadaveric recipients from time of transplant.

To compare rejection episodes between LDLT and cadaveric transplant recipients.

1. To determine the incidence and severity of rejection episodes occurring within one year after transplantation in recipients undergoing LDLT.
2. To determine the incidence of steroid resistant rejection
3. To determine the incidence of recurrent rejection occurring within 1 year after transplantation

3.3. Retrospective Hepatitis C Virus (HCV) Study

3.3.1. Primary Aim

To determine if recurrent HCV disease at 1 yr (± 3 months), as observed histologically, is more severe in patients undergoing LDLT as compared to cadaveric transplant.

3.3.2. Secondary Aims

To compare the rate of fibrosis progression (comparison of 1 yr. and most recent biopsy) in LDLT and cadaveric transplant

To determine if cholestatic hepatitis in transplanted patients with HCV occurs at a higher rate following LDLT as compared to cadaveric transplant controls.

To determine if rejection requiring treatment occurs at a higher rate in HCV patients who undergo LDLT as compared to cadaveric transplant and to correlate this frequency of treatment of rejection to aggressive recurrence of HCV as defined histologically.

To compare rate of graft loss secondary to HCV between LDLT recipients and cadaveric recipients.

3.4. Retrospective Hepatocellular Carcinoma (HCC) Study

3.4.1. Primary Aim

To compare the outcomes for patients with HCC from the time of LDLT donor evaluation for those receiving LDLT versus those not receiving LDLT. Outcomes considered will include survival, hospitalizations, ablative treatments, and HCC status/recurrence.

3.4.2. Secondary Aim

To compare the demographic characteristics, HCC stage, and outcome (patient survival and cancer-free patient survival) in patients receiving LDLT or cadaveric transplant with HCC as either a primary or secondary pre-transplant diagnosis (excluding incidental tumors discovered at the time of transplant).

3.5. SRTR Data Validation Study

3.5.1. Primary Aim

To estimate the completeness and correctness of selected data elements submitted by the transplant centers to the Organ Procurement and Transplantation Network (OPTN) and subsequently transmitted to the Scientific Registry of Transplant Recipients (SRTR).

3.5.2. Secondary Aims

To ascertain which data elements collected via the OPTN data collection process can be reliably employed for use in the prospective A2ALL Cohort Study.

To provide feedback to the SRTR and OPTN on the accuracy and completeness of selected data elements.

3.6. Retrospective Post-surgical Complications Study

3.6.1. Primary Aim

To determine the rate of the major donor post-operative complications associated with planned right lobe liver donation

To compare the major recipient post-operative complications after LDLT versus cadaveric transplant.

3.7. Retrospective Resource Utilization Study

3.7.1. Primary Aim

To compare the resource utilization for patients who proceed to LDLT versus those for whom living donation does not occur and thus proceed toward cadaveric transplant.

4. Investigational Plan

4.1. Overall Study Design

Most of the specific aims require LDLT recipients and control patients who did not undergo LDLT. However, the identification of these controls and study start time (time 0) for following LDLT patients and controls will differ for the various objectives. All, or nearly all, of the LDLT recipients will be included in all analyses, which will simplify chart review. Many of the control patients will also be included in several analyses. LDLT donors will be evaluated for surgical complications.

For the primary survival and resource utilization objectives, the study entry point is at initial evaluation of a potential living donor that includes history and physical examination at the transplant center. The overall design of the retrospective cohort study is predicated on this definition as the starting point for inclusion in the cohort. In the primary analysis (see below), the mortality of LDLT patients will be compared to mortality of patients who have not yet had LDLT, regardless of subsequent events (cadaveric transplant, death, or removal from waitlist for any other reason). This cohort will include all those evaluated for LDLT transplants from 1/1/98 until 2/28/03. Among the 9 transplant centers in the A2ALL project, approximately 40% of individuals who had a potential living donor identified went on to undergo LDLT, leaving 60% as controls (see Feasibility Study report [Appendix A]). Based on this report, we estimate that approximately 800 patients were evaluated for LDLT at the 9 A2ALL transplant centers, of which approximately 300 subsequently received LDLT and 500 did not. A subset of this cohort with diagnoses of HCC at entry will also be used.

Other objectives regarding the post-transplant experience will compare LDLT to contemporaneous cadaveric transplants beginning at the time of transplantation. The analysis will control for center and date of transplantation as well as age, sex, disease (HCC, cholestatic, HCV/HBV, alcoholic, other), and severity of illness (MELD score, OPTN/UNOS status, CTP score). This comparison would involve approximately 300

LDLT recipients and approximately 250 cadaveric liver recipients. A subset of this cohort with diagnoses of HCV at entry will also be used.

Living donor liver transplantation presents unique immunological setting that is determined by three major variables that are different from the cadaveric setting, with the potential to impact on short and long term graft and patient survival. First, regeneration may be associated with different pattern of lymphocyte trafficking in and out the graft resulting in a differential repopulation of the liver with donor cells, and unknown effects on the extent of peripheral chimerism. Second, transplantation of a lobe from a living donor is done under conditions allowing extremely short cold ischemic time (60 vs. 500 minutes), a variable that may affect the severity of the inflammatory and immune response. Finally, it is estimated that 40% of LDLT are done in between genetically related individuals, resulting in a potentially more favorable HLA matching.

Previous single center studies have suggested a reduced rate of rejection after adult to adult LDLT. These observations should be validated by a carefully designed retrospective analysis of rejection rate and severity in AALDLT recipients. The clinical findings will determine the opportunities for appropriate clinical modifications in the immunosuppression protocol for the prospective study, aiming at better outcomes for graft rejection and recurrent disease. Moreover, they will set the stage for hypothesis-driven experimental studies, aiming to determine pattern of immune response and the potential development of favorable induction of tolerance.

For certain endpoints, supplementation of cadaveric controls above those identified in the retrospective cohort component of the study may be necessary. Augmentation with contemporaneous cadaveric controls would most likely occur for the first one to two years of a program's experience. If additional patients are required, they will be identified using SRTR data, frequency matching to the characteristics of recipients undergoing LDLT. Potentially, a few LDLT patients could be included in this group but excluded from the primary objective analysis. This situation would arise if a donor evaluation occurred in 1997, resulting in LDLT in early 1998, although this comprises a very small number of patients. We anticipate supplementation with no more than 100 to 200 transplant recipients.

The final cohort will include the LDLT donors (approximately 300).

4.2. Comparison of mortality between LDLT and non-LDLT recipients

4.2.1. Study Methods

The primary aim will use the cohort of subjects evaluated for LDLT. Survival from time of donor evaluation will be compared among those receiving and not receiving LDLT. In addition, we will compare both survival and rejection episodes for LDLT vs. cadaveric recipients from time of transplant.

Primary endpoint: Time of death or last known alive.

Secondary endpoint: Time from transplant to rejection episode, or last known time without rejection, incidence, number and severity of rejection and incidence of steroid-resistant rejection during the 1st post-transplant year.

4.2.2. Participant Selection

The cohort will include all of the following:
Potential recipient listed for liver transplantation

- age >= 18
- single organ

Potential donor evaluated with history and physical examination occurring between 1/1/1998 and the start date of the A2ALL-Cohort-01 Study enrollment. This date will be different for each clinical site and will be determined once site initiation is completed and the site is ready to begin enrollment of prospective subjects.

4.2.3. Data Elements

Two limitations of chart reviews must be kept in mind: Information may be missing, and information may be inaccurate. Because these problems can occur systematically, results can be biased. A2ALL will be circumspect about collecting information that is limited in either respect. Sample records will be examined for completeness and ease of obtaining information on all data elements before formal data collection begins.

a. At listing
Date of listing
DOB, sex, ethnicity (PHS categories)
Reasons for transplantation (list primary and secondary diseases)
MELD/UNOS status/CTP score at time of listing

b. Potential Donor
Date of each donor evaluation
Information on potential donor. Data collection on donors will largely be limited to clinically significant pre- and post-donation events and a small amount of operative information.
Donor outcome information
Reasons for not donating for those who do not donate

- Medical or psychological for donor
  - Medical condition (liver related vs. co-morbid medical conditions)
  - Anatomical
  - Size
  - Blood type
  - Psychological
- Donor declines/changes mind
- Recipient became too sick (or too well)
- Recipient received cadaveric transplant
- Other

Date of decision not to donate

c. Pre-transplant
Complications (treated ascites, treated SBP, variceal bleed, other GI bleeds requiring transfusion, hepatorenal, hepatopulmonary, treated encephalopathy, TIPS, portopulmonary hypertension, bony fracture [yes or no for each])
SBP Prophylaxis (yes/no)
Antiviral therapy (specific to HBV and HCV)
Changes in MELD, CTP, OPTN/UNOS status
Hospitalization admission and discharge date
Days in ICU
Death
Dates for each of these

d. Transplantation and beyond
Date of transplant
Selected intra-operative data
Hospitalization dates
Days in ICU
Retransplantation
Baseline immunosuppression regimen (tacrolimus, cyclosporine, or non-calcineurin antagonist based); antibody induction (yes/no)
Treated rejection episodes within one year of transplant:

1. Date of rejection (treated rejection episodes separated by less than 22 days will be considered the same event for analysis purposes).
2. Liver biopsy (when performed): Acute rejection severity as recorded in the original pathology reading (mild, moderate, severe or undetermined)
3. Immunosuppression at transplant and at the initiation of anti-rejection therapy
4. Drugs used to treat rejection

4.2.4. Sample Size and Power Calculations

We will compare the survival experience between those receiving a living donor liver transplant (LDLT) and those considered for an LDLT but not receiving one. Although the analysis will involve a fairly complex method of matching LDLT recipients with sets of non-recipients, for the purpose of power calculations, we will assume a much simpler 2-group design. We anticipate having at least 300 LDLT recipients and 500 non-recipients. Power calculations are based on the (two-sided) logrank test, an exponential survival distribution, and alpha=0.05. Assuming a one-year survival probability of 0.875 in the LDLT group, we have 82% power to detect as significant a survival probability among non-recipients as high as 0.83 or as low as 0.91, and 93% power to detect a survival probability among non-recipients as high as 0.82 or as low as 0.92.

For a comparison of rejection probabilities in the first year after transplant between LDLT (n=300) and cadaveric (n=250) transplants, we assume a two-sided test of binomial proportions with alpha=0.05. We also assume that approximately 32% of cadaveric transplants experienced a rejection episode. We will have 44% power to detect

a difference between LDLT and cadaveric transplants if the LDLT proportion is 25%, and 83% power if the LDLT proportion is only 21%.

4.2.5. Statistical Analysis

A comparison of survival between LDLT recipients and those evaluated for LDLT but not receiving a living donor organ will be made. An initial, approximate analysis comparing these groups will use Cox regression, with the time axis starting at time of donor evaluation, a time-dependent covariate for LDLT transplantation, and covariate adjustment for age, gender, race, calendar year of initial evaluation, liver disease etiology and severity, comorbidities and other variables. This analysis assumes that most candidates evaluated for LDLT either receive the transplant or do not receive it due to problems with the donor. In particular, it assumes that non-progression to LDLT due to cadaveric transplantation or because the recipient becomes too sick to transplant is rare. These assumptions can be evaluated when the data are available.

A second, more difficult but preferred analysis will be performed to compare survival from the time of LDLT surgery among LDLT recipients to a set of controls who were evaluated for LDLT, and were alive and eligible for transplant at the same time following donor evaluation as the LDLT patient was when they received their transplant. This analysis will involve a different set of controls for each patient, with many control patients re-used in several control sets. A modified Cox regression will be performed, with statistical adjustment for the re-use of controls. In both Cox analyses, variables will be checked to ensure that the proportional hazards assumption is met. If non-proportional hazards are detected, particularly for the LDLT effect, they will be modeled using time-dependent covariates. Interactions between covariates and the LDLT effect will be tested.

Survival from date of surgery for LDLT versus cadaveric transplant will also be compared using Cox regression, adjusted for prognostic variables. The distributions of time from transplant to rejection episode between LDLT and cadaveric transplant will be similarly compared.

We will also analyze the incidence, timing, and diagnosis (biopsy-proven or not) of clinically evident liver transplant rejection requiring treatment. Analyses of rejection will include subsets restricted to biopsy-proven and steroid-resistant rejection episodes.

4.3. Study of Hepatitis C Virus Infection

4.3.1. Study Methods

LDLT recipients transplanted for HCV will be compared to an approximately equal number of contemporaneous cadaveric controls selected from SRTR based on a diagnosis of HCV. If SRTR data are not complete for HCV identification, identification of HCV patients at the facility level may be required.

(Note: Post-transplant biopsies will be re-read by the local pathologist for grade, stage, and other characteristics of recurrent HCV. The biopsy performed closest to the one-year anniversary of transplant (+/- 3 months) will be employed for histologic scoring)

Primary end-point

a) Severity of disease based upon Knodell (necroinflammatory) and Ishak (fibrosis) scores on liver biopsy at 1 year (± 3 months) post-transplant in LDLT and cadaveric transplant.

Secondary end-points

a) Rate of fibrosis progression (comparison of 0, 1 year and most recent biopsy [the latter must be a minimum of 12 months after the 1-year biopsy] in LDLT and cadaveric transplants)
b) Proportion with cholestatic hepatitis
c) Proportion with treated acute rejection episodes
d) Graft loss due to recurrent hepatitis C

4.3.2. Participant Selection

All right lobe LDLT patients age >= 18 with documented positive HCV RNA prior to transplantation whose donors were evaluated between 1/1/1998 and the start date of enrollment into the A2ALL-Cohort-01 Study, and excluding those receiving anti-HCV positive or anti-HB_c positive organ. Cadaveric transplant controls transplanted for hepatitis C will be identified from cadaveric transplant controls in the retrospective study. Additional HCV-infected cadaveric transplant recipients will be identified by SRTR if there are insufficient matched controls in the retrospective study population. The analysis will adjust for center and time of transplant (both calendar time and time from donor identification).

Inclusion criteria

a) LDLT patients and cadaveric transplant patients with HCV
b) HCV RNA positive (within 12 months if no antiviral therapy or if HCV RNA positive post-transplant)

Exclusion criteria (cases and controls)

Anti-HCV positive controls who received anti-HBc positive or anti-HCV positive organs. Patients who are HCV RNA negative at last assessment prior to the time of transplant

Controls will be selected as above.

4.3.3. Data Elements

Verification of diagnosis with report of positive HCV RNA either pre- or post-transplant. Identification of anti-HB_c and anti-HCV status for both donor and recipient.

Histology 1 year post-transplant (± 3 mos), at start of antiviral therapy (if on treatment), and at last histological follow-up.

Data elements (donor and recipient) that will be collected for the retrospective study, plus the following:

Pre-transplant:

- HCV RNA level pre-transplant (within 12 months of transplant and in whatever units available – IU/mL preferred).
- HCV genotype
- History of antiviral therapy for hepatitis C prior to transplant (start and stop dates, specific therapy used, treatment response [ETR, SVR])
- HBV markers in recipient
- Graft size
- Donor age, BMI, steatosis, DM

Post-transplant (immunosuppressive therapy, treatment of rejection and other data collected as part of retrospective study)
HCV RNA levels at 1 year ± 3 months, at time of onset of cholestatic hepatitis, at time of re-transplant)

ALT levels (liver panel) within one month of transplant and at 1,3,6,9 and 12 months post transplant.
Antiviral treatment (start and stop dates, specific drugs and doses used and response [ETR, SVR])

Pre-transplant and post transplant treatment in both groups

HLA matching with donor

Pathology interpretation: Re-review by local pathologist and scoring using Knodell (necroinflammatory) and Ishak (fibrosis) scores.

Working definition of cholestatic hepatitis:

1. Bilirubin ≥4 mg/dl x 2 wks minimum, at least 8 weeks post-transplant, PLUS .
2. Pathology features of
   (i) cholestasis
   (ii) lobular or portal inflammation
   (iii) absence of features of acute rejection and chronic rejection. PLUS
3. Absence of the following:
   - hepatic artery thrombosis
   - biliary stricture
   - sepsis

4.3.4. Sample Size and Power Calculations

Primary endpoint: Comparison of Knodell (necroinflammatory) and Ishak (fibrosis) scores in LDLT or cadaveric transplant at 1 year post-transplant. Predictors of disease severity will be investigated using ordinal logistic regression analysis. We anticipate having at least 300 LDLT recipients and 250 cadaveric recipients, but only about 1/3 of these will have HCV prior to transplant. We assume sample sizes of 100 LDLT and 83 cadaveric recipients with prior HCV. Because sample size calculations for ordinal logistic regression are difficult, we base power calculations on a two-sample t-test (2-sided, alpha=0.05). For fibrosis score (0 to 6) as an outcome variable, we have 91% power to detect a difference of 0.5 in fibrosis score between LDLT and cadaveric recipients, assuming a standard deviation of 1.0.

Secondary endpoints: To compare rate of fibrosis in LDLT and cadaveric transplants (use last available biopsy). All biopsies scored for fibrosis using Ishak (0-6) and rate is based on time between transplant and last available biopsy. For the presence of severe histologic fibrosis at 1 year, we expect approximately 10% overall with bridging fibrosis (Ishak>=3). We will have 83% power to detect proportions as different as 0.05 for cadaveric transplant and 0.20 for LDLT, based on a chi-square test of equality of proportions with alpha=0.05.

We consider the power for comparing time to graft loss due to HCV based on a logrank test with alpha=0.05. We will have 84% power to detect a difference in the probability of graft loss at one year as large as 15% for LDLT versus 5% for cadaveric recipients.

4.3.5. Statistical Analysis

Fibrosis score will be analyzed using both ordinal and ordinary regression analyses, with the LDLT versus cadaveric recipients as the variable of primary interest. Ordinal logistic regression will be used to accommodate the ordinal nature of the fibrosis scale. Ordinary regression analysis will supplement the ordinal analysis and will facilitate interpretation, but does assume that the ordinal scale has roughly equal increments.

The proportions of patients with fibrosing cholestatic hepatitis and treated acute rejection episodes will be analyzed using chi-square tests of equality of proportions between LDLT and cadaveric groups. Logistic regression will be used to compare LDLT versus cadaveric transplants, adjusted for other covariates. Finally, time to graft loss will be analyzed using Cox regression, again comparing LDLT versus cadaveric recipients and adjusting for other prognostic factors. Graft loss or death due to causes other than HCV will be censored.

4.4. Study of Hepatocellular Carcinoma

4.4.1. Study Methods

LDLT recipients transplanted for HCC will be compared to HCC patients who had a donor evaluated for possible LDLT but who did not receive a LDLT. The analysis will adjust for cirrhosis etiology diagnosis, center, age, CTP/MELD score, use of ablation pretransplant, and pre transplant ablation method (i.e. chemoembolization, RFA, etc.). In

addition, a comparative analysis of LDLT and cadaveric transplant patients with HCC will be conducted.

4.4.2. Participant Selection

All right lobe LDLT patients age >= 18 whose donor was evaluated between January 1, 1998 and the start date of enrollment into the A2ALL-Cohort-01 Study at one of the A2ALL transplant centers, with patient diagnosis either primary or secondary of cirrhosis and HCC. Excluded subjects include any patient who was transplanted with a preoperative diagnosis of HCC and cirrhosis where no HCC was found at explant histology, and no prior ablation is recorded that may have caused complete necrosis of tumor leading to pathologic disappearance. For the comparative study of LDLT and cadaveric transplant recipients, no supplemental contemporaneous cadaveric controls will be used.

4.4.3. Data Elements

Maximum size and number by radiology pre-transplant and at transplant (explant)
Whether Milan criteria were met
Whether HCC was an incidental finding.
Date of diagnosis of disease recurrence post-transplant.
Number and type of HCC ablation procedures.

4.4.4. Sample Size and Power Calculations

We anticipate approximately 75 hepatocellular carcinomas among the ~300 LDLT cases, and approximately 125 among the ~500 non-LDLT cases who were also evaluated for LDLT. With 75 LDLT cases and 125 non-LDLT cases, we will have 90% power to detect a difference in recurrence (or presence) of HCC of 10% versus 30%. Since reduction of HCC in the non-LDLT group will be due to subsequent cadaveric transplantation, this statistical test will compare the strategy of LDLT versus waiting for a cadaveric transplant.

4.4.5. Statistical Analysis

Initial analysis of HCC will be primarily descriptive. The characteristics of HCC patients described will include TNM explant pathologic stage, use of ablation pretransplant, and pre transplant ablation method (i.e. chemoembolization, RFA, etc.). The proportion recurring within one year will be presented, with 95% CI. Predictors of one-year recurrence will be explored using logistic regression for patients with at least one year of follow-up. The difference between recurrence (or presence) proportions for LDLT versus non-LDLT patients will also be estimated using a 95% confidence interval. A comparison of survival between these two groups will be performed using Cox regression, adjusted for various prognostic covariates. A comparison of survival between LDLT and cadaveric transplant recipients will also be performed.

4.5. SRTR Data Validation Study

(This section does not apply to subjects who have the first living donor evaluated after 2/28/03)

4.5.1. Study Methods

We will investigate records for all patients with LDLT, and a subset of patients not receiving LDLT. These patients will be selected as needed to develop comparison cohorts for the other Retrospective research aims. All patients to be studied as part of any Retrospective cohort will be included in this validation study.

For each included patient, the A2ALL study coordinator will be asked to provide the data, based on chart review, for a selected subset of SRTR data items. The coordinator will be asked NOT to refer to copies of SRTR forms, but to provide the data based on chart review (or personal knowledge) alone. These data will be entered in a web-based data entry module. The module will have access to the original SRTR data, and will check the new data against the original SRTR data and provide immediate feedback if a discrepancy is found. The data coordinator will then resolve the difference, and either confirm the new value or enter a corrected value. The original SRTR record, as well as the final online entry, will be recorded in a special validation database.

The current SRTR data may be incomplete, and we have documented serious omissions in the reporting of HCC data. However, because the SRTR data were submitted closer to the time of listing and transplant, they may benefit from information available at those times that was not documented in the patient charts. Thus, if a discrepancy is found between the old SRTR data and the newly entered data, the coordinator will be given the opportunity to decide which is correct.

Potential for bias may arise if the A2ALL coordinator is the same person who enters the SRTR/OPTN data, or is a co-worker of that person. In that case, the A2ALL coordinator may be more likely to simply validate the SRTR data, rather than checking to make sure it is correct. We will attempt to minimize this bias by addressing the problem in the coordinator training session. Coordinators will be instructed in the importance of obtaining the data from chart review.

4.5.2. Participant Selection

All patients waitlisted for liver transplantation and considered for living donor transplantation between 1/1/1998 and 2/28/2003 at any of the nine A2ALL centers. If supplemental cadaveric transplant cases are used for any other specific aims, their data may also be included in the validation study.

4.5.3. Data Elements

Validation of SRTR data elements will incorporate information from patients included in all of the above studies.

4.5.4. Sample Size and Power Calculations

For an estimated proportion correct near 0.95 (95% correct), sample size of 300 will yield a 95% confidence interval (CI) for the true proportion will have a CI width of approximately +/- 0.025. For estimated proportions near 0.50 (50% correct), a 95% CI for the true proportion will have CI width of approximately +/- 0.057.

4.5.5. Statistical Analysis

The purpose of the data analysis is to document the correctness of the SRTR database. For each data element we will calculate: (1) the percent missing in the original SRTR data that were completed in the new data, (2) the percent of values that were not missing in the original data but were changed (corrected) in the new data, and (3) the percent of values that were correct in the original data. These percents should total 100%, unless an original SRTR data value was deemed to be incorrect and replaced with a missing value.

An additional analysis will investigate whether data quality changed after introduction of the electronic OPTN data submission system (UNet).

This validation study will tell us which of the SRTR data elements are reliable, and which are not. For each data element, we will assume that the A2ALL centers are representative of the other SRTR centers. Any data elements shown to be less than 95% correct in the A2ALL centers should be analyzed with caution in the full SRTR database.

We will also investigate center variability, to determine if error rates are center-specific or if they are similar across centers. This information will allow us to confidently use the full SRTR database for selected retrospective analyses.

4.6. Retrospective Post-surgical Complications Study

4.6.1. Study Methods

The major objective of this portion of the study is to define the incidence of donor morbidity in right lobe living donors in a retrospective cohort of patients and to compare recipient morbidity after LDLT or cadaveric transplant.

The charts of all right lobe donors will be retrospectively reviewed using a defined worksheet. The records of all patients who underwent a general anesthetic with the intent to proceed with living donation will be included. This will allow us to capture patients whose donation was aborted for various reasons. The hospital records, as well as any outpatient ambulatory medical records, will be included in the review. Visits to outside medical groups including visits to the emergency room department at other hospitals will be documented. Also, any subsequent medical care, such as physical therapy, will also be noted. It is the intent of this process to be inclusive of all potential complications that either required intervention or continuous monitoring. No control group will be used.

For the study of recipient complications, treated post-transplant complications (bile leaks, re-operation, treated rejection, and treated CMV infection) will be examined. The recipient complications study will focus on post-operative complications requiring intervention.

4.6.2. Participant Selection

All donors who were evaluated for right hepatic lobectomy between 1/1/1998 and the start date of enrollment into the A2ALL-Cohort-01 Study at any of the nine A2ALL centers and subsequently underwent the procedure will be included. All waitlisted

candidates for liver transplantation who had a potential donor considered for living donor transplantation and subsequently underwent either an LDLT or cadaveric transplant will be included. Supplementation of contemporaneous controls above those identified in the cohort component of the study may be necessary. If additional patients are needed, they will be selected using SRTR data. Controls will be frequency matched on center and date of transplantation (6 month window). In analysis, we will control for these variables as well as age, sex, disease (HCC, cholestatic, HCV/HBV, alcoholic, other), and severity of illness (MELD score, OPTN/UNOS status).

4.6.3. Data Elements

Data elements for the donor morbidity study will be taken from a donor morbidity/outcomes worksheet. Data elements for the comparative study of recipient morbidity will be taken from a recipient morbidity data collection form.

4.6.4. Sample Size and Power Calculations

Estimation of proportions of donor complications will be made using 95% confidence intervals (CI) based on the binomial distribution. Assuming 300 donors, 95% CI widths will be no larger than +/- 0.057.

Comparisons of recipient complications after LDLT and cadaveric transplants will be based on chi-square tests of equality of proportions. Assuming n=300 LDLT, n=250 cadaveric, and alpha=0.05, we will have 89% power to detect a difference in the proportion of bile leaks, for example, of 0.18 in the cadaveric group versus 0.30 in the LDLT group (a difference of 0.12). Physician estimates of this difference are closer to 0.20, so power is more than sufficient for this endpoint. If we more conservatively assume complication proportions near 0.5, we will have 89% power to detect a difference of 0.14 (such as 0.43 versus 0.57).

4.6.5. Statistical Analysis

Analysis of LDLT donor post-operative complications will be descriptive. We will report the proportions of donors with complications such as bile leak, primary non-function, graft failure, pneumonia, and urinary tract infection, as well as any complication requiring hospital admission, re-operation, or other intervention. Confidence intervals will be included with all estimates. We will also report follow-up outcomes including wound healing, pain medications, blood laboratory values, and the proportion of patients who returned to work/school. Some attempt will be made to correlate complications with patient characteristics and operative procedures, but any such analyses will be limited by the quality of available data.

LDLT recipient post-operative complications will be reported in the same way as the donor complications described above. In addition, a comparison of LDLT complications with complications following cadaveric transplant will be made. Depending on the type of complication (event occurrence, time to event, or continuous outcome), a comparison of the events between LDLT and cadaveric transplants will be made using logistic regression, Cox regression, or ordinary regression, respectively, each adjusted for other predictive variables as needed.

4.7. Retrospective Resource Utilization Study

4.7.1. Study Methods

Length of hospitalization, days in ICU, and major interventions will be used as measures of resource utilization. Note: Incorporation of cost and charge data is not planned. Such information is both difficult to obtain and to interpret.

4.7.2. Participant Selection

The cohort will include all of the following:
Potential recipient listed for transplantation

- age >= 18
- single organ

Potential donor evaluated between 1/1/1998 and the start date of enrollment into the A2ALL-Cohort-01 Study.

4.7.3. Data Elements

Hospitalization admission and discharge dates (pre-transplant and post-transplant). Number of ICU days. Major interventions performed during inpatient hospitalizations

4.7.4. Sample Size and Power Calculations

For comparing hospitalization between LDLT recipients and non-recipients we consider the number of hospital days in one year. Although the analysis will take into account the possibility that some patients may be included in both groups, both pre- and post-LDLT, the power calculations consider a similar but simplified design based on a two-sample t-test (2-sided, alpha=0.05), assuming 300 LDLT recipients and 500 non-recipients. We have no preliminary data on means or standard deviations (s.d.s) for number of hospital days in a year, but assuming a fairly large s.d. of 25 days, we will have 93% power to detect a difference of 5 days (effect size = 0.20 s.d.) between LDLT and non-LDLT groups.

4.7.5. Statistical Analysis

Resource utilization, particularly hospitalization (number of hospitalizations and number of hospital days) will be compared for those with and without LDLT using a repeated measures logistic regression analysis. In addition, a comparison of hospitalization after LDLT versus cadaveric transplant will be made.

5. Human Subjects

5.1. Protection of Human Subjects

5.1.1. Institutional Review Board

This data collection and analysis will be performed under Institutional Review Board (IRB) oversight. Prior to the initiation of the study, an IRB approval for study of human subjects will be obtained separately from the IRB of each of the participating transplant

centers and the DCC. Revisions to the study protocol and changes in the study design will also be submitted to IRBs for approval prior to implementation.

Each center will complete an application to their own IRB to allow receipt of the center-specific SRTR-identified data set and the abstraction of additional information from the medical record and release of this identified information to the DCC for analysis. The application will request a waiver of written informed consent for this retrospective project. The DCC will also have in place an IRB approved protocol to complete its responsibilities for the study. The DCC will, in turn, receive identifiable data from the centers to allow for linking to the prospective study in the future to avoid the need for duplicative data collections.

In order to plan a successful prospective study it is important to include all adult-to-adult donors and recipients of living donor liver transplants. Because the numbers are large and span a five-year period it would be extremely difficult to obtain written informed consent for all subjects in the data set. Therefore, each transplant center will request a waiver of informed consent for this data collection and release of patient identified information. The following paragraphs delineate the rationale for requesting a waiver of informed consent for the retrospective study.

Waiver of project-specific written informed consent is possible if a project meets the following four criteria derived from Section 45 CFR 46.116 (d). "An IRB may … waive the requirements to obtain informed consent, provided the IRB finds and documents that:"

1. The research involves no more than minimal risk to the research subjects. 45 CFR 46.102 (I) defines minimal risk as: the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life of during the performance of routine physical or psychological examinations or tests.

2. The waiver or alteration will not adversely affect the rights and welfare of the research subjects.

3. The research could not be practicably be carried out without the waiver or alteration; and;

4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

The proposed A2ALL retrospective study meets the above four criteria necessary for consideration of a waiver of consent.

1. The research will abstract information that was collected in standard medical records during routine medical evaluation and follow-up. The risk to the subject of this data abstraction is judged to be minimal. Safeguards are in place to keep the information

confidential utilizing a secure server for web-based data entry. The data will be stored on a secure server within the University of Michigan computer system.

2. A waiver of written informed consent will not adversely affect the rights or welfare of the research subjects. These data will consist of routine laboratory and procedure results, complications and outcomes of surgery and overall level of health that have been recorded in the subject's medical record. It is important to keep this data linked to the subject to avoid the need to "recollect" the data for use in the planned prospective clinical trial.

3. The inclusion of every living donor liver recipient and donor from each of the A2ALL transplant centers is necessary for the planning the prospective study. There are well-documented investigations of the bias introduced by the informed consent process. In order to avoid this bias and examine the overall effect of this procedure, every patient that has participated in this procedure must be examined. Successfully locating, contacting and securing informed consent from each subject is "impracticable". The results of this retrospective analysis will guide the development of a 5-year prospective longitudinal investigation of this study population. All eligible retrospective study subjects will be approached and informed consent will be documented for the prospective study. Only the retrospective study subjects that are able to be contacted and provide written informed consent will be enrolled into the prospective study.

4. Information that is revealed from this study will be presented at transplant meetings and published in scientific periodicals. The NIH will also utilize press releases to communicate the study findings. In this manner, information that may affect the previous subjects will be communicated.

Additionally, this study meets the requirements for a waiver of consent under the new HIPAA guidelines.

The HIPAA requirements for a waiver of consent (164.512(i)(2)(ii)) are:

1. No more than minimal risk to subject *(addressed above)*

2. Plan to protect identifiers from improper use/disclosure

   Secure web servers and limited access to the data will protect the data from improper use/disclosure

3. Plan to destroy identifiers at earliest opportunity consistent with conduct of research unless retention required by law or research design

   The links will be removed as soon as determination of ability to contact subject for prospective study has been made. Any subject contacted and not interested in participating, any subject that is deceased and any subject that can not be located

will have identifiers destroyed. The remainder will have the links maintained after consent is obtained and they will be enrolled into the prospective study. Data sets for this retrospective study will be coded and have identifiable information removed prior to analysis by the DCC.

4. Written assurances that Private Health Information (PHI) will not be reused or disclosed except as required by law or oversight

   The DCC will provide a written assurance that the information will be not reused or disclosed.

5. Can't do research without waiver

   Significant bias introduced without waiver is addressed above.

6. Can't do research without access to and use of PHI.

   The need to link to potential prospective data in the next study is discussed above. The DCC will be requesting data sets from the SRTR that contain identifiable information and will distribute these to the individual transplant centers that originally submitted the data. The DCC will receive the data set back from the transplant centers with corrections and additions of the original data as well as additional data elements obtained from medical record review. The DCC will maintain these links until the prospective study begins and will destroy the links for non-participators in the prospective study. At all times the data will be stored and transferred via secure data servers that require username and password access.

5.1.2. Patient confidentiality

Special procedures for ensuring patient confidentiality will be implemented. Data transmission and the distributed data systems have multiple layers of security as discussed in the study management section. Each study subject will be assigned an identification number. Only this number will be used to identify subjects in any individual tabulation. It is expected that only group data will be published. If individual subject data are to be published, no identifying information will be included. The study files will be maintained in a secure location as described above. Access to computerized data will be restricted to study personnel. Password authorization will be enforced. These passwords will be changed on a quarterly basis and whenever the Database Administrator makes a determination for a security change. Previous use of this security system and secured server indicates that this technique is very successful in assuring the protection of confidential information.

Authorized representatives of the Sponsor, the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK), National Institute of Health (NIH), participating clinical institution, DCC monitoring staff, as well as the IRB, have access to medical records and records from participation in this study. Such access is necessary to ensure the accuracy of the findings.

5.1.3. Risks to the patient

This data collection represents no more than minimal risk to the subjects and does not contain sensitive information. All data scheduled for collection and analysis have already been collected and documented as a part of standard clinical care. It would be impracticable to find, contact and obtain informed consent from each subject in the study group. This study meets the federal guidelines for a waiver of informed consent.

5.1.4. Unauthorized data release

The data sets will be stored on a secure server with restricted access (requires a unique username and password) at the DCC and every precaution will be taken to keep the information private. However, there is always the possibility of unauthorized release of data about subjects. Such disclosure would be extremely unlikely to involve a threat to life, health, or safety but would be a serious invasion of the subject's privacy. It is conceivable that such disclosure could have psychological, social, or legal effects on the patient. Using the standard security procedures (described above under patient confidentiality) can effectively minimize the risk of unauthorized disclosure of data. All study personnel who have access to patient data will be educated regarding the need to protect confidentiality and the procedures to be followed to ensure such protection. All staff will also be required to sign a standard medical record confidentiality agreement. The computer system on which data are maintained uses standard password protection procedures to limit access to authorized users. It is envisaged that the DCC will provide a second level of security checks. Data to be used for analysis will contain only the assigned identification numbers. All patient identifiers such as name, address and hospital record identification number will not be accessible to the staff involved in carrying out data analysis.

5.2. Benefits to the Patients

There are no direct benefits to the patients for participation in the study.

5.3. Inclusion of Women

This is a multi-center study drawing on a clinical population from nine transplant institutions across the United States. The demographics of the study population are pre-determined due to the retrospective all-inclusive nature of the study. Women will be included in the retrospective study as living liver donors and recipients. It is anticipated that the representation of women will correspond to the fraction of females in the living liver donor and recipient population.

5.4. Inclusion of Minorities

This is a multi-center study drawing on a clinical population from nine transplant institutions across the United States. The demographics of the study population are pre-determined due to the retrospective all-inclusive nature of the study. Racial and ethnic minority groups will be included in the donor and recipient components of the retrospective study and will be proportional to their representation in the donor and recipient population.

5.5. Inclusion of Children

The Adult-to-adult living donor liver transplantation cohort study specifically excludes children.

5.6. Data and Safety Monitoring Plan

Accepted principles of data and safety monitoring will be observed throughout the conduct of the A2ALL retrospective study. Since the retrospective study is restricted to review of information in the medical record, no adverse events will occur or be reported.

Each transplant center principal investigator will be responsible for monitoring the A2ALL retrospective study, as will the DCC. Monitoring responsibility will extend to determination of accurate and effective conduct of the protocol and to recommendations regarding closure of the study.

Oversight of monitoring will be performed to ensure that: 1) monitoring activities are appropriate to the study, 2) monitoring is accomplished in a regular, timely and effective way and 3) recommendations that result from study monitoring are completed.

IRBs will be provided feedback on a regular basis.

Training of study coordinators and study monitoring activities will be conducted by the DCC to ensure patient confidentiality and privacy and to maximize the reliability, accuracy, and timeliness of study data.

6. Study Organization

6.1. Clinical Transplant Centers

The participating Clinical Centers will have primary responsibility for developing the study protocol, maintaining high rates of follow-up and data collection, obtaining data of high quality, and interpreting, presenting, and publishing findings from the study.

1. Columbia University Health Sciences
   New York, NY
   Principal Investigator: Jean Emond, MD
2. Northwestern University
   Chicago, IL
   Principal Investigator: Michael Abecassis, MD
3. University of Pennsylvania
   Philadelphia, PA
   Principal Investigator: Abraham Shaked, MD
4. University of Colorado Health Sciences
   Denver, CO
   Principal Investigator: James Trotter, MD
5. University of California, Los Angeles
   Los Angeles, CA
   Principal Investigator: Mark Ghobrial, MD

6. University of California, San Francisco
   San Francisco, CA
   Principal Investigator: Christopher Freise, MD
7. University of North Carolina
   Chapel Hill, NC
   Principal Investigator: Roshan Shrestha, MD
8. University of Virginia
   Charlottesville, VA
   Principal Investigator: Carl Berg, MD
9. Virginia Commonwealth University
   Richmond, VA
   Principal Investigator: Robert Fisher, MD

6.2. Data Coordinating Center

The Data Coordinating Center (DCC) contributes content area expertise and shares in scientific leadership of the research group. The DCC has developed a communication infrastructure that includes meetings, teleconferences, electronic mail and bulletins, interactive web-based encounters and written correspondence. The DCC assists in protocol development and preparation of scientific publications. The DCC has the major responsibility of creating a database and data collection systems for the transplant centers, ongoing evaluation of data quality and performance monitoring of the transplant centers and statistical analyses of the data. The DCC will also create a comprehensive Manual of Operations (MOO) that will govern the conduct of the study. The manual will detail the protocols, protocol clarifications and amendments, summary of the regulatory requirements for the study, instructions for enrollment, data collection, data management, visit schedules and detailed instructions on the use of the electronic data submission.

University of Michigan
Ann Arbor, MI
Principal Investigator: Robert M. Merion, MD

6.3. Steering Committee

The primary governing body of the study is the Steering Committee, comprised of each of the Principal Investigators of the transplant centers, the Principal Investigator of the DCC and the NIDDK Project Scientist. The Steering Committee develops policies for the study pertaining to access to patient data and specimens, ancillary studies, performance standards, and publications and presentations. They develop the study protocol and meet to discuss the progress of the study and to consider problems arising during its conduct. The Steering Committee may establish subcommittees to further develop specific components of the study protocol and propose ancillary areas of study. Small working groups may be established to prepare manuscripts and presentations.

6.4. Retrospective Study Subcommittees

The following subcommittees have been established to address specific issues in the Retrospective study.

- Retrospective Protocol Design

- Hepatitis C Virus (HCV) Workgroup
- Hepatocellular Carcinoma (HCC) Workgroup
- Outcomes/Endpoints/Definitions Workgroup

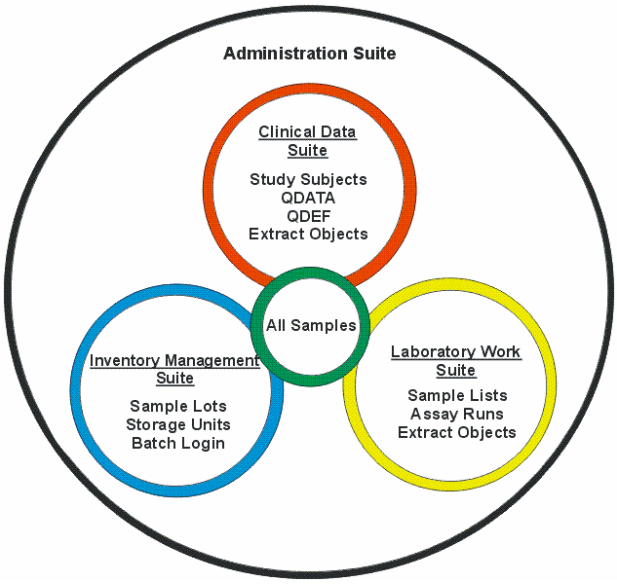
Other possible subcommittees include:

- A2ALL Study Policies
- Ancillary Study Policy
- Publication and Presentations
- Access to Study Data
- Others as required

7. Study Management

7.1. Data collection, Data Collection Forms, and Data Entry – BioDBx

The DCC will utilize the web-based BioDBx program as the data management nucleus for the A2ALL studies. This system, developed specifically for multicenter clinical trials management, was created by Dr. Stephen Gruber and Mr. Joseph Bonner at the University of Michigan, both of whom will be participating as consultants to the DCC. Briefly, BioDBx is a highly flexible database application that allows investigators to organize their research operations and perform common actions on research data within a single database. There are three main suites: the Clinical Data Suite, which manages clinical data, the Inventory Management Suite, which manages inventory such as acquired specimens, and the Laboratory Workspace, which manages laboratory operations. An Administrative Suite is the overall manager for the foregoing three suites.



The Clinical Data Suite manages clinical data within a defined hierarchy, the highest level of which is termed Active Studies. From Active Studies, study subjects and study data are managed and clinical data can be viewed. There is a QDef module where study set-up occurs and a QData module where clinical data are entered after being defined by QDef. The Study Subjects module is used to enter and manage demographic data for study participants and the Study Samples module allows entry and edit of data for samples obtained from the subjects in the study.

The primary mechanism by which a study is set up in BioDBx is through a four-component QDef (Question Definition) module. The four components are: 1) definition,

2) validation, 3) extraction, and 4) navigation. Definition functions to determine where and why a variable or question appears. Validation determines acceptable values for a variable or acceptable answers to a question. Extraction defines where the data from a particular element will go for statistical analysis. Navigation is a characteristic that determines what data element is requested next.

QData is the module within the Clinical Data Suite used to enter and edit data from Case Report Forms or study questionnaires. QData can only be utilized for a given study when the entire battery of questions for a study have been defined (in QDef) and tested. For the complement of data defined, QData prepares individual data entry screens for users to key responses for specific study subjects. After responses have been entered, they can be printed and reviewed or extracted into extract objects for statistical analysis.

The DCC will utilize the BioDBx QDef module to create electronic case report forms to capture all relevant study data for the main A2ALL cohort study, the study of previously transplanted A2ALL recipients, the A2ALL donor study, and all investigational/research protocols that are developed and implemented during the course of the study. The BioDBx system allows real-time monitoring of study data for protocol adherence, quality assurance, adverse event reporting, discrepancy reporting, and other trends.

7.2. Data Management

All study data will be entered into the BioDBx electronic data entry system by study coordinators at each study site. This data will be encrypted and transferred to the DCC and stored on a secure server at the University of Michigan. Access to the server and BioDBx system is limited and requires a unique username and password combination. The servers are backed up daily and physically stored in a locked facility.

All analysis of the data sets will utilize de-identified (coded) data sets.

7.3. Quality Control and Database Management

The first steps in ensuring protocol compliance are good protocol design and careful orientation of study personnel. Following final agreement on protocols, and prior to study initiation at any of the transplant centers, the DCC will organize a Training and Certification session for transplant center study coordinators/data entry personnel.

The BioDBx electronic data entry system will have built-in data checks as part of study quality assurance. Protocol compliance will be assessed by monitoring the submission of data at required intervals. Data inconsistencies and discrepancy reports will be reviewed by the Clinical Monitor so that necessary queries can be generated and sent to the transplant center study sites for verification and resolution.

Periodic requests may be generated for the submission of random source documents to assess the quality of data acquisition and data entry at each site. In addition, the Clinical Monitor or Project Manager will visit each site at least once to review source documents, monitor regulatory compliance, and assess protocol adherence.

In addition to source document verification, the Clinical Monitor and Project Manager will produce reports from the BioDBx system to look for inconsistencies in submitted data, particularly for repeated measures data elements, even if data do not fall outside of built-in validation routines.

Studies of intra-subject and inter-subject data variability by transplant center as well as intra-transplant center and inter-transplant center data variability will be used to further ascertain random or systematic data quality issues.

Comparisons of major endpoints from the current study to national data from the SRTR will be used to assess the extent to which participants in the A2ALL study are representative of the general population of patients undergoing these procedures in the United States.

7.4. Data Security/Data Transfer

Personnel at each study center will collect and enter data into BioDBx, a web-based data entry system. Authentication is currently enabled from Oracle Developer Form Server to the Oracle database. Between the web server and client browser, secure socket layer technology is in place. This will ensure safety and confidentiality of data by using secure encrypted data transmission from the transplant centers to the BioDBx database server.

The database logs every modification of every cell in the database to ensure the ability to monitor access to the data and audit transactions. The system is accessible only via an established account with a logon and password for security and confidentiality. Authorized study personnel will be assigned an account on the system. Passwords will have defined expiration dates and must be changed regularly to permit continuing access.

The BioDBx database server is located in a locked cabinet in a locked room at the University of Michigan Medical Center. The hardware administrator and his designated backup are the only individuals who have keys. The data will be transferred via the secure network to the Kidney Epidemiology Cost Center (KECC) at the University of Michigan. The A2ALL project staff is physically located in the KECC office suite. The office suite is kept locked with entry control 24 hours a day to prohibit unauthorized entry.

The computer system at KECC currently is used for research projects that involve processing large volumes of identified and re-identifiable patient-specific data. The KECC system has a comprehensive security plan based on the guidelines in OMB Circular A-130, "Security of Federal Automated Information Resources" and NIST Publication 800-18 "Guide for Developing Security Plans for Information Technology Systems." This plan has undergone extensive review by HRSA for security certification for maintaining patient-identified data. The A2ALL project will be covered by this security plan and will be required to comply.

8. Procedures and Instructions

BioDBx will be utilized for electronic submission of data for this study. Detailed instructions on the use of BioDBx, data element definitions and a code list will be provided in a Manual Of Operations (MOO). Each study site will be provided a copy of the MOO and the entire manual will be available on the study web site.

9. Expected Publications

A. Mortality and major morbidity consequent to choosing LDLT (primary objective)
B. Recurrence of and other outcomes of hepatitis C post-LDLT
C. Descriptive experience of post-LT HCC outcomes according to pre-LDLT variables.
D. Donor complications
E. Post-LDLT recipient outcomes (requires prospective identification of the outcomes that would be reported).
F. Validation of SRTR (a longer report could be provided to HRSA, OPTN)

APPENDICES

Appendix A. Feasibility Study

Summary	Total	Received LDLT		Received CAD		Died/Removed from List		Still Waiting	
Year	LDLT Candidates	Number	%	Number	%	Number	%	Number	%
1998	35	27	77%	4	11%	4	11%	0	0%
1999	99	54	55%	26	26%	16	16%	3	3%
2000	155	61	39%	37	24%	28	18%	29	19%
2001	275	99	36%	53	19%	40	15%	83	30%
2002	298	94	32%	61	20%	19	6%	124	42%
Total	862	335	39%	181	21%	107	12%	239	28%

Northwestern	Total	Received LDLT		Received CAD		Died/Removed from List		Still Waiting	
Year	LDLT Candidates	Number	%	Number	%	Number	%	Number	%
1998	0	0		0		0		0	
1999	5	2	40%	2	40%	1	20%	0	0%
2000	17	7	41%	4	24%	2	12%	4	24%
2001	13	9	69%	1	8%	2	15%	1	8%
2002	23	10	44%	6	26%	3	13%	4	17%
Total	58	28	48%	13	23%	8	14%	9	16%

VCU	Total	Received LDLT		Received CAD		Died/Removed from List		Still Waiting	
Year	LDLT Candidates	Number	%	Number	%	Number	%	Number	%
1998	17	12	71%	1	6%	4	24%	0	0%
1999	36	25	69%	5	14%	4	11%	2	6%
2000	16	11	69%	3	19%	1	6%	1	6%
2001	21	7	33%	3	14%	7	33%	4	19%
2002	29	9	31%	4	14%	1	3%	15	52%
Total	119	64	54%	16	13%	17	14%	22	18%

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UVA	Total	Received LDLT		Received CAD		Died/Removed from List		Still Waiting	
Year	LDLT Candidates	Number	%	Number	%	Number	%	Number	%
1998	0	0	0%	0	0%	0	0%	0	0%
1999	6	3	50%	3	50%	0	0%	0	0%
2000	10	6	60%	3	30%	1	10%	0	0%
2001	16	9	56%	3	19%	3	19%	1	6%
2002	7	3	43%	2	29%	1	14%	1	14%
Total	39	21	54%	11	28%	5	13%	2	5%

UNC	Total	Received LDLT		Received CAD		Died/Removed from List		Still Waiting	
Year	LDLT Candidates	Number	%	Number	%	Number	%	Number	%
1998	4	2	50%	2	50%	0	0%	0	0%
1999	17	9	53%	7	41%	1	6%	0	0%
2000	25	6	24%	4	16%	7	28%	8	32%
2001	31	5	16%	8	26%	4	13%	14	45%
2002	12	1	8%	5	42%	0	0%	6	50%
Total	89	23	26%	26	29%	12	14%	28	31%

Penn	Total	Received LDLT		Received CAD		Died/Removed from List		Still Waiting	
Year	LDLT Candidates	Number	%	Number	%	Number	%	Number	%
1998	0	0		0		0		0	
1999	3	2	66%	1	33%	0	0%	0	0%
2000	17	5	29%	2	12%	8	47%	2	12%
2001	15	5	33%	5	33%	4	27%	1	6%
2002	12	7	58%	2	16%	0	0%	3	25%
Total	47	19	40%	10	21%	12	26%	6	13%

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Colorado	Total	Received LDLT		Received CAD		Died/Removed from List		Still Waiting	
Year	LDLT Candidates	Number	%	Number	%	Number	%	Number	%
1998	0	0		0		0		0	
1999	0	0		0		0		0	
2000	0	0		0		0		0	
2001	35	19	54%	7	20%	4	11%	5	14%
2002	24	9	38%	6	25%	0	0%	9	38%
Total	59	28	47%	13	22%	4	7%	14	24%

UCLA	Total	Received LDLT		Received CAD		Died/Removed from List		Still Waiting	
Year	LDLT Candidates	Number	%	Number	%	Number	%	Number	%
1998	0	0		0		0		0	
1999	18	2	11%	6	33%	9	50%	1	6%
2000	28	6	21%	8	29%	6	21%	8	29%
2001	32	12	38%	5	16%	8	25%	7	22%
2002	41	7	17%	9	22%	6	15%	19	46%
Total	119	27	23%	28	24%	29	24%	35	29%

UCSF	Total	Received LDLT		Received CAD		Died/Removed from List		Still Waiting	
Year	LDLT Candidates	Number	%	Number	%	Number	%	Number	%
1998	0	0	0%	0	0%	0	0%	0	0%
1999	1	0	0%	1	100%	0	0%	0	0%
2000	17	6	35%	7	41%	3	18%	1	6%
2001	66	21	32%	15	23%	5	8%	25	38%
2002	103	23	22%	18	18%	6	6%	56	54%
Total	187	50	27%	41	22%	14	7%	82	44%

1073

Columbia	Total	Received LDLT		Received CAD		Died/Removed from List		Still Waiting	
Year	LDLT Candidates	Number	%	Number	%	Number	%	Number	%
1998	14	13	93%	1	7%	0	0%	0	0%
1999	13	11	85%	1	8%	1	8%	0	0%
2000	25	14	56%	6	24%	0	0%	5	20%
2001	46	12	26%	6	13%	3	7%	25	54%
2002	47	25	53%	9	19%	2	4%	11	23%
Total	145	75	52%	23	16%	6	4%	41	28%

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Investigator Document Requirements Checklist
A2ALL:Retrospective Study

- ☐ **Study Protocol**

- ☐ **CV: Investigators and sub-investigators**
  Must include start and end dates (or "to present") for all appointments and positions (No date gaps)
  CV should be signed and dated by the investigator (sub-investigator) to verify document is current
  CV SHOULD INCLUDE MEDICAL LICENSE NUMBER AND EXPIRATION DATE

- ☐ **Medical License**
  A copy of current medical license with expiration date, must be submitted for the PI and all sub-investigators IF NOT included with the CV

- ☐ **IRB/ERC Approvals**
  IRB/ERC approval letter MUST specifically state approval of the ***PROTOCOL***
  Must be on IRB/ERC Letterhead
  Actual date of IRB/ERC approval must appear on letter
  Protocol number, title and Version must appear on letter
  Renewal date or statement indicating when the approval must be renewed MUST be included in the letter
  Signature of the IRB/ERC Chairperson or designee must appear on the letter

- ☐ **IRB Membership List**
  Must be current
  If your IRB/ERC does not release its membership list, a DHHS Multiple Assurance Number must be submitted on the IRB/ERC letterhead

- ❑ **Monitor Log**

- ❑ **Human Research Subject Participation Certification**

- ❑ **HIPAA Training Certification**

- ❑ **Major Correspondence**

Monitor's Name (Print): _____ **Date:** _____

Monitor's Signature: _____

Data and Safety Monitoring Plan
Accepted principles of data and safety monitoring will be observed throughout the conduct of the A2ALL retrospective study. Since the retrospective study is restricted to review of information in the medical record, no adverse events will occur or be reported.

Each transplant center principal investigator will be responsible for monitoring the A2ALL retrospective study, as will the DCC. Monitoring responsibility will extend to determination of accurate and effective conduct of the protocol and to recommendations regarding closure of the study.

Oversight of monitoring will be performed to ensure that: 1) monitoring activities are appropriate to the study, 2) monitoring is accomplished in a regular, timely and effective way and 3) recommendations that result from study monitoring are completed.

IRBs will be provided feedback on a regular basis.

Training of study coordinators and study monitoring activities will be conducted by the DCC to ensure patient confidentiality and privacy and to maximize the reliability, accuracy, and timeliness of study data.
Data Management
All study data will be entered into the BioDBx electronic data entry system by study coordinators at each study site. This data will be encrypted and transferred to the DCC and stored on a secure server at the University of Michigan. Access to the server and BioDBx system is limited and requires a unique username and password combination. The servers are backed up daily and physically stored in a locked facility.

All analysis of the data sets will utilize de-identified (coded) data sets.

Quality Control and Database Management
The first steps in ensuring protocol compliance are good protocol design and careful orientation of study personnel. Following final agreement on protocols, and prior to study initiation at any of the transplant centers, the DCC will organize a Training and Certification session for transplant center study coordinators/data entry personnel.

The BioDBx electronic data entry system will have built-in data checks as part of study quality assurance. Protocol compliance will be assessed by monitoring the submission of data at required intervals. Data inconsistencies and discrepancy reports will be reviewed by the Clinical Monitor so that necessary queries can be generated and sent to the transplant center study sites for verification and resolution.

Periodic requests may be generated for the submission of random source documents to assess the quality of data acquisition and data entry at each site. In addition, the Clinical Monitor or Project Manager will visit each site at least once to review source documents, monitor regulatory compliance, and assess protocol adherence.

In addition to source document verification, the Clinical Monitor and Project Manager will produce reports from the BioDBx system to look for inconsistencies in submitted data, particularly for repeated measures data elements, even if data do not fall outside of built-in validation routines.

Studies of intra-subject and inter-subject data variability by transplant center as well as intra-transplant center and inter-transplant center data variability will be used to further ascertain random or systematic data quality issues.

Comparisons of major endpoints from the current study to national data from the SRTR will be used to assess the extent to which participants in the A2ALL study are representative of the general population of patients undergoing these procedures in the United States.

Data Security/Data Transfer

Personnel at each study center will collect and enter data into BioDBx, a web-based data entry system. Authentication is currently enabled from Oracle Developer Form Server to the Oracle database. Between the web server and client browser, secure socket layer technology is in place. This will ensure safety and confidentiality of data by using secure encrypted data transmission from the transplant centers to the BioDBx database server.

The database logs every modification of every cell in the database to ensure the ability to monitor access to the data and audit transactions. The system is accessible only via an established account with a logon and password for security and confidentiality. Authorized study personnel will be assigned an account on the system. Passwords will have defined expiration dates and must be changed regularly to permit continuing access.

The BioDBx database server is located in a locked cabinet in a locked room at the University of Michigan Medical Center. The hardware administrator and his designated backup are the only individuals who have keys. The data will be transferred via the secure network to the Kidney Epidemiology Cost Center (KECC) at the University of Michigan. The A2ALL project staff is physically located in the KECC office suite. The office suite is kept locked with entry control 24 hours a day to prohibit unauthorized entry.

The computer system at KECC currently is used for research projects that involve processing large volumes of identified and re-identifiable patient-specific data. The KECC system has a comprehensive security plan based on the guidelines in OMB Circular A-130, "Security of Federal Automated Information Resources" and NIST Publication 800-18 "Guide for Developing Security Plans for Information Technology Systems." This plan has undergone extensive review by HRSA for security certification for maintaining patient-identified data. The A2ALL project will be covered by this security plan and will be required to comply.

Adult-to-Adult Living Donor Liver Transplant Cohort Study

Study Coordinator Training
Retrospective Study
May 16-17, 2003
Ann Arbor, MI

A2ALL

History & Overview of A2ALL Study

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Introductions/Expectations

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A2ALL Study

- Funded by NIH, HRSA and American Society of Transplant Surgeons
- First organized multi-center study of adult-to-adult living liver transplantation.
- A2ALL consists of 9 transplant centers and a Data Coordinating Center
- Study began in 2002 and is funded for 7 years.
- There is a retrospective study and a prospective study.

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Retrospective Study: Updated Timelines

Main Task	Deadline
Final Protocol Approval	Feb 20, 2003
IRB submission by TC	March 3, 2003
IRB Approval by all TC	April 30, 2003
Approval of Data Modules	April 19,2003
Central Coordinator training	May 16-17, 2003
Start enrollment	June 2003

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Revised Cohort Study Timeline

Task	Date
Study Design Approval	Done
Protocol Approval	May '03 SC
Incorporate Final Edits	6/13/03
Consent Form Review by DCC	6/25/03
IRB Submission	6/30/03
CRF Design & Testing	August 2003
BioDBx Data Screen Builds	September 2003
Approval of CRF	Sep '03 SC
IRB Approval at all TC's	9/20/03 (12 wks)
Operations Manual Deployment	10/1/03
Study Coordinator Training	mid-October 2003
Enrollment/Data Collection	November 2003

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HIPAA-Privacy and Research

- Issued: Dec. 28, 2000
- Final: 04-15-01
- Really Final: 08-14-02
- Enforceable: 04-14-03
- Location: 65 FR 82462-82829 www.hhs.gov/ocr/hipaa/
- Office of Civil Rights will enforce

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Theory of HIPAA Privacy

"An individual's rights and welfare must never be sacrificed for scientific or medical progress".

12/02 Comments page 974

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HIPAA-Definitions

"Health Information" is any information created or received by a health plan, health care provider, public health authority, employer, life insurer, school or university, or health plan clearinghouse that relates to physical/mental health or a condition of an individual, provision of health care, or health care billing/payment

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HIPAA-Definitions

"Individually Identifiable Health Information" (IIHI) is anything that allows the patient/subject to be identified.

"Protected Health Information" is IIHI transmitted or maintained in any form or medium.

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What is not covered

De-identified information

Human biological tissue (obtained with specific authorization) except that PHI derived from tissue is covered

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Exclusions continued

Public health Data required by a State or Federal law (CDC, FDA, UNET) all continue to exist under the Privacy regulations

Data may be sent to a public health agency because HIPAA says PHI may be disclosed to a public health authority to prevent disease or injury

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Who are Covered Entities (CE)

- Health care providers who transmit information in electronic format including researchers who provide treatment to research participants
- Health plans (entities who pay for or provide medical care)
- Health care clearinghouses (Ex:billing services)

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What the Rule Does

- It says that any patient must be given a Notice of Privacy Protections, and must sign an acknowledgment that the Notice has been received
- Then treatment, billing and health care operations (TPO) can occur
- Any other use of PHI can only occur with specific patient authorization

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Definition of Research

164.502: "A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

Same as Common Rule 46.102(d).

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Use or Disclosure for Research

164.512(i) has the permitted uses rules.

PHI may be used for research with:

1. **subject consent; OR**
2. **IRB approval of an alteration or waiver**

NOTE: Waiver not for mere convenience

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Waiver criteria:164.512(i)(2)(ii)

1. No more than minimal risk to subject
2. Plan to protect identifiers from improper use/disclosure
3. Plan to destroy identifiers at earliest opportunity consistent with conduct of research unless retention required by law or research design

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Waiver Criteria continued

4. Written assurances that PHI will not be reused or disclosed except as required by law or oversight
5. Can't do research without waiver and
6. Can't do research without access to and use of PHI

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Common Rule Waiver Criteria

1. **No more than minimal risk.**
2. **Will not adversely affect rights of subject.**
3. **Could not practicably do the research.**
4. **Subject gets added information after participation (deception research).**

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Retrospective Study

Protocol Overview

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Retrospective study components

- Retrospective cohort study
- HCV
- HCC
- Donor Morbidity/mortality
- SRTR validation

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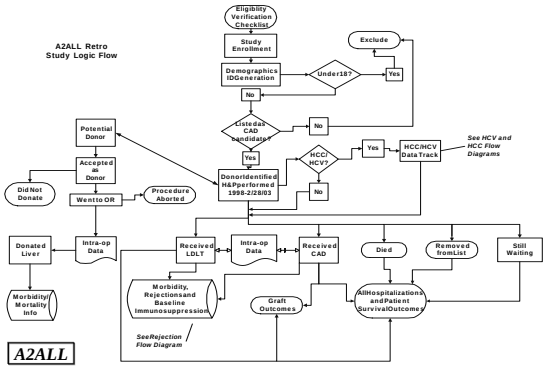

Retrospective cohort study

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Retrospective cohort study

Primary Aim:

To determine if choosing LDLT is beneficial for a recipient who pursues such a choice

Secondary Aim:

To compare, from the time of operation, the outcomes of cohort members who receive LDLT v. cadaveric transplants

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Retrospective cohort study

- **Inclusion criteria**
  - **Age ≥ 18 y.o.**
  - **Single organ recipient**
  - **Donor H and P performed between Jan 1 1998 and February 28, 2003**

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Hypothesis

- **Receipt of a living liver allograft leads to better long term outcomes for liver transplant candidates than pursuit of cadaveric transplant.**
  - **Improved pre-transplant morbidity/mortality?**
  - **Improved overall mortality?**

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Donor Identification Entry Point

- **Permits assessment of potential recipient benefit from shortened waiting time**
- **Permits inclusion of candidates who expire/are removed from list prior to liver transplant**
- **Allows homogeneous potential candidate group to be analyzed**
  - **All patients in cohort were felt by center to be possible LDLT candidate**

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Retrospective core study data elements (4.2.3)

- **Recipient data at listing**
- **Donor information**
- **Pre-transplant recipient complications**
- **Intra-operative data**
- **Post-operative course**

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HCV recurrence

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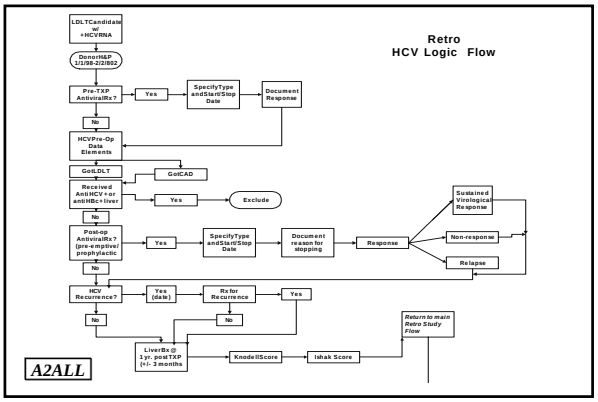

HCV recurrence

- **Primary Aim:**
  - **To determine whether HCV recurrence at 1 year (+/- 3 mos) defined histologically is more severe in LDLT recipients compared with contemporaneous cadaveric LT recipients.**

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HCV recurrence

Secondary Aims:

- **To compare rate of fibrosis progression in LDLT v. cad LT at one year and most recent biopsies**
- **To compare rate of cholestatic hepatitis in LDLT v. cad LT**
- **To compare rate of graft loss in HCV recipients between LDLT and cad LT**

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HCV study inclusion criteria

- **Cohort participants with HCV and selected contemporaneous cadaveric controls**
- **HCV RNA positive within 1 year of transplant (in absence of therapy) or recurrent HCV post-transplant**
- **Matched for center and time of transplant (+/- 6 mos)**

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HCV study exclusion criteria

- **Receipt of HCV, or Hep B cAb positive organ**
- **Hep B sAg positive**
- **HCV RNA negative at time of last measure before transplant**

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HCV data elements (4.3.3)

- **Pre-transplant characteristics**
  - **Age, gender, genotype, viral load, pre-emptive therapy**
- **Transplant characteristics**
  - **Graft volume**
- **Post-transplant immunosuppression**
  - **Number of treated rejections, immunosuppression regimen**
- **Post-transplant anti-viral therapy, ALTs, and viral loads**

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HCV data elements

- **Liver biopsies**
  - **Re-read by local pathologist using Knodell and Ishak scoring**
  - **Biopsies from 1 year (+/- 3 mos) post-LT and most recent biopsy to be reviewed, as well as pre-therapy biopsy**
  - **Covered by waiver of consent**

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Retrospective HCC Study

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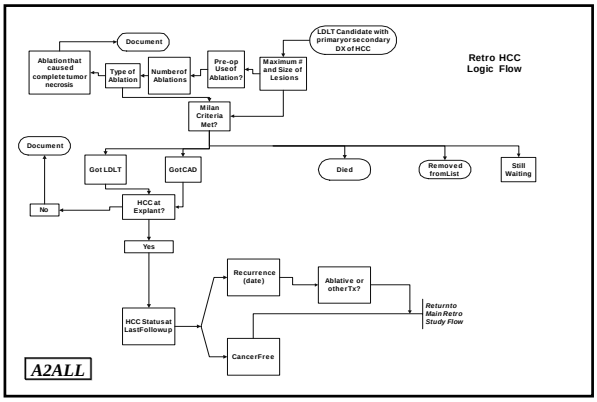

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Retrospective HCC Study

- **Primary Aim:**
  - **Observe recurrence of HCC following LDLT**
  - **Describe rates of recurrence of HCC in relationship to pre-operative staging and therapy following LDLT**

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HCC inclusion criteria

- **All cohort LDLT recipients with pre-operative diagnosis of HCC**
- **Must have identifiable HCC at explant unless ablative therapy performed pre-operatively**

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Data elements (4.4.3)

- **Maximum size and number of tumors pre-transplant**
- **Size and number of lesions found at explant**
- **Maximum AFP pre-transplant**
- **Type of pre-operative ablation (if any)**
- **Disease free survival post-transplant**

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Retrospective post-surgical complications study

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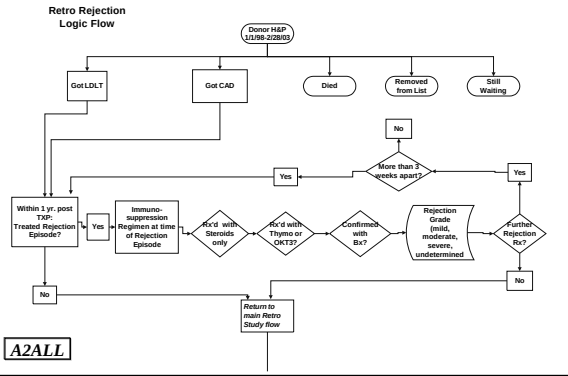

Retrospective post-surgical complications study

- **Primary aims:**
  - **To determine the rate of major donor post-operative complications associated with planned right lobe donation**
  - **To determine the major recipient post-operative complications associated with LDLT v. cadaveric LT**

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Donor inclusion criteria

- **All donors who undergo general anesthesia with intent to donate right lobe**

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Donor complications

- **Aim to quantify major complications that require intervention of continuous monitoring**
- **No control group**

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Recipient complications

- **All transplanted core cohort members eligible**
- **Supplement with contemporaneous controls if needed**
- **Compare complications in LDLT v. cadaveric recipients**

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Recipient complications

- **Focus on complications that require intervention**

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SRTR data validation study

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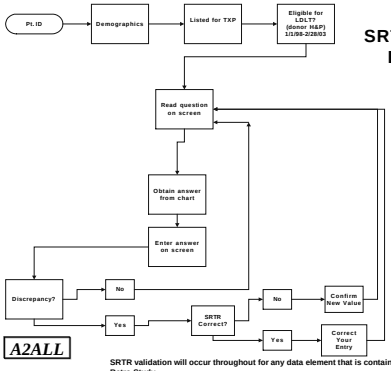

SRTR Validation Logic Flow

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SRTR validation will occur throughout for any data element that is contained in the SRTR and is required for the Retro Study.

SRTR data validation study

Primary Aim:

To estimate the correctness and completeness of selected data elements submitted to the OPTN and transmitted to the SRTR

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SRTR data validation study

Secondary Aims:

- **To ascertain which elements collected by the OPTN may reliably be employed in the prospective study**
- **To provide feedback to the OPTN and SRTR regarding the accuracy of selected data elements**

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SRTR validation methodology

- **Include all LDLT recipients in cohort and selected non-recipients**
- **Enter selected SRTR data elements based on chart review without knowledge of original SRTR responses**
- **If discordant, coordinator asked to choose correct response**

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Gathering Data for a Retrospective Study

Advantages and Challenges

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Retrospective Studies

- Looks back and captures a time interval that occurred in the past.
- No patient contact
- All information is gleaned from chart review/patient records
- You are limited by the quantity, quality and timing of the data contained in the patient records.

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Hints & Tips

- Look for a documented diagnosis in the chart.
- You do not have to be a diagnostician.
- For help with question interpretation, call DCC.
- For help with chart/record interpretation, talk to your PI.
- There will be missing information.

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So… How many charts are we looking at, here??!

- Prior to writing the protocol, the DCC conducted a feasibility study.
- Purpose was to make sure we had enough LDLT candidates and CAD candidates for controls

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Feasibility Questionnaire

Summary Year	Total LDLT Candidates	LDLT Txp N	LDLT Txp %	CAD Txp N	CAD Txp %	Died/Removed N	Died/Removed %	Still Waiting N	Still Waiting %
1998	35	27	77%	4	11%	4	11%	0	0%
1999	99	54	55%	26	26%	16	16%	3	3%
2000	155	61	39%	37	24%	28	18%	29	19%
2001	275	99	36%	53	19%	40	15%	83	30%
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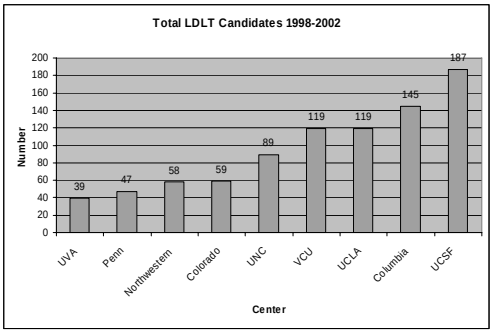

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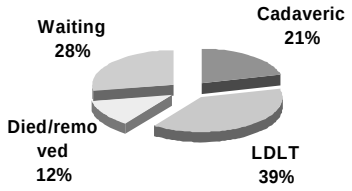

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Data Modules - Recipients

- Eligibility Checklist
- Study Enrollment
  - Assign Study ID
- Demographics
- Condition at Listing
- Condition at Enrollment
- Listing & TXP Information
- Condition at TXP
- HCC Pre-op Data
  - At listing
  - At enrollment
  - At transplant
- HCV Pre-op Data
  - At enrollment
  - At transplant
- Intraoperative Data
- HCC Explant Assessment
- Baseline Immunosuppression & Rejection Episodes
- Multiple Rejection Episodes
- Morbidity
- Complication Severity
- Hospitalizations
- HCV Post-op Recurrence and Rx Data
- HCC Post-op Recurrence and Rx Data
- Graft Outcomes
- Survival

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Data Modules - Donors

- Enrollment Checklist
- Study Enrollment
- Demographics
- Intraoperative Data
- Hospitalizations
- Morbidity
- Complication Severity
- Survival

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Core Modules

- **Recipients**
  - Eligibility Checklist
  - Study Enrollment
  - Demographics
  - Condition at Listing
  - Condition at Enrollment
  - Hospitalizations
  - Patient Survival
  - Listing and TXP Info
- **Donors**
  - Eligibility Checklist
  - Study Enrollment
  - Demographics
  - Evaluation
  - Patient Survival

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Trigger Modules

- Answers to some questions in some data modules will require you to fill out additional modules.
- For now, you will have to depend on the chart in your manual to prompt you.
- We plan to have a way to prompt you in the computer

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Data Element Definition and Format

- Name of data element
- Definition
- Format of answer
- Location in chart
- SRTR element?
- Data Module

A2ALL

Example

Name	Definition	Format Answer	Location in Chart	SRTR Element Y/N	Data Module
Gender	What is the patient's gender?	1= Male 2 = Female	Face Sheet	Y	Recipient Demographics, Donor Demographics
Cancer Recurrence	Did the patient develop cancer recurrence post-transplant	1= Yes 2 = No 3= Unknown	Post transplant medical record Imaging Studies Lab Reports	N	HCC Postoperative Recurrence and Treatment Data

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Example (cont'd)

Name	Definition	Format Answer	Location in Chart	SRTR Element Y/N	Data Module(s)
Pleural Effusion	Did the patient develop a pleural effusion severe enough to require either chest tube placement or thoracocentesis?	1= Yes 2 = No 3=Unknown	Progress Notes Procedure Notes Imaging Studies	N	Donor Morbidity Recipient Morbidity
Cold Ischemia Time	What was the cold ischemia time (from time of donor cross clamp to the time the liver was taken out of ice) in minutes?	00 Minutes	Operative Notes	Y	Recipient Intraoperative Data

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Purpose of Each Module

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- **Eligibility Checklist (Recipient and Donor): To confirm eligibility prior to enrollment.**
  - **Will not be data-entered, but should be kept with patient records at your center.**
  - **To generate a study ID number, and link potential recipients with their SRTR record.**
  - **Can be completed now (as soon as it is provided by the DCC) to document your set of eligible patients.**
- **Study Enrollment & Demographics (Recipient and Donor):**
  - **We will test our ability to match SRTR records.**
- **Donor Evaluation:**
  - **To collect baseline information about donors at evaluation**
  - **To validate SRTR elements regarding donors**

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- **Recipient Condition at Listing: Collects information about the recipients' condition when first listed for transplant. Validates some SRTR elements.**
- **Recipient Condition at Enrollment: Captures changes in the recipients' status in the interval between listing and enrollment.**
- **Recipient Condition at Txp: To collect baseline covariates for LDLT vs CAD analyses. Captures changes in the recipients' status in the interval between enrollment and transplant.**
  - **These three intervals give us a picture of what happens to the patient while on the waiting list.**

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- **Listing & Transplant Data**
  - **Validates SRTR transplant date**
  - **Tells us whether we need to fill out intraoperative or morbidity data**
- **HCC Pre-op Data at Listing:**
  - **To collect baseline characteristics of HCC, and ablative treatments prior to Enrollment.**
- **HCC Pre-op Data at Enrollment:**
  - **To collect characteristics of HCC, and ablative treatments between listing and enrollment. Shows disease progression while on the waiting list.**
- **HCC Pre-op Data at TXP:**
  - **To collect baseline characteristics of HCC, and ablative treatments between enrollment and TXP. Shows disease progression while on the waiting list.**

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- **HCC Explant Assessment:**
  - **To exclude patients who did not have HCC at the time of transplant**
  - **To confirm pre-operative assessment of cancer stage**
- **HCC Post-op Recurrence & Rx Data:**
  - **HCC Recurrence (Aim 3.4.2)**
  - **HCC post-op ablations**

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- **HCV Pre-op Data at Enrollment:**
  - **To collect characteristics of HCV.**
  - **Possible covariate for analysis of survival or hospitalization**
- **HCV Pre-op Data at Txp:**
  - **To collect baseline characteristics of HCV for LDLT vs CAD analysis.**
  - **Shows the progression of disease in the interval between enrollment and transplant.**
- **HCV Post-op Recurrence & Rx Data:**
  - **To collect HCC recurrence (Aim 3.3.1)**
  - **HCV severity at 1 year post Txp**
  - **Fibrosis progression at 1 year and most recent follow-up**
  - **Presence of cholestatic hepatitis**

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- **Recipient & Donor Intraoperative Data:**
  - **To collect possible predictors of outcomes comparing LDLT vs. CAD (recipient)**
  - **To collect possible predictors of morbidity for donors.**
- **Baseline Immunosuppression & Rejection Episodes:**
  - **To collect information on rejection (Aim 3.2.2)**
  - **To collect information on post-operative complications (Aim 3.6.1)**

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- **Multiple Rejection Episodes:**
  - **To collect information on rejection (Aim 3.2.2)**
  - **To collect information on post-operative complications (Aim 3.6.1)**
- **Donor & Recipient Morbidity, Complication Severity and Hospitalizations:**
  - **To collect information on post-operative complications (Aim 3.6.1)**
  - **To collect information on frequency of specific complications**
  - **To collect information on post-operative resource utilization**
- **Graft Outcomes:**
  - **To compare graft outcomes in LDLT and CAD recipients**
  - **To collect information on graft loss (Aim 3.3.2)**
- **Recipient & Donor Survival:**
  - **To compare survival between LDLT & CAD recipients**
  - **To collect information on donor outcomes**

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Assigning a Recipient Study ID#

- **Review and confirm the requirements on the Eligibility Checklist**
- **Find your Center ID#**
- **The Study ID for recipients is a 6-character code.**

- **Character 1,2 = Center ID#**
- **Character 3 = R**
- **Character 4,5,6 = sequential 3-digit code 001-999.**
- **e.g. If you're from Columbia, and this is your first recipient, then the Study ID# would be: 01R001**

A2ALL

Assigning a Donor Study ID#

- **Review and confirm the requirements on the Eligibility Checklist**
- **Find your Center ID#**
- **The Study ID for recipients is a 7-character code.**

- **Character 1,2 = Center ID#**
- **Character 3 = D**
- **Character 4,5,6 = last 3 digits of the recipient's Study ID#.**
- **Character 7 = chronological order that this donor was for that recipient**
- **e.g. If you are from Columbia, and this is the second donor evaluated for the recipient we identified above, then the Study ID number would be: 01D0012**

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Study Coordinator Quizbowl!

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Question 1

LDLT recipient candidate Bob Badliver had 3 donors evaluated. Assign him a Study ID number. Then assign his prospective donors their Study ID numbers.

First donor, Clark Kent, DOB 4/21/60 had his H&P on 12/22/97.

Second Donor, Paul Pureliver, DOB 3/3/61, had his H&P on 2/2/98.

Third Donor, Batman Jones, DOB 11/5/57, had his H&P on 6/7/98.

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Bonus Question

- What is Bob Badliver's date of enrollment?

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Regulatory Binder

- Retrospective Study Protocol
- Investigator's and sub-investigators' CV's
  - No date gaps
  - Must be signed by investigator to verify correctness
  - Should include medical license number and expiration date. If not included in CV, include copy of actual license in binder.
- IRB/ERC Approvals
  - Must specifically state approval of the protocol (protocol number, title and version)
  - Date of approval
  - Renewal date
  - Signed by IRB/ERC chair

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Regulatory Binder

- Current IRB Membership List
  - If your IRB/ERC does not release its membership list, a DHHS Multiple Assurance Number must be submitted on the IRB/ERC letterhead.
- Monitor Log
- Human Research Subject Participation Certification
- HIPAA Training Certification
- Major Correspondence

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The BioDBx System

Web-based Data Entry

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BioDBx Basics

- Every center has its own ID number
- Each of you will have your own password.
- You will access BioDBx through the A2ALL website.
- You will only be able to see your own center's data.

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Return of Study Coordinator Quizbowl!

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Case Hx 2: Horace Heppa

- 48 y.o., presented for liver TXP eval. 1/2/00, listed 1/30/00
- 7/97: Dx'd with HCV. Bx showed cirrhosis, genotype 1b. HCV RNA 1.5 million copies/ml
- 9/99: developed ascites, Tx'd with diuretics
- 7/97-12/97: received interferon monotherapy, no response
- Antiviral Tx discussed at 1/2/00 visit, but not pursued
- 3/2/00: living donor presented for evaluation, excluded because of comorbid medical conditions
- 9/1/00: CAD liver TXP performed. Uneventful. Discharged from hospital on 10/3/00.

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Horace (cont'd)

- 1/3/01: Increase in LFT noted during routine labs, called back for evaluation
- 1/10/01 Liver Bx showed mild inflammation and mild fibrosis
- 1/20/01 Anti-viral Tx started x 42 weeks (Intron & Ribavirin), then DC'd because of extreme fatigue and depression.
- 10/1/01: Antiviral Tx stopped. HCV RNA +

2/27/03 LFT's increased again. Liver Bx showed increased inflammation and fibrosis

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Horace's 2000 Labs

Test/Date	1/2/00	3/2/00	9/1/00	11/25/00
Alb	3.1	2.9	2.7	3.6
Tbil	2.0	3.1	4.5	0.8
SAP	135	154	139	110
AST	125	130	128	39
ALT	99	90	100	45
INR	1.3	1.4	1.6	N/A
HCV RNA	+	N/A	N/A	N/A
HCV Genotype	N/A	N/A	N/A	N/A

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Horace's 2001 Labs

Test/Date	1/3/01	1/10/01	4/1/01	7/5/01	10/1/01	12/2/01
Alb	3.6	3.5	3.3	3.5	3.2	3.6
Tbil	1.1	1.8	1.1	0.9	0.7	0.5
SAP	128	150	130	120	99	102
AST	115	126	87	56	45	76
ALT	164	190	120	78	62	99
INR	N/A	1.2	N/A	N/A	1.1	N/A
HCV RNA (IU/ml	4,056,720	N/A	N/A	738,500	201,450	N/A

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Horace's 2002/03 Labs

Test/Date	4/10/2	8/3/02	12/2/02	2/27/02
Alb	3.6	3.8	3.6	3.7
Tbil	0.8	0.7	1.1	1.3
SAP	112	132	96	148
AST	69	57	88	154
ALT	75	68	100	170
INR	N/A	N/A	N/A	1.2
HCV RNA (IU/ml)	N/A	N/A	N/A	3,256,740

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Horace's Biopsy Results

Liver Bx/Date	1/10/01	2/27/03
Periportal necrosis	1	3
Lobular inflammation	3	1
Portal inflammation	1	3
Ishak Fibrosis	1	3

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Case Hx 3: Sally Sirrosis

- 9/00: Dx'd with HCV, Bx showed cirrhosis. No antiviral Rx.
- 6/01: US showed single 2cm nodule in rt. lobe. PV & HV patent. No enlarged lymph nodes. AFP = 15ng/ml. Chest CT & bone scan neg. for metastases.
- 8/2/01: Listed for liver TXP
- 8/10/01: AFP 19ng/ml, Radiofrequency ablation performed
- 10/1/01 Living donor evaluated and accepted (donor is Sally's sister Sasha)
- 11/5/01: repeat MRI, 3.5cm necrotic cavity in place of tumor. PV and HV patent. No nodes or evidence of metastases. AFP 9ng/dl
- 11/20/01: LDLT performed.

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Sally (cont'd)

- Explant Liver showed 3.5cm necrotic cavity in rt. Lobe. One 0.5cm satellite nodule that showed dysplasia, but no HCC. HV & PV patent. No lymph node or peritoneal seeding noted. Histology: scanty neoplastic cells (fewer than 10 under high power field), characteristic of well-differentiated HCC.
- 5/6/02: Well post TXP. AFP 5ng/ml. Repeat MRI abdomen, CT chest and bone scan WNL.
- 12/1/02: Continues to do well. Repeat imaging studies show no tumor recurrence

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First Tasks

- Locate charts of all LDLT candidates who had a donor identified and evaluated between 1/1/98 and 2/28/03.
- Do the Eligibility Checklist and assign them a Study ID#
- Associate the prospective donors with the candidates and assign them each a Study ID#
- Enter the patients into the BioDBx data base.
- DCC will match this information to that contained in the SRTR and import that data back into BioDBx
- Once this has occurred, then you can begin answering questions and adding clinical data.
- Please note: YOU MUST HAVE SENT A COPY OF YOUR IRB APPROVAL LETTER TO THE DCC BEFORE YOU CAN ENTER DATA (OR EVEN LOOK AT CHARTS) FOR THIS STUDY!

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1 # Adult-to-Adult Living Donor Liver Transplant Cohort Study

Study Coordinator Training

Retrospective Study

May 16-17, 2003

Ann Arbor, MI

2 # History & Overview of A2ALL Study

3 # Introductions/Expectations

4 # A2ALL Study

1
- **Funded by NIH, HRSA and American Society of Transplant Surgeons**
- **First organized multi-center study of adult-to-adult living liver transplantation.**
- **A2ALL consists of 9 transplant centers and a Data Coordinating Center**

2
- **Study began in 2002 and is funded for 7 years.**
- **There is a retrospective study and a prospective study.**

5 **Retrospective Study: Updated Timelines**

6 **Revised Cohort Study Timeline**

7 # HIPAA-Privacy and Research

- **Issued: Dec. 28, 2000**
- **Final: 04-15-01**
- **Really Final: 08-14-02**
- **Enforceable: 04-14-03**
- **Location: 65 FR 82462-82829 www.hhs.gov/ocr/hipaa/**
- **Office of Civil Rights will enforce**

8 # Theory of HIPAA Privacy

"An individual's rights and welfare must never be sacrificed for scientific or medical progress".

12/02 Comments page 974

9

HIPAA-Definitions

"Health Information" is any information created or received by a health plan, health care provider, public health authority, employer, life insurer, school or university, or health plan clearinghouse that relates to physical/mental health or a condition of an individual, provision of health care, or health care billing/payment

10

HIPAA-Definitions

"Individually Identifiable Health Information" (IIHI) is anything that allows the patient/subject to be identified.

"Protected Health Information" is IIHI transmitted or maintained in any form or medium.

11

What is not covered

De-identified information

Human biological tissue (obtained with specific authorization) except that PHI derived from tissue is covered

12

Exclusions continued

Public health Data required by a State or Federal law (CDC, FDA, UNET) all continue to exist under the Privacy regulations

Data may be sent to a public health agency because HIPAA says PHI may be disclosed to a public health authority to prevent disease or injury

13

Who are Covered Entities (CE)

Health care providers who transmit information in electronic format including researchers who provide treatment to research participants

Health plans (entities who pay for or provide medical care)

Health care clearinghouses (Ex:billing services)

14

What the Rule Does

It says that any patient must be given a Notice of Privacy Protections, and must sign an acknowledgment that the Notice has been received

Then treatment, billing and health care operations (TPO) can occur

Any other use of PHI can only occur with specific patient authorization

15 ☐ # Definition of Research

164.502: "A systematic investigation, <u>including research development, testing</u> <u>and evaluation</u>, designed to develop or contribute to generalizable knowledge."

Same as Common Rule 46.102(d).

16 ☐ # Use or Disclosure for Research

164.512(i) has the permitted uses rules.

PHI may be used for research with:

1. subject consent; OR

2. IRB approval of an alteration or waiver

NOTE: Waiver not for mere convenience

17 ☐ # Waiver criteria:164.512(i)(2)(ii)

1. No more than minimal risk to subject

2. Plan to protect identifiers from improper use/disclosure

3. Plan to destroy identifiers at earliest opportunity consistent with conduct of research unless retention required by law or research design

18 ☐ # Waiver Criteria continued

4. Written assurances that PHI will not be reused or disclosed except as required by law or oversight

5. Can't do research without waiver and

6. Can't do research without access to and use of PHI

19 ☐ # Common Rule Waiver Criteria

1. No more than minimal risk.

2. Will not adversely affect rights of subject.

3. Could not practicably do the research.

4. Subject gets added information after participation (deception research).

20 ☐ # Retrospective Study

Protocol Overview

21

22

23 # Retrospective cohort study

24 ## Retrospective cohort study

Primary Aim:

To determine if choosing LDLT is beneficial for a recipient who pursues such a choice

Secondary Aim:

To compare, from the time of operation, the outcomes of cohort members who receive LDLT v. cadaveric transplants

25 ## Retrospective cohort study

- **Inclusion criteria**
  - **Age ≥ 18 y.o.**
  - **Single organ recipient**
  - **Donor H and P performed between Jan 1 1998 and February 28, 2003**

26 # Hypothesis

- **Receipt of a living liver allograft leads to better long term outcomes for liver transplant candidates than pursuit of cadaveric transplant.**
  - **Improved pre-transplant morbidity/mortality?**
  - **Improved overall mortality?**

27 ## Donor Identification Entry Point

- **Permits assessment of potential recipient benefit from shortened waiting time**
- **Permits inclusion of candidates who expire/are removed from list prior to liver transplant**
- **Allows homogeneous potential candidate group to be analyzed**
  - **All patients in cohort were felt by center to be possible LDLT candidate**

28 ## Retrospective core study data elements (4.2.3)

- **Recipient data at listing**
- **Donor information**
- **Pre-transplant recipient complications**
- **Intra-operative data**

- **Post-operative course**

29 HCV recurrence

30

31 HCV recurrence

- **Primary Aim:**
  - **To determine whether HCV recurrence at 1 year (+/- 3 mos) defined histologically is more severe in LDLT recipients compared with contemporaneous cadaveric LT recipients.**

32 HCV recurrence

Secondary Aims:

- **To compare rate of fibrosis progression in LDLT v. cad LT at one year and most recent biopsies**
- **To compare rate of cholestatic hepatitis in LDLT v. cad LT**
- **To compare rate of graft loss in HCV recipients between LDLT and cad LT**

33 HCV study inclusion criteria

- **Cohort participants with HCV and selected contemporaneous cadaveric controls**
- **HCV RNA positive within 1 year of transplant (in absence of therapy) or recurrent HCV post-transplant**
- **Matched for center and time of transplant (+/- 6 mos)**

34 HCV study exclusion criteria

- **Receipt of HCV, or Hep B cAb positive organ**
- **Hep B sAg positive**
- **HCV RNA negative at time of last measure before transplant**

35 HCV data elements (4.3.3)

- **Pre-transplant characteristics**
  - **Age, gender, genotype, viral load, pre-emptive therapy**
- **Transplant characteristics**
  - **Graft volume**
- **Post-transplant immunosuppression**
  - **Number of treated rejections, immunosuppression regimen**
- **Post-transplant anti-viral therapy, ALTs, and viral loads**

36 HCV data elements

- **Liver biopsies**
  - **Re-read by local pathologist using Knodell and Ishak scoring**
  - **Biopsies from 1 year (+/- 3 mos) post-LT and most recent biopsy to be reviewed, as well as pre-therapy biopsy**
  - **Covered by waiver of consent**

37 Retrospective HCC Study

38

39 Retrospective HCC Study

- **Primary Aim:**
  - **Observe recurrence of HCC following LDLT**
  - **Describe rates of recurrence of HCC in relationship to pre-operative staging and therapy following LDLT**

40 HCC inclusion criteria

- **All cohort LDLT recipients with pre-operative diagnosis of HCC**
- **Must have identifiable HCC at explant unless ablative therapy performed pre-operatively**

41 Data elements (4.4.3)

- **Maximum size and number of tumors pre-transplant**
- **Size and number of lesions found at explant**
- **Maximum AFP pre-transplant**
- **Type of pre-operative ablation (if any)**
- **Disease free survival post-transplant**

42 Retrospective post-surgical complications study

43

44 Retrospective post-surgical complications study

- **Primary aims:**
  - **To determine the rate of major donor post-operative complications associated with planned right lobe donation**
  - **To determine the major recipient post-operative complications associated with LDLT v. cadaveric LT**

45 Donor inclusion criteria

- **All donors who undergo general anesthesia with intent to donate right lobe**

46 ## Donor complications

- **Aim to quantify major complications that require intervention of continuous monitoring**
- **No control group**

47 ## Recipient complications

- **All transplanted core cohort members eligible**
- **Supplement with contemporaneous controls if needed**
- **Compare complications in LDLT v. cadaveric recipients**

48 ## Recipient complications

- **Focus on complications that require intervention**

49 ## SRTR data validation study

50

51 ## SRTR data validation study

Primary Aim:

To estimate the correctness and completeness of selected data elements submitted to the OPTN and transmitted to the SRTR

52 ## SRTR data validation study

Secondary Aims:

- **To ascertain which elements collected by the OPTN may reliably be employed in the prospective study**
- **To provide feedback to the OPTN and SRTR regarding the accuracy of selected data elements**

53 ## SRTR validation methodology

- **Include all LDLT recipients in cohort and selected non-recipients**
- **Enter selected SRTR data elements based on chart review without knowledge of original SRTR responses**
- **If discordant, coordinator asked to choose correct response**

54 # Gathering Data for a Retrospective Study

Advantages and Challenges

55

Retrospective Studies

- Looks back and captures a time interval that occurred in the past.
- No patient contact
- All information is gleaned from chart review/patient records
- You are limited by the quantity, quality and timing of the data contained in the patient records.

56

Hints & Tips

- Look for a documented diagnosis in the chart.
- You do not have to be a diagnostician.
- For help with question interpretation, call DCC.
- For help with chart/record interpretation, talk to your PI.
- There will be missing information.

57

So… How many charts are we looking at, here??!

- Prior to writing the protocol, the DCC conducted a feasibility study.
- Purpose was to make sure we had enough LDLT candidates and CAD candidates for controls

58

Feasibility Questionnaire

59

60

Total Retro cohort 1998-2002

61

Data Modules - Recipients

1

- Eligibility Checklist
- Study Enrollment
  - Assign Study ID
- Demographics
- Condition at Listing
- Condition at Enrollment
- Listing & TXP Information
- Condition at TXP
- HCC Pre-op Data
  - At listing
  - At enrollment
  - At transplant
- HCV Pre-op Data
  - At enrollment
  - At transplant

2

- Intraoperative Data
- HCC Explant Assessment
- Baseline Immunosuppression & Rejection Episodes
- Multiple Rejection Episodes
- Morbidity
- Complication Severity
- Hospitalizations
- HCV Post-op Recurrence and Rx Data
- HCC Post-op Recurrence and Rx Data
- Graft Outcomes
- Survival

62 Data Modules - Donors

- **Enrollment Checklist**
- **Study Enrollment**
- **Demographics**
- **Intraoperative Data**
- **Hospitalizations**
- **Morbidity**
- **Complication Severity**
- **Survival**

63 Core Modules

1
- **Recipients**
  - **Eligibility Checklist**
  - **Study Enrollment**
  - **Demographics**
  - **Condition at Listing**
  - **Condition at Enrollment**
  - **Hospitalizations**
  - **Patient Survival**
  - **Listing and TXP Info**

2
- **Donors**
  - **Eligibility Checklist**
  - **Study Enrollment**
  - **Demographics**
  - **Evaluation**
  - **Patient Survival**

64 Trigger Modules

- **Answers to some questions in some data modules will require you to fill out additional modules.**
- **For now, you will have to depend on the chart in your manual to prompt you.**
- **We plan to have a way to prompt you in the computer**

65 Data Element Definition and Format

- **Name of data element**
- **Definition**
- **Format of answer**
- **Location in chart**
- **SRTR element?**
- **Data Module**

66 Example

67 Example (cont'd)

68

Purpose of Each Module

69

- **Eligibility Checklist (Recipient and Donor): To confirm eligibility prior to enrollment.**
  - **Will not be data-entered, but should be kept with patient records at your center.**
  - **To generate a study ID number, and link potential recipients with their SRTR record.**
  - **Can be completed now (as soon as it is provided by the DCC) to document your set of eligible patients.**
- **Study Enrollment & Demographics (Recipient and Donor):**
  - **We will test our ability to match SRTR records.**
- **Donor Evaluation:**
  - **To collect baseline information about donors at evaluation**
  - **To validate SRTR elements regarding donors**

70

- **Recipient Condition at Listing: Collects information about the recipients' condition when first listed for transplant. Validates some SRTR elements.**
- **Recipient Condition at Enrollment: Captures changes in the recipients' status in the interval between listing and enrollment.**
- **Recipient Condition at Txp: To collect baseline covariates for LDLT vs CAD analyses. Captures changes in the recipients' status in the interval between enrollment and transplant.**
  - **These three intervals give us a picture of what happens to the patient while on the waiting list.**

71

- **Listing & Transplant Data**
  - **Validates SRTR transplant date**
  - **Tells us whether we need to fill out intraoperative or morbidity data**
- **HCC Pre-op Data at Listing:**
  - **To collect baseline characteristics of HCC, and ablative treatments prior to Enrollment.**
- **HCC Pre-op Data at Enrollment:**
  - **To collect characteristics of HCC, and ablative treatments between listing and enrollment. Shows disease progression while on the waiting list.**
- **HCC Pre-op Data at TXP:**
  - **To collect baseline characteristics of HCC, and ablative treatments between enrollment and TXP. Shows disease progression while on the waiting list.**

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- **HCC Explant Assessment:**
  - **To exclude patients who did not have HCC at the time of transplant**
  - **To confirm pre-operative assessment of cancer stage**
- **HCC Post-op Recurrence & Rx Data:**
  - **HCC Recurrence (Aim 3.4.2)**
  - **HCC post-op ablations**

73

- **HCV Pre-op Data at Enrollment:**
  - **To collect characteristics of HCV.**
  - **Possible covariate for analysis of survival or hospitalization**
- **HCV Pre-op Data at Txp:**
  - **To collect baseline characteristics of HCV for LDLT vs CAD analysis.**
  - **Shows the progression of disease in the interval between enrollment and transplant.**
- **HCV Post-op Recurrence & Rx Data:**
  - **To collect HCC recurrence (Aim 3.3.1)**
  - **HCV severity at 1 year post Txp**
  - **Fibrosis progression at 1 year and most recent follow-up**
  - **Presence of cholestatic hepatitis**

74

- **Recipient & Donor Intraoperative Data:**
  - **To collect possible predictors of outcomes comparing LDLT vs. CAD (recipient)**
  - **To collect possible predictors of morbidity for donors.**
- **Baseline Immunosuppression & Rejection Episodes:**
  - **To collect information on rejection (Aim 3.2.2)**
  - **To collect information on post-operative complications (Aim 3.6.1)**

75

- **Multiple Rejection Episodes:**
  - **To collect information on rejection (Aim 3.2.2)**
  - **To collect information on post-operative complications (Aim 3.6.1)**
- **Donor & Recipient Morbidity, Complication Severity and Hospitalizations:**
  - **To collect information on post-operative complications (Aim 3.6.1)**
  - **To collect information on frequency of specific complications**
  - **To collect information on post-operative resource utilization**
- **Graft Outcomes:**
  - **To compare graft outcomes in LDLT and CAD recipients**
  - **To collect information on graft loss (Aim 3.3.2)**
- **Recipient & Donor Survival:**
  - **To compare survival between LDLT & CAD recipients**
  - **To collect information on donor outcomes**

76

Assigning a Recipient Study ID#

1

- **Review and confirm the requirements on the Eligibility Checklist**
- **Find your Center ID#**
- **The Study ID for recipients is a 6-character code.**

2

- **Character 1,2 = Center ID#**
- **Character 3 = R**

- **Character 4,5,6 = sequential 3-digit code 001-999.**
- **e.g. If you're from Columbia, and this is your first recipient, then the Study ID# would be: 01R001**

77 ☐ # Assigning a Donor Study ID#

1
- **Review and confirm the requirements on the Eligibility Checklist**
- **Find your Center ID#**
- **The Study ID for recipients is a 7-character code.**

2
- **Character 1,2 = Center ID#**
- **Character 3 = D**
- **Character 4,5,6 = last 3 digits of the recipient's Study ID#.**
- **Character 7 = chronological order that this donor was for that recipient**
- **e.g. If you are from Columbia, and this is the second donor evaluated for the recipient we identified above, then the Study ID number would be: 01D0012**

78 ☐ # Study Coordinator Quizbowl!

79 ☐ # Question 1

LDLT recipient candidate Bob Badliver had 3 donors evaluated. Assign him a Study ID number. Then assign his prospective donors their Study ID numbers.
First donor, Clark Kent, DOB 4/21/60 had his H&P on 12/22/97.
Second Donor, Paul Pureliver, DOB 3/3/61, had his H&P on 2/2/98.
Third Donor, Batman Jones, DOB 11/5/57, had his H&P on 6/7/98.

80 ☐ # Bonus Question

- **What is Bob Badliver's date of enrollment?**

81 ☐ # Regulatory Binder

1
- **Retrospective Study Protocol**
- **Investigator's and sub-investigators' CV's**
  - **No date gaps**
  - **Must be signed by investigator to verify correctness**
  - **Should include medical license number and expiration date. If not included in CV, include copy of actual license in binder.**

2
- **IRB/ERC Approvals**
  - **Must specifically state approval of the protocol (protocol number, title and version)**
  - **Date of approval**
  - **Renewal date**
  - **Signed by IRB/ERC chair**

82 ☐ # Regulatory Binder

1
- **Current IRB Membership List**
  - **If your IRB/ERC does not release its membership list, a DHHS Multiple Assurance Number must be submitted on the IRB/ERC letterhead.**

2
- **Monitor Log**
- **Human Research Subject Participation Certification**
- **HIPAA Training Certification**
- **Major Correspondence**

83 The BioDBx System

Web-based Data Entry

84 BioDBx Basics

- **Every center has its own ID number**
- **Each of you will have your own password.**
- **You will access BioDBx through the A2ALL website.**
- **You will only be able to see your own center's data.**

85 Return of Study Coordinator Quizbowl!

86 Case Hx 2: Horace Heppa

1
- **48 y.o., presented for liver TXP eval. 1/2/00, listed 1/30/00**
- **7/97: Dx'd with HCV. Bx showed cirrhosis, genotype 1b. HCV RNA 1.5 million copies/ml**
- **9/99: developed ascites, Tx'd with diuretics**
- **7/97-12/97: received interferon monotherapy, no response**
- **.**

2
- **Antiviral Tx discussed at 1/2/00 visit, but not pursued**
- **3/2/00: living donor presented for evaluation, excluded because of comorbid medical conditions**
- **9/1/00: CAD liver TXP performed. Uneventful. Discharged from hospital on 10/3/00.**

87 Horace (cont'd)

1
- **1/3/01: Increase in LFT noted during routine labs, called back for evaluation**
- **1/10/01 Liver Bx showed mild inflammation and mild fibrosis**
- **1/20/01 Anti-viral Tx started x 42 weeks (Intron & Ribavirin), then DC'd because of extreme fatigue and depression.**

2
- **10/1/01: Antiviral Tx stopped. HCV RNA +**

2/27/03 LFT's increased again. Liver Bx showed increased inflammation and fibrosis

88 Horace's 2000 Labs

89 Horace's 2001 Labs

90 Horace's 2002/03 Labs

91 ☐ # Horace's Biopsy Results

92 ☐ # Case Hx 3: Sally Sirrosis

1
- **9/00: Dx'd with HCV, Bx showed cirrhosis. No antiviral Rx.**
- **6/01: US showed single 2cm nodule in rt. lobe. PV & HV patent. No enlarged lymph nodes. AFP = 15ng/ml. Chest CT & bone scan neg. for metastases.**
- **8/2/01: Listed for liver TXP**

2
- **8/10/01: AFP 19ng/ml, Radiofrequency ablation performed**
- **10/1/01 Living donor evaluated and accepted (donor is Sally's sister Sasha)**
- **11/5/01: repeat MRI, 3.5cm necrotic cavity in place of tumor. PV and HV patent. No nodes or evidence of metastases. AFP 9ng/dl**
- **11/20/01: LDLT performed.**

93 ☐ # Sally (cont'd)

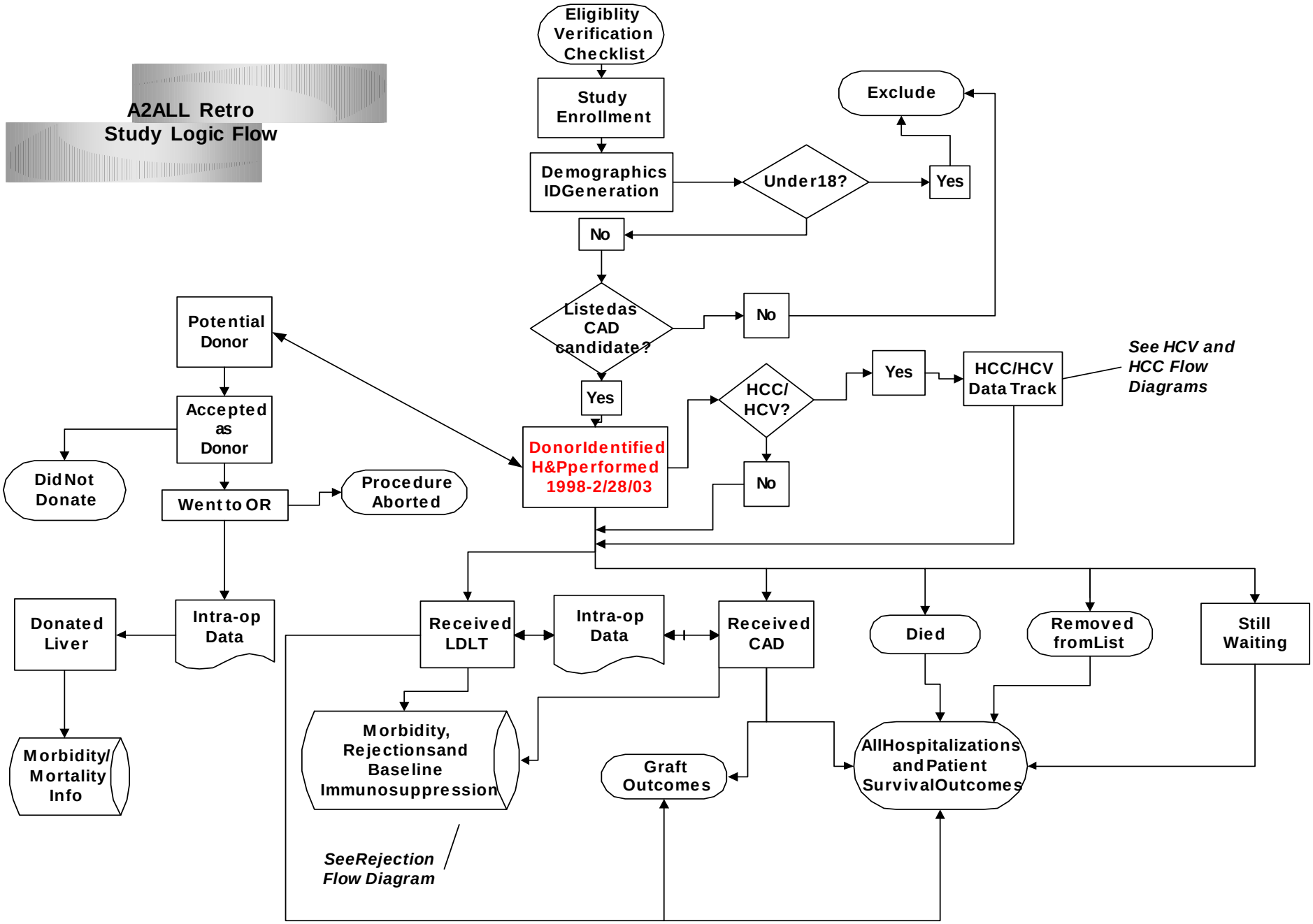
1
- **Explant Liver showed 3.5cm necrotic cavity in rt. Lobe. One 0.5cm satellite nodule that showed dysplasia, but no HCC. HV & PV patent. No lymph node or peritoneal seeding noted. Histology: scanty neoplastic cells (fewer than 10 under high power field), characteristic of well-differentiated HCC.**

2
- **5/6/02: Well post TXP. AFP 5ng/ml. Repeat MRI abdomen, CT chest and bone scan WNL.**
- **12/1/02: Continues to do well. Repeat imaging studies show no tumor recurrence**

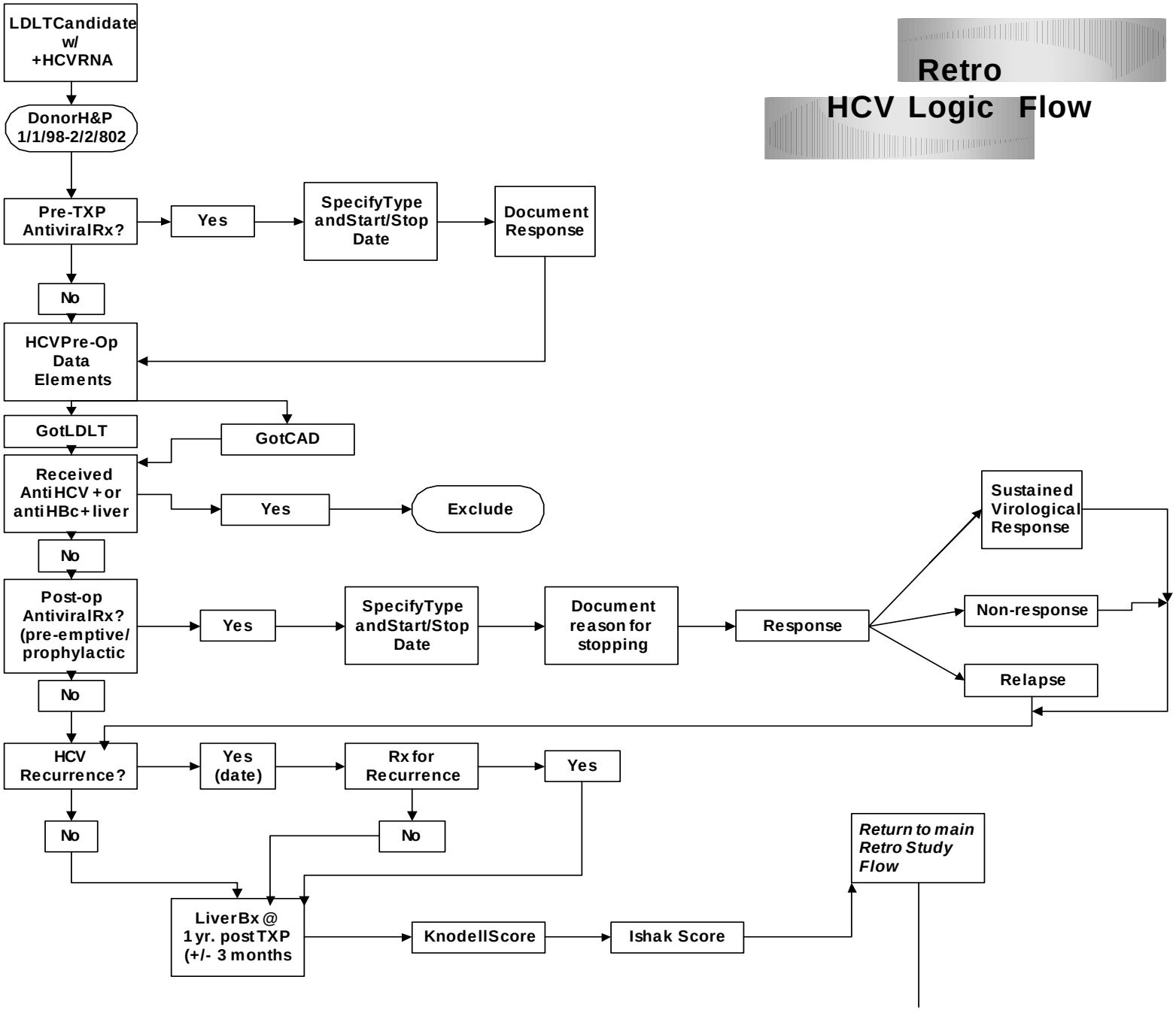
94 ☐ # First Tasks

- **Locate charts of all LDLT candidates who had a donor identified and evaluated between 1/1/98 and 2/28/03.**
- **Do the Eligibility Checklist and assign them a Study ID#**
- **Associate the prospective donors with the candidates and assign them each a Study ID#**
- **Enter the patients into the BioDBx data base.**
- **DCC will match this information to that contained in the SRTR and import that data back into BioDBx**
- **Once this has occurred, then you can begin answering questions and adding clinical data.**
- **Please note: YOU MUST HAVE SENT A COPY OF YOUR IRB APPROVAL LETTER TO THE DCC BEFORE YOU CAN ENTER DATA (OR EVEN LOOK AT CHARTS) FOR THIS STUDY!**

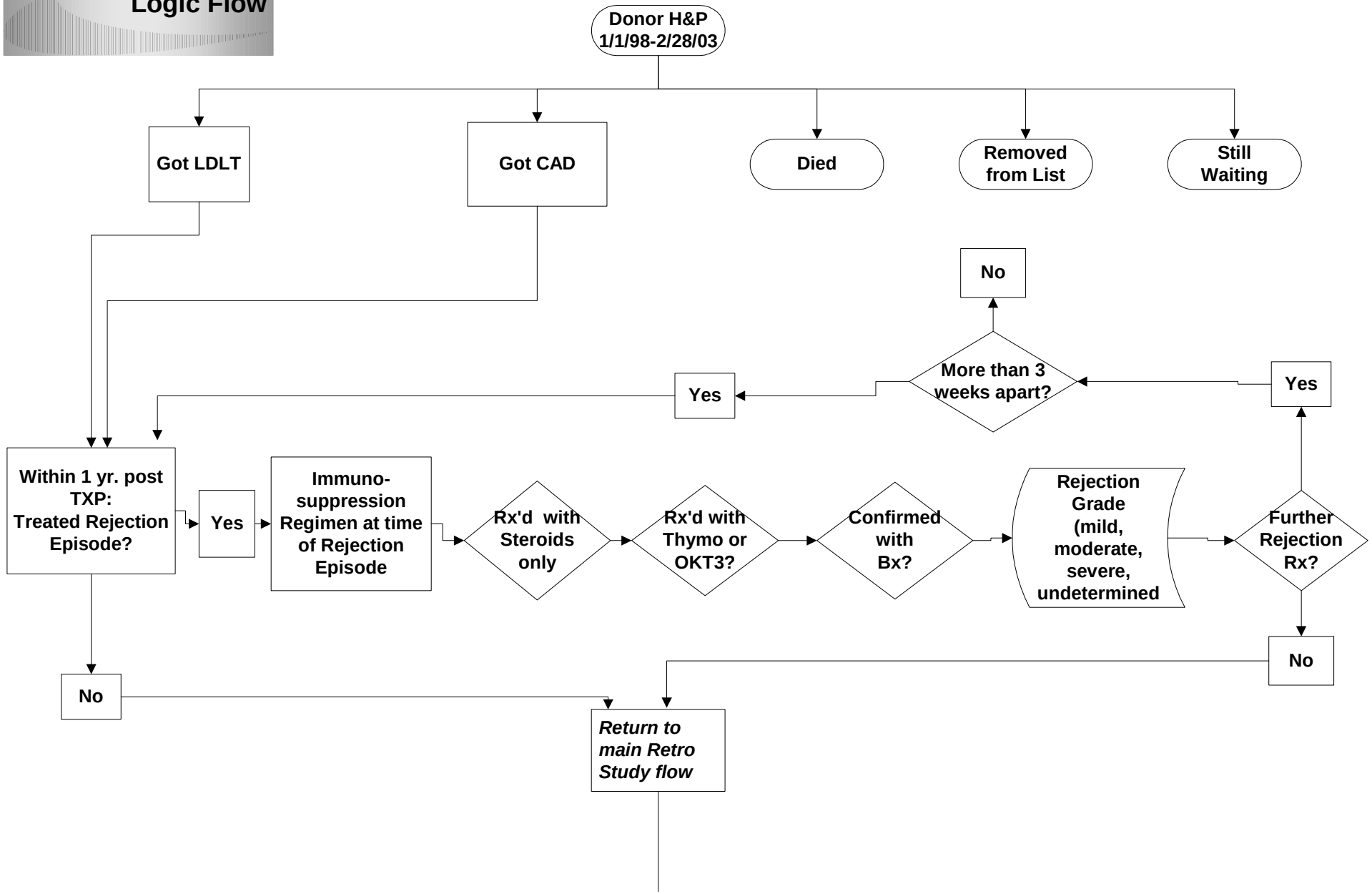
A2ALL Retro Study Logic Flow



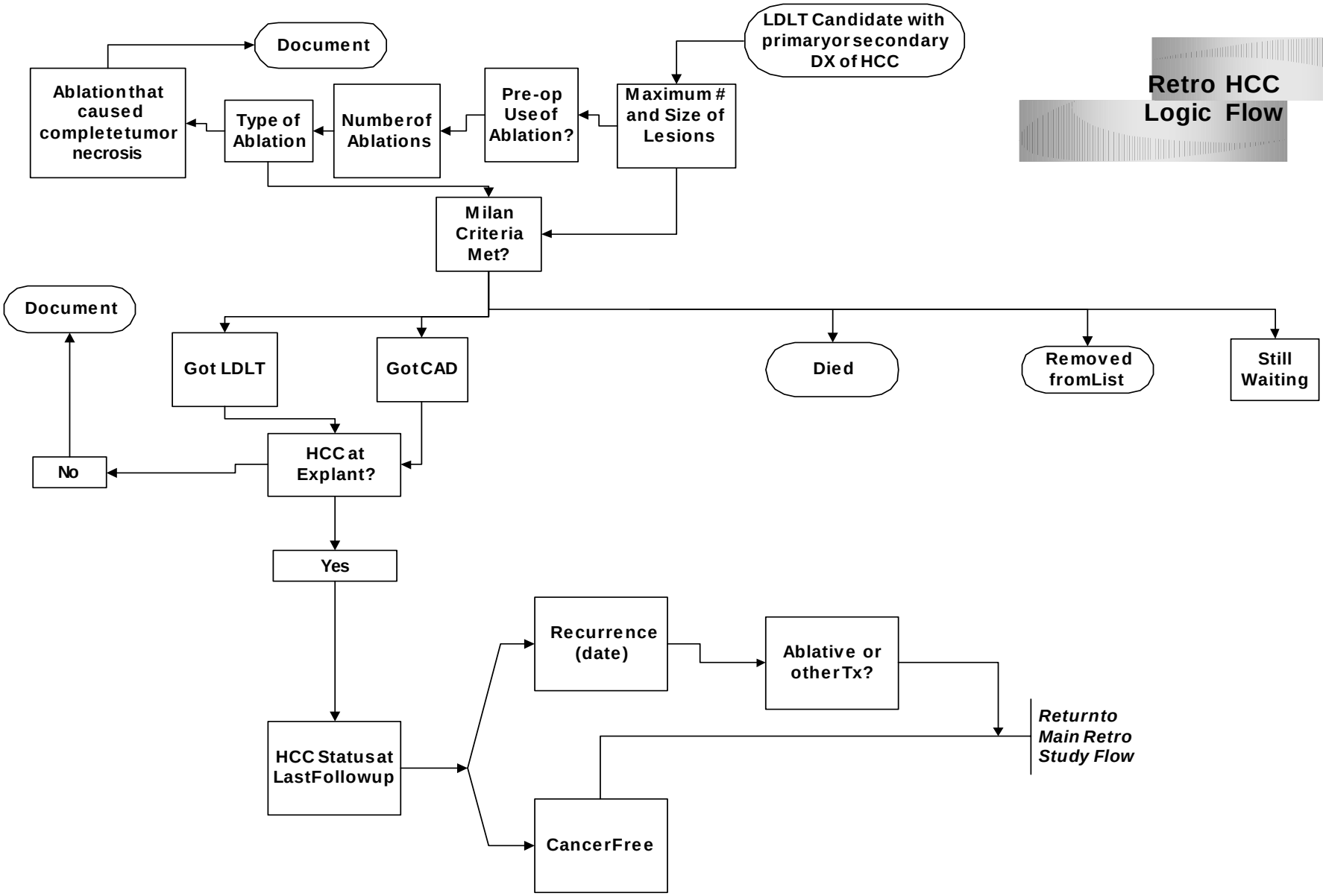
Retro HCV Logic Flow



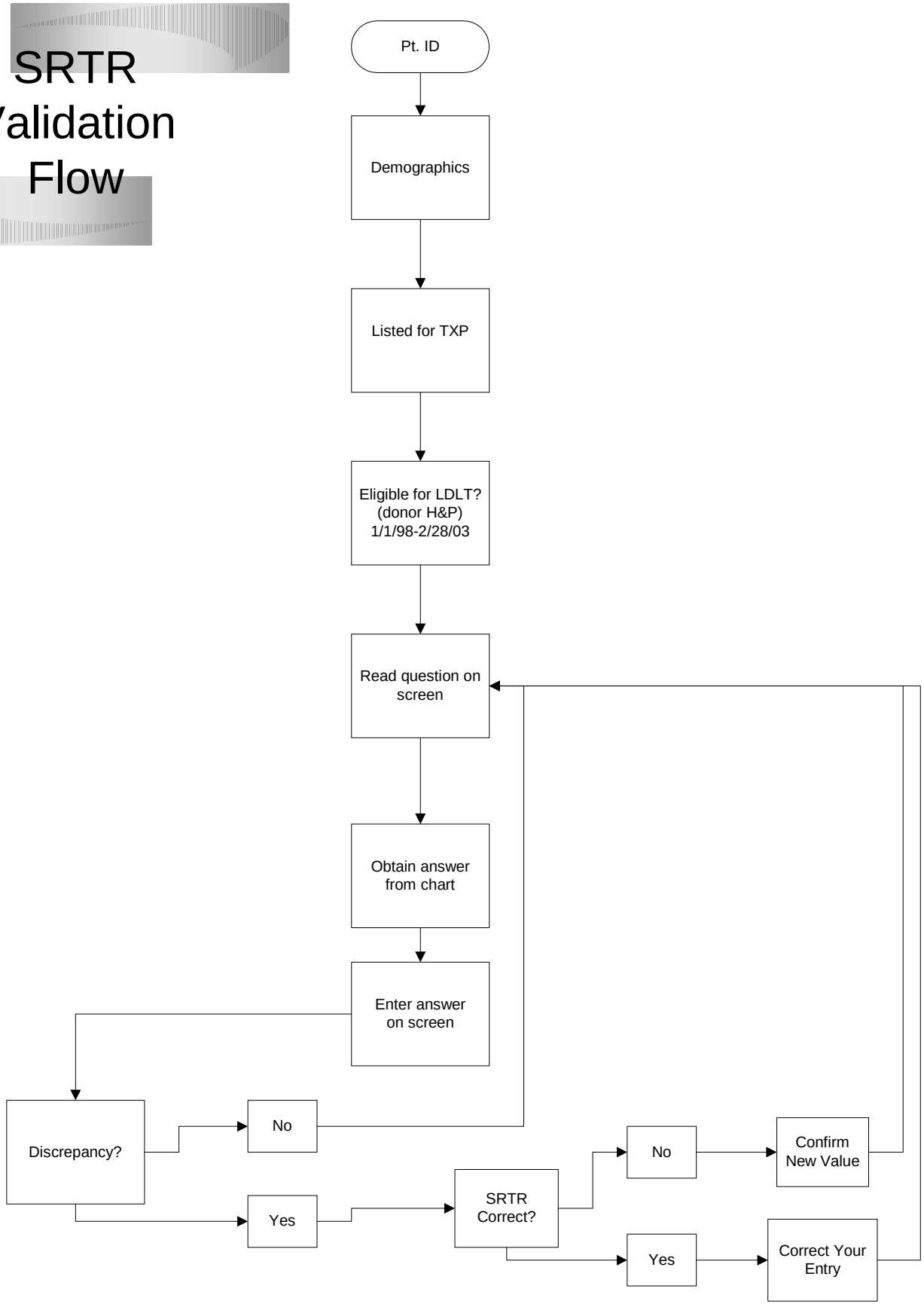
Retro Rejection Logic Flow



Retro HCC Logic Flow



SRTR Validation Flow



General Inclusion and Exclusion Criteria for the Retrospective Study

Inclusion Criteria

1. Subject ≥ 18 years of age
2. Recipient of a single organ
3. Potential donor evaluated with history and physical examination occurring between 1/1/1998 and 2/28/2003.

Exclusion Criteria

1. Subject < 18 years of age
2. Recipient of multiple organs

Inclusion and Exclusion criteria for HCV study

Inclusion Criteria

1. LDLT and cadaveric transplant patients with diagnosed HCV.
2. HCV RNA positive (within 12 months of transplant if no antiviral therapy or HCV RNA positive post-transplant).

Exclusion Criteria

1. Patients who received anti-HBc positive or anti-HCV positive organ.
2. Patients who are HCV RNA negative at last assessment prior to the time of transplant.
3. Patients who are Hep B sAg positive.

Inclusion and Exclusion criteria for HCC study

Inclusion Criteria

1. LDLT and cadaveric transplant patients with diagnosis either primary or secondary of cirrhosis and HCC.
2. Identifiable HCC at explant unless ablative therapy performed pre-operatively.

Exclusion Criteria

1. Any patient who was transplanted with a preoperative diagnosis of HCC and cirrhosis where no HCC was found at explant histology, and no prior ablation is recorded that may have caused complete necrosis of tumor leading to pathologic disappearance.

Retrospective Study Recipient Eligibility Checklist

Name: _____ **Study ID*** _____
(insert if eligible)

☐ Patient is age 18 or older at enrollment

☐ Had a donor evaluated between 1/1/98 and 2/28/03.

☐ Was listed for single-organ cadaver transplant**.

**The Study ID for recipients is a 6-character code.*

- *Character 1,2 = Center # (assigned by DCC)*
- *Character 3 = R*
- *Character 4, 5, 6 = sequential number 001-999*

** Contact DCC if otherwise eligible patient was never listed.

Retrospective Study Donor Eligibility Checklist

Name: _____ **Study ID** _____

☐ Patient is age 18 or older at enrollment

☐ Was evaluated as a donor between 1/1/98 and 2/28/03.

- *The Study ID for donors is a 7-character code.*
  - *Character 1,2 = Center Number (assigned by DCC)*
  - *Character 3 = D*
  - *Character 4,5,6 = Last 3 digits of recipient's Study ID*
  - *Character 7 = Chronologic order that this donor was evaluated for the recipient (1 = first donor evaluated, 2 = 2nd donor evaluated)*

Assigning a Study ID Number

Recipients

1. Complete the "Retrospective Study Recipient Eligibility Checklist".
    - Make sure a donor H&P occurred between 1/1/98 and 2/28/03.
    - Check the recipient's age and make sure s/he was 18 years or older at the time the living donor underwent a pre-donation H&P.
    - The patient should only have been listed for a single organ transplant.
2. Find your institution's center ID number on the list.
3. Assign a study ID number to this patient. It will be a 6-character code.
    - Character 1,2 = Center #
    - Character 3 = R
    - Character 4,5,6 = sequential three-digit code 001-999.

e.g. If you're from Columbia and this is your first recipient, the number would be: **01R001.**

Donors

1. Complete the "Retrospective Study Donor Eligibility Checklist".
    - Make sure the donor was evaluated for donation and underwent a history and physical between 1/1/98 and 2/28/03.
    - Make sure the patient was 18 years of age or older at the time of the evaluation.
2. Find your institution's center ID number on the list.
3. Assign a study ID number to this patient. The donor's Study ID is linked to the recipient. There may be several donors linked to a single recipient, and the only way for the DCC to be able to analyze along these links is if you provide accurate Study ID numbers. The donor Study ID will be a 7-character code.
    - Character 1, 2 = Center #
    - Character 3 = D
    - Character 4,5,6 = Last 3 digits of the *recipient's* Study ID
    - Character 7 = Chronologic order that this donor was evaluated for that recipient (i.e. 1 = first donor evaluated, 2 = 2nd donor evaluated, etc.

e.g. If you are from Columbia, and this is the second donor evaluated for the recipient we identified above, then the Study ID number would be: **01D0012**

Transplant Center Study ID Numbers

01 Columbia University
02 Northwestern University
03 University of Pennsylvania
04 University of Colorado
05 University of California – Los Angeles
06 University of California – San Francisco
07 University of North Carolina
08 University of Virginia
09 Virginia Commonwealth University

BioDBx

Installation instructions for the Java Initiator Certificate

Pre-Installation Step:

You must have Internet Explorer 5.5 or higher installed. To find out what version you have you can go to The Help-> About Internet Explorer and it will tell you. To update you can go to http://windowsupdate.microsoft.com and follow the links to upgrade Internet Explorer.

You must have proxy servers disabled in order to connect to the secure forms server. To disable proxy servers in IE go to Tools->Options Menu, select the Connections tab, and turn off both the "Automatic configuration script" and the "Proxy server" checkboxes.

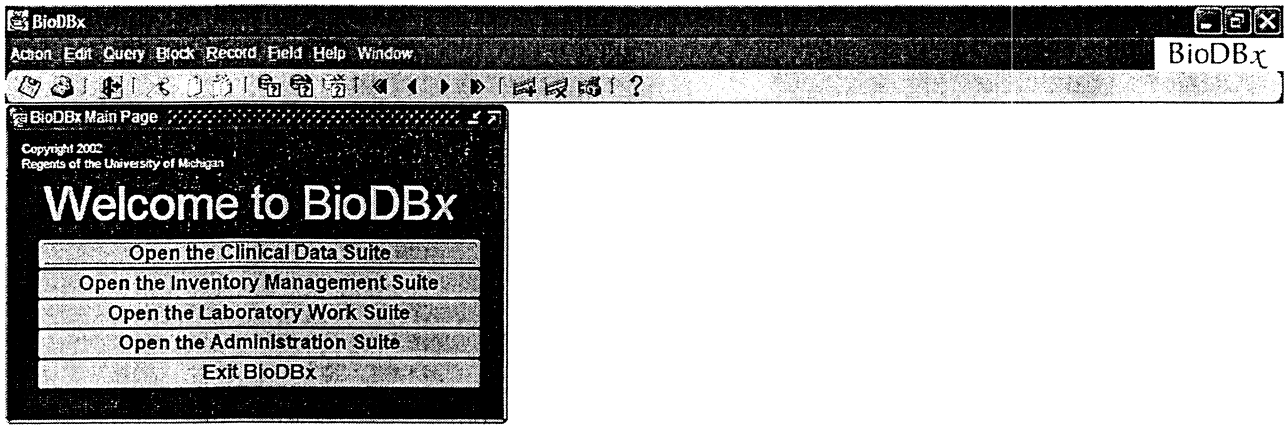
Installation Step	Comment/Description
1) Access the following URL https://biodbx.medgen.med.umich.edu . Choose a database hyper link from this site.	This should happen with no trouble. If it is the first time you've tried to run BioDBx from this location you'll see several notices. One says you're leaving a secure environment - just say OK. The second is that you need to download the Java Initiator. Just continue the Test Steps at this point.
2) Download jini.exe	Sometimes this takes a couple attempts.
3) Run jini.exe which will install Oracle Java Initiator Version 1.1.8.16	There are several steps but choose the defaults. Press NEXT all the way through. Sometimes you have to stop and restart your internet explorer session after the install.
4) Users might intermittently experience a frm-92050 error at this point. • If so Press OK and Close internet explorer. • Re-access https://biodbx.medgen.med.umich.edu and access the Certificate Installer hyper link instead of a database hyperlink. • Choose run from current location. This will install the MEDGEN certificate so that your machine chooses to trust BioDBx. • When you see the message "BioDBx ... for a new age" and the dos window is titled "finished" then you have successfully installed the certificate. • These instructions do not work for a MAC.	This step is not always required. When it is required, the outlined steps will suffice. This error is caused, in this context, by an error to communicate with the https version of the application. It is remedied by downloading and installing the certificate

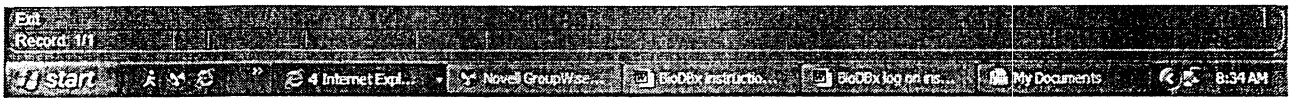
5) After the certificate is installed re-access https://biodbx.medgen.med.umich.edu and choose a database hyper link. The application should now run nicely. You'll see a new graphic as a splash screen, a new logo, and a new background.	

BioDBx

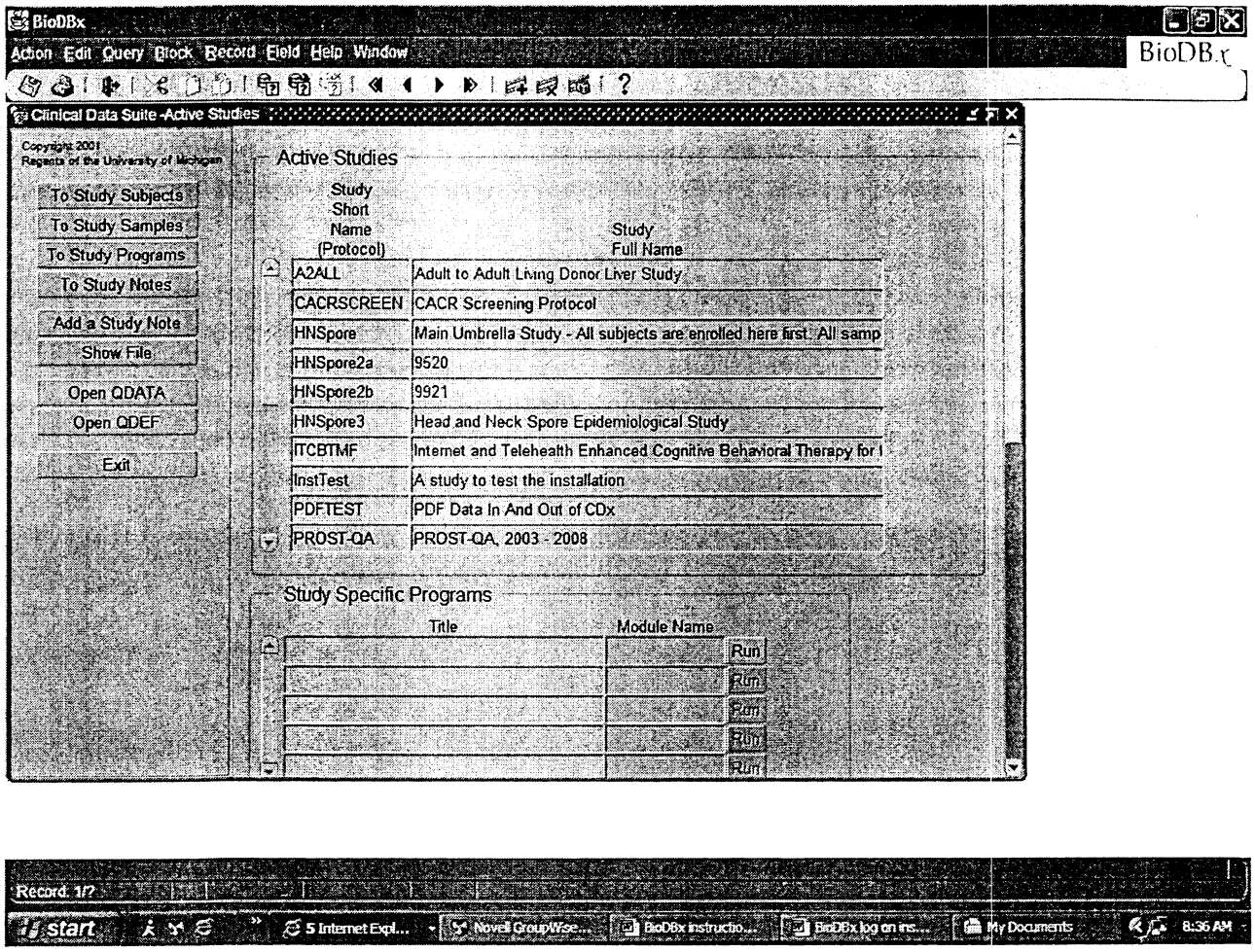
Access to BioDBx is controlled by your username and password. You must safeguard your login information and your computer when you are signed into BioDBx to prevent unauthorized changes to the study data.

Access to BioDBx is obtained through the A2ALL website www.nih-a2all.org . At the bottom of the page are links to access the certificate installer and to log on to the system. Initially this link will direct you to Java-managed portion of the system. You should see a logon screen that asks for your username and password and has the letters CACR on the bottom. You may encounter a "Security Alert" box that asks you about the Java Certificate and whether you want to continue. Please select "YES-Continue". After you logon you will see a Welcome to BioDBx message.



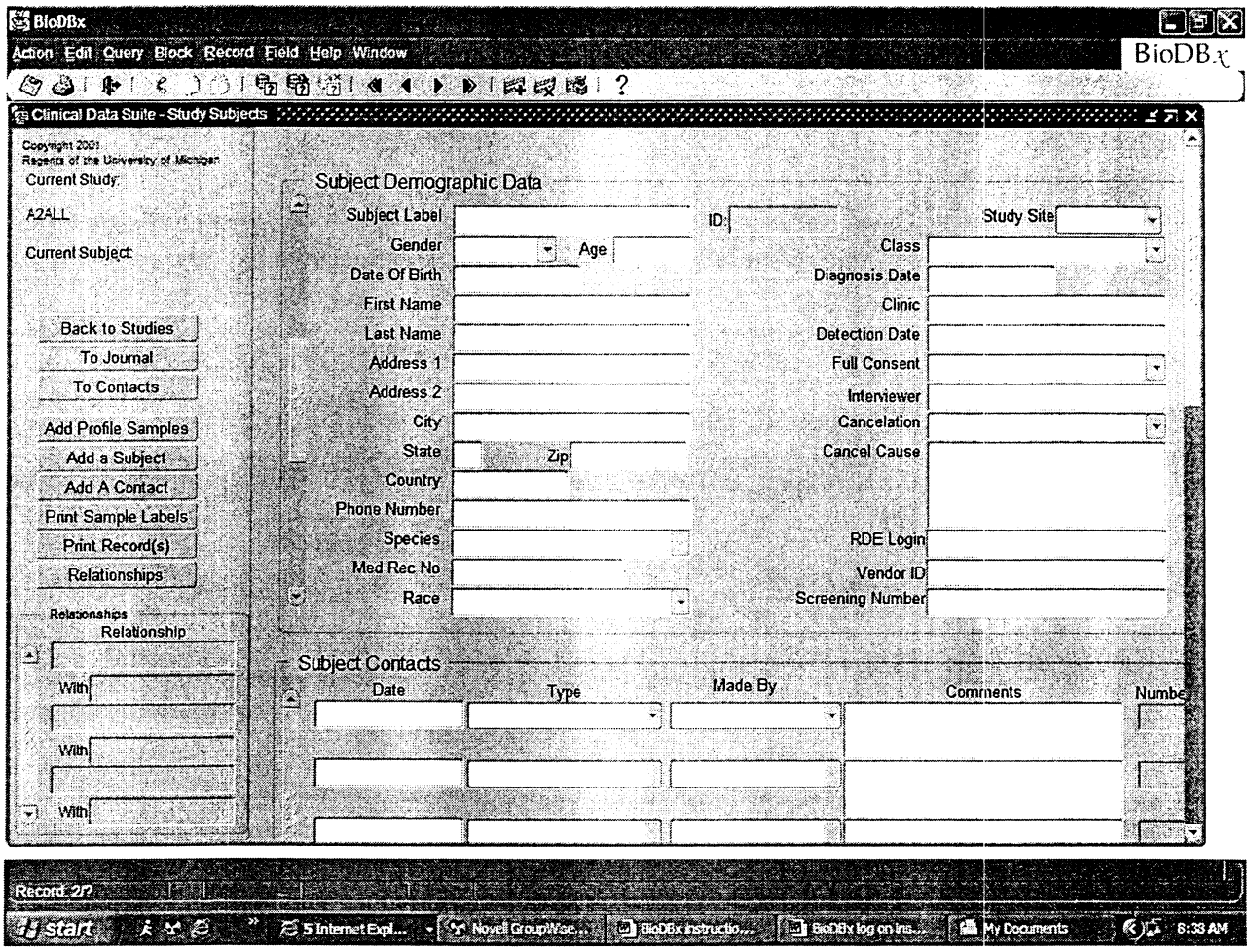


Select "Open the Clinical Data Suite" and you will see a list of studies.



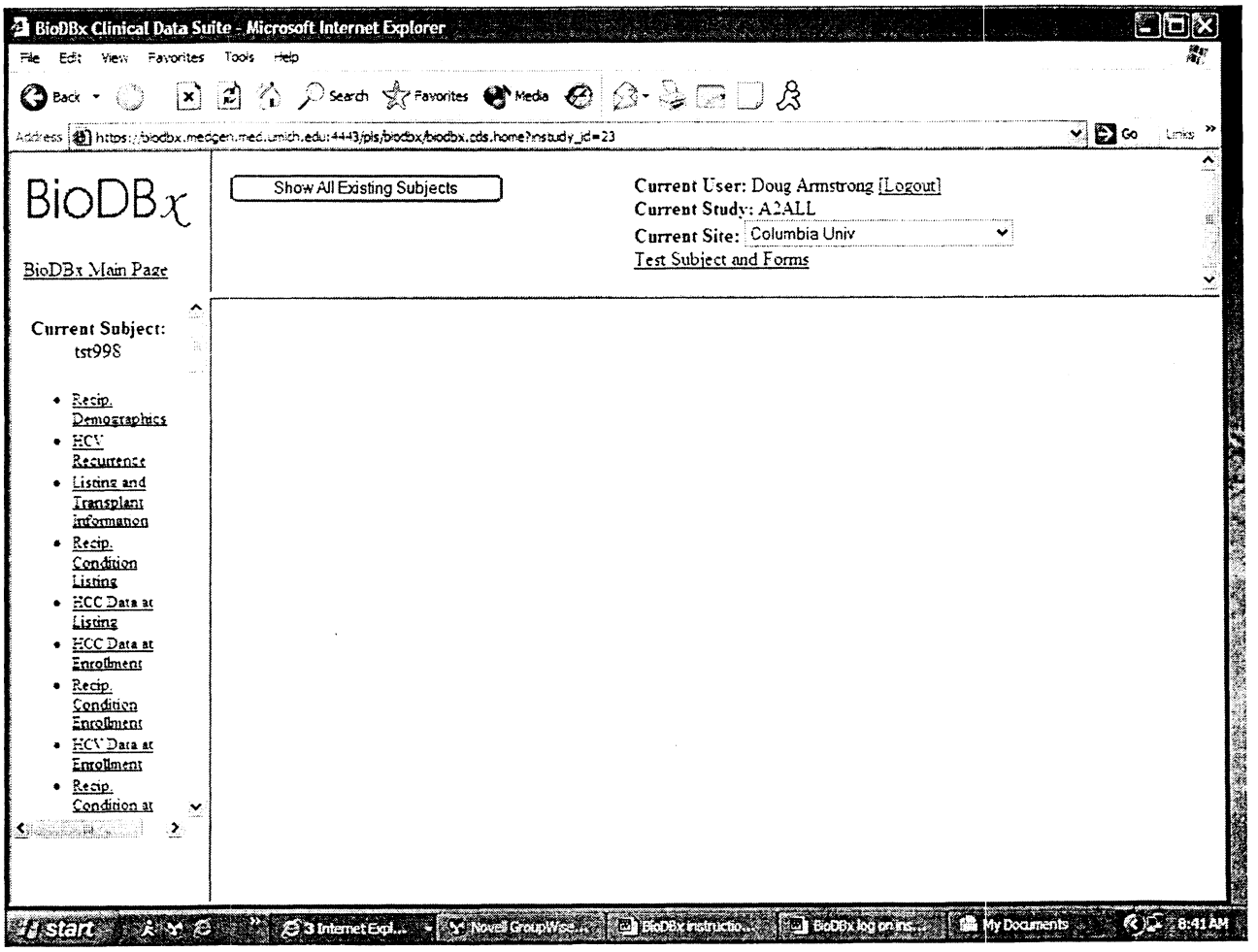
Make sure A2ALL is highlighted and then click on "To Study Subjects" button. Click on the "Add a Subject" button and this will allow you to enter the Name, DOB, SSN, Gender, Class (Donor or

Recipient), Site and Study ID number for all of your patients. There is no need to enter any of the other information on the page-please leave it blank.



Once all patients have been entered into the system (and ID numbers created) this link will be changed to direct you to the data entry portion of the study. You will not have to use the Java system after all study patients are entered.

Once the database is ready to accept clinical data entry the link on the A2ALL page will be changed. You will again be asked for your BioDBx username and password and will be directed to a Data entry web page. You will see:



Subject selection and search functions are accessed by the top buttons and data entry page selections are made from the list of links on the left. This portion of the system is currently undergoing revision so it may look slightly different on your computer screen.

You must click save after each data change before exiting the system or changing forms. BioDBx will not prompt you to save changes. Once you navigate away from a form without saving, any data that you entered will be lost.

For BioDBx or data module questions please contact:

Terri Howell 734 998-6109 email: thowell@umich.edu

or

Doug Armstrong 734 998-6588 email: darms@umich.edu

Gathering Data in a Retrospective Study

For some of you, gathering data in a retrospective study may be a new experience. Remember that a retrospective study looks back and reviews a time interval in the past. There is no patient contact involved, and all information is gathered via chart review. This means you are limited by the quantity, quality and timing of the information contained within the patient record. It is our hope that this training will help you develop strategies and systems that will enable you to gather retrospective data in an effective and efficient manner. Below are some points to remember as you approach this task.

1. Look for a documented diagnosis when gathering data on complications and morbidity. We have given you extensive definitions of what factors, symptoms and treatments might accompany these data elements. However, we do not expect you to be a diagnostician. The treating or consulting physician(s) already diagnosed the patient. Your task will be to find that in the chart. If you do not see a documented diagnosis of a complication's existence, then you should not answer "Yes" to its presence (even if you do see elements in the chart that may make up its description).
2. Sometimes events may be under-reported, and that possibility is frustrating for all of us who care about good research and usable results. Remember that we will have the opportunity to gather information on the same data elements in a much more organized and controllable fashion in the prospective study.
3. Chart review will get easier as you gain experience. It takes several trials to learn all of the eccentricities of your center's chart organization and the surgeons' and physicians' charting. While we can give you general hints where you might find certain information, the location where you actually locate it in your center's charts may differ.
4. If you have questions about the meaning of a question or data element, you should contact the DCC for definition. We would like to keep interpretation of data elements consistent so that we have consistent responses to the questions and therefore end up with good data that we can analyze and interpret.
5. If you have questions about what a notation means on a chart, then you should contact your PI for definition and interpretation.

Retrospective Study Data Modules

Recipient Data Modules

1. Recipient Enrollment Checklist
2. Recipient Study Enrollment
3. Recipient Demographics
4. Listing and Transplant Information
5. Recipient Condition at Listing
6. Recipient Condition at Enrollment
7. Recipient Condition at Transplant
8. HCC at Listing - 8a. HCC Assessment Form
9. HCC at Enrollment
10. HCC at Transplant
11. HCV at Enrollment - 11a. Knodell Score
12. HCV at Transplant
13. Recipient Intraoperative Data
14. HCC Explant Assessment
15. Recipient Baseline Immunosuppression and Rejection Episodes
16. Multiple Rejection Episodes and Treatment
17. Recipient Hospitalizations - 17a. Liver Diagnosis Codes
18. Recipient Morbidity
19. Recipient Complication Severity - 19a. Definitions of Recipient Adverse Events
20. HCV Post-op Recurrence and Rx Data
21. HCC Post-op Recurrence and Rx Data
22. Graft Outcomes
23. Recipient Patient Survival - 23a. Recipient Cause of Death Codes

Donor Data Modules

24. Donor Enrollment Checklist
25. Donor Study Enrollment
26. Donor Demographics
27. Donor Evaluation
28. Donor Intraoperative Data
29. Donor Hospitalizations- 29a. Liver Diagnosis Codes
30. Donor Morbidity
31. Donor Complication Severity - 31a. Definitions of Donor Adverse Events
32. Donor Patient Survival

Core Modules – Recipients

1. Eligibility Checklist
2. Study Enrollment
3. Demographics
4. Condition at Listing
5. Condition at Enrollment
6. Hospitalizations
7. Patient Survival
8. Listing and TXP Info

Core Modules – Donors

1. Eligibility Checklist
2. Study Enrollment
3. Demographics
4. Evaluation
5. Patient Survival

Retro Study Triggering Modules

Triggering Module	Data Element	Trigger Answer	Opened Module(s)
Recipient Condition at Listing	Recipient Hepatocellular Carcinoma at the time of listing	Yes	HCC Data at Listing
Recipient Condition at Enrollment	Recipient Hepatocellular Carcinoma at the time of enrollment	Yes	HCC Data at Enrollment
Recipient Condition at Enrollment	Recipient HCV at the time of enrollment	Yes	HCV Data at Enrollment
Listing & TXP Information	TXP Surgery	Yes	Recipient Intraoperative Data Recipient Condition at TXP
Listing & TXP **AND** Recipient Condition at TXP	TXP Surgery Recipient HCC at time of TXP	Yes Yes	HCC Data at Transplant
Listing & TXP **AND** Recipient Condition at TXP	TXP Surgery Recipient HCV at time of TXP	Yes Yes	HCV Data at Transplant
Listing & TXP Information	Liver TXP Performed	Yes	Recipient Post-operative Morbidity Graft Outcomes Basic Immunosuppression and Rejection Information
Recipient Post-Operative Morbidity	Multiple Data Elements that direct you to fill out a severity form.	Yes	Recipient Complication Severity
Graft Outcomes	Retransplantation	Yes	Graft Outcomes
HCC Data at Transplant **AND** Listing & TXP Information	Presence of Module/CRF Liver TXP Performed	Yes Yes	HCC Explant Assessment HCC Post-op Recurrence and Rx Data
HCV Data at Transplant **AND** Listing & TXP Information	Presence of Module/CRF Liver TXP Performed	Yes Yes	HCV Post-op Recurrence and Rx Data
Baseline Immunosuppression and Rejection Episodes	Number of Rejection Episodes	>1	Multiple Rejection Episodes and Treatment (fill out for each episode)
Donor Evaluation	Donor Acceptance	Yes	Donor Intraoperative Data
Donor Intraoperative Data	Procedure Aborted	No	Donor Morbidity Donor Hospitalizations
Donor Morbidity	Each Complication	Yes	Donor Complication Severity

Retro Study Triggering Modules

Donor Intraoperative Data	Procedure Aborted	Yes	Donor Hospitalizations

Retrospective Study Recipient Eligibility Checklist

Name: _____ **Study ID*** _____
(insert if eligible)

☐ Patient is age 18 or older at enrollment

☐ Had a donor evaluated between 1/1/98 and 2/28/03.

☐ Was listed for single-organ cadaver transplant**.

**The Study ID for recipients is a 6-character code.*

- *Character 1,2 = Center # (assigned by DCC)*
- *Character 3 = R*
- *Character 4, 5, 6 = sequential number 001-999*

** Contact DCC if otherwise eligible patient was never listed.

Recipient Study Enrollment

Revised 03/27/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Recipient Study ID Number	Record the Recipient's Study ID number from the Eligibility checklist	00R000	Enrollment Checklist	No
Recipient last name	Recipient surname	Text	Face sheet	No*
Recipient first name	Recipient first name	Text	Face sheet	No*
Recipient middle initial	Recipient middle initial	Text	Face sheet	No*
Recipient date of birth	Recipient date of birth	mmddyyyy	Face sheet	No*
Recipient SSN	Recipient SSN	000000000	Face sheet	No*
Recipient gender	Recipient gender	Male Female	Face sheet	No*
Potential donor H&P date	Date that recipient's potential donor had their H&P (defines enrollment date for recipient)	mmddyyyy	Donor records	No

N.B. Not included, but present in SRTR (from TCR): Previous surname, permanent zip code, waiting zip code

* These data elements will be used to identify each participant in the SRTR database. Once the link is established, selected SRTR data will be compared with newly-entered A2ALL data for validation

Recipient Demographics

Revised 04/09/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Recipient state of permanent residence at enrollment	Recipient state of permanent residence at enrollment	Two-character state abbreviation	Face sheet	No
Recipient ethnicity	Recipient ethnicity	Hispanic/Latino Non-Hispanic/Non-Latino	Face sheet	Yes
Recipient race	Recipient race (select one or more)	White Black or African-American American Indian or Alaskan Native Asian Native Hawaiian or Other Pacific Islander Mid-east or Arabian Indian sub-continent	Face sheet	Yes
Recipient ABO blood type	Recipient ABO blood type	A B O AB	Laboratory	Yes
Recipient highest education level at enrollment	Recipient highest education level at enrollment	None Grade school (0-8) High school (9-12) Attended college/Technical school Associate/Bachelor degree Post-college graduate degree Unknown	Social history	Yes

Listing and Transplant Information

Revised 04/15/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Date of Listing	What is the date of listing for liver transplant? If patient has had previous liver transplants, see MOO for further instructions.	mmddyyyy	Outpatient Notes	Y
De-Listing Information	Has the patient been removed from the waiting list since the date of listing?	Y N	Outpatient Notes	Y
(if Yes to de-listing) Reason for removal from list	What was the reason(s) the patient was removed from the waiting list from your TC?	Medically Unsuitable Refused Transplant Transferred to Another Center Died Candidate listed in error Candidate condition worsened Candidate condition improved Candidate removed in error Changed to KP (by system) Program inactive for 2+ years Patient died during transplant procedure Non Compliant Financial Issues Psychosocial Issues Other	Outpatient Notes Autopsy Social Work Notes Lab result	Y
Transplant Surgery	Was the patient brought to the operating room with the intention of receiving a liver transplant after the date of study enrollment?	Y N	Outpatient Notes Operative Notes Inpatient Notes Anesthesia Record Autopsy Record	N
Liver Transplant Information	Did the patient receive a liver transplant after the date of study enrollment?	Y N	Outpatient Notes	Y

Recipient Condition at Listing

Revised 04/25/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Recipient previous liver transplants	Recipient previous liver transplants	Yes No	Inpatient/outpatient notes Transplant evaluation	Yes
Recipient medical condition at listing	Recipient medical condition at listing	Patient in ICU Hospitalized, not in ICU Not Hospitalized	Inpatient/outpatient notes Transplant evaluation	Yes
Recipient on life support at listing	Recipient on life support at listing	Yes No	Inpatient/outpatient notes Transplant evaluation	Yes
(if yes to life support) Recipient on ventilator at listing	Recipient on ventilator at listing	Yes No	Inpatient/outpatient notes Transplant evaluation	Yes
Recipient functional status at listing	At the time of listing how well did patient perform daily activities of daily living?	No activity limitations. (NYHA Class I or Class II) Performs activities of daily living with some assistance. (NYHA Class III) Performs activities of daily living with total assistance. (NYHA Class IV) N/A Patient hospitalized Unknown	Inpatient/outpatient notes Social History	Yes
Recipient employment status at listing	Select the one choice that best describes the Recipient employment status at time of listing. **Working** indicates that patient is employed inside/outside the home or attending school. **Not Working** indicates that patient is unemployed and not attending school.	Working full time Working part time by choice Working part time due to disease Working part time reason unknown Not working by choice Not working due to disease Not working, unable to find employment Not working, reason unknown Retired Employment status unknown	Inpatient/outpatient notes Social History	Yes

Recipient height	Recipient height	0.0	Inpatient/outpatient notes Transplant evaluation	Yes
Recipient height units	Recipient height units	Inches Centimeters	Inpatient/outpatient notes Transplant evaluation	Yes
Recipient weight at listing	Recipient weight closest to the date of listing	0.0	Inpatient/outpatient notes Transplant evaluation	Yes
Recipient weight units at listing	Recipient weight units at listing	Pounds Kilograms	Inpatient/outpatient notes Transplant evaluation	Yes
Recipient primary diagnosis at listing	Recipient diagnosis 1 at the time of listing (order does not matter)	OPTN diagnosis codes*	Inpatient/outpatient notes Transplant evaluation	Yes**
Recipient secondary diagnosis at listing	Recipient diagnosis 2 at the time of listing (order does not matter)	OPTN diagnosis codes*	Inpatient/outpatient notes Transplant evaluation	Yes**
Recipient tertiary diagnosis at listing	Recipient diagnosis 3 at the time of listing (order does not matter)	OPTN diagnosis codes*	Inpatient/outpatient notes Transplant evaluation	Yes**
Recipient hepatocellular carcinoma diagnosis at the time of listing	Recipient hepatocellular carcinoma diagnosis at the time of listing	Yes No	Inpatient/outpatient notes Biopsy/pathology reports	No
Recipient hepatitis C diagnosis at the time of listing	Recipient hepatitis C diagnosis at the time of listing	Yes No	Inpatient/outpatient notes Biopsy/pathology reports	No
Recipient encephalopathy	Recipient experiencing signs/symptoms of encephalopathy at the time of listing	Yes No Unknown	Inpatient/outpatient notes Transplant evaluation	Yes
Recipient variceal bleeding within 2 weeks prior to listing	Recipient was experiencing variceal bleeding from varices present in the esophagus	Yes No Unknown	Inpatient/outpatient notes Procedure Reports (ERCP, EGD)	Yes

	and/or stomach within 2 weeks prior to listing			
Recipient ascites	More than one pint (500 ml) of fluid in recipient abdominal cavity within 2 weeks prior to listing	Yes No Unknown	Inpatient/outpatient notes Procedure Reports (CT, US)	Yes
Recipient previous upper abdominal surgery	Recipient previous upper abdominal surgery prior to listing	Yes No Unknown	Inpatient/outpatient notes Transplant evaluation	Yes
(If Yes to Previous Upper Abdominal Surgery) Type of Upper Abdominal Surgery	What type(s) of upper abdominal surgery has the patient had prior to listing?	Cholescystectomy Gastric Resection Ulcer Operation Small Bowel Resection Other	Inpatient/outpatient notes Transplant Evaluation	N
Recipient spontaneous bacterial peritonitis	Recipient currently being treated or exhibiting signs/symptoms of spontaneous bacterial peritonitis at time of listing	Yes No Unknown	Inpatient/outpatient notes Transplant evaluation	Yes
Recipient history of TIPSS	Recipient history of TIPSS (Transjugular intrahepatic portacava stent shunt) prior to listing	Yes No Unknown	Inpatient/outpatient notes Transplant evaluation	Yes
Recipient diabetes mellitus	Recipient diabetes mellitus at time of listing	No Insulin-dependent Non-insulin dependent Yes, type unknown Unknown diabetes mellitus status	Inpatient/outpatient notes Transplant evaluation	Yes
(If “insulin-dependent”, “non-insulin dependent”, or “Yes, type unknown) answered on previous question) Diabetes Treatment	What diabetic treatment is the patient receiving?	Insulin Oral Agent Both insulin and oral agent No Medications	Inpatient/outpatient Notes Transplant Evaluation Drug Orders	No
Recipient dialysis	Recipient receiving dialysis at time of listing	No Hemodialysis/CVVHD Peritoneal dialysis Dialysis – unknown type was performed Unknown	Inpatient/outpatient notes Transplant evaluation	Yes
Recipient angina/coronary artery disease	Documented signs/symptoms of Angina or CAD prior to or at	Yes No Unknown	Inpatient/outpatient notes. Cardiology stress test, EKG,	No

	listing.		functional tests. Transplant evaluation	
Recipient drug treated systemic hypertension	Recipient drug treated systemic hypertension	Yes No Unknown	Inpatient/outpatient notes Transplant evaluation Medication Orders	Yes
Recipient serum creatinine at listing	Recipient serum creatinine closest and prior to listing (mg/dL)	0.0	Laboratory	Yes
Recipient total serum albumin	Recipient total serum albumin closest and prior to listing (g/dL)	0.0	Laboratory	Yes
Recipient total serum bilirubin	Recipient total serum bilirubin closest and prior to listing (mg/dL)	0.0	Laboratory	No
Recipient INR	Recipient INR closest and prior to listing	0.0	Laboratory	No

N.B. Not included, but present in SRTR (from TCR): Citizenship, life support modalities other than ventilator (mostly cardiac), previous transplant other than liver, source of payment data, liver medical factors: marked muscle wasting, history of portal vein thrombosis, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, drug treated COPD, pulmonary embolism within last 6 months, any previous transfusion, any previous malignancy, PRA>10%,

* See appendix A (LiverDGNFormatList.xls).
** Edit check will look for any diagnosis match regardless of field position (SRTR captures up to 2 diagnoses).

Recipient Condition at Enrollment

Revised 04/25/2003

Data element	Definition	Answer format	Location in chart	SRTR validation	Data module
Donor H&P date	Pre-populated from Study Enrollment form	mmddyyyy	N/A	N/A	Study enrollment
Recipient medical condition at enrollment	Recipient medical condition on the date that the potential donor had their H&P	Patient in ICU Hospitalized, not in ICU Not Hospitalized	Inpatient/outpatient notes	No	Recipient condition at enrollment
Recipient on life support at enrollment	Recipient on life support on the date that the potential donor had their H&P	Yes No	Inpatient/outpatient notes	No	Recipient condition at enrollment
(If yes to life support) Recipient on ventilator at enrollment	Recipient on ventilator on the date that the potential donor had their H&P	Yes No	Inpatient/outpatient notes	No	Recipient condition at enrollment
Recipient functional status at enrollment	At the time of enrollment how well did patient perform activities of daily living at the time of the potential donor's H&P?	No activity limitations. (NYHA Class I or Class II) Performs activities of daily living with some assistance. (NYHA Class III) Performs activities of daily living with total assistance. (NYHA Class IV) N/A Patient hospitalized Unknown	Inpatient/outpatient notes	No	Recipient condition at enrollment
Recipient employment status at enrollment	Select the one choice that best describes the Recipient employment status at time of donor H&P. **Working** indicates that patient is employed inside/outside the home or attending school. **Not Working** indicates that patient is unemployed andnot attending school.	Working full time Working part time by choice Working part time due to disease Working part time reason unknown Not working by choice Not working due to disease Not working, unable to find employment Not working, reason unknown Retired Employment status unknown	Inpatient/outpatient notes	No	Recipient condition at enrollment
Recipient weight at enrollment	Recipient weight closest to the date that the potential donor had their H&P	0.0	Inpatient/outpatient notes	No	Recipient condition at enrollment

Recipient weight units at enrollment	Recipient weight units	Pounds Kilograms	Inpatient/outpatient notes	No	Recipient condition at enrollment
Recipient primary diagnosis at listing	Pre-populated from Recipient Condition at Listing form	OPTN diagnosis codes*	N/A	N/A	Recipient condition at listing
Recipient secondary diagnosis at listing	Pre-populated from Recipient Condition at Listing form	OPTN diagnosis codes*	N/A	N/A	Recipient condition at listing
Recipient tertiary diagnosis at listing	Pre-populated from Recipient Condition at Listing form	OPTN diagnosis codes*	N/A	N/A	Recipient condition at listing
Recipient diagnoses changed between listing and enrollment	Recipient diagnoses changed between listing and enrollment	Yes No	Inpatient/outpatient notes	No	Recipient condition at enrollment
Recipient primary diagnosis at enrollment (only if changed)	Recipient diagnosis 1 at the time of enrollment (order does not matter)	OPTN diagnosis codes*	N/A	N/A	Recipient condition at enrollment
Recipient secondary diagnosis at enrollment (only if changed)	Recipient diagnosis 2 at the time of enrollment (order does not matter)	OPTN diagnosis codes*	N/A	N/A	Recipient condition at enrollment
Recipient tertiary diagnosis at enrollment (only if changed)	Recipient diagnosis 3 at the time of enrollment (order does not matter)	OPTN diagnosis codes*	N/A	N/A	Recipient condition at enrollment
Recipient hepatocellular carcinoma diagnosis at the time of enrollment	Recipient hepatocellular carcinoma diagnosis at the time of enrollment	Yes No	Inpatient/outpatient notes Biopsy/pathology results	No	Recipient condition at enrollment
Recipient hepatitis C diagnosis at the time of enrollment	Recipient hepatitis C diagnosis at the time of enrollment	Yes No	Inpatient/outpatient notes Biopsy/pathology results	No	Recipient condition at enrollment
Recipient encephalopathy	Recipient had encephalopathy prior to enrollment	Yes No Unknown	Inpatient/outpatient notes	No	Recipient condition at enrollment
Recipient variceal bleeding	Recipient had variceal bleeding prior to enrollment	Yes No Unknown	Inpatient/outpatient notes Procedure Reports (ERCP, ERGD)	No	Recipient condition at enrollment
Recipient ascites	Recipient had ascites prior to enrollment	Yes No Unknown	Inpatient/outpatient notes Procedure Reports (CT, US)	No	Recipient condition at enrollment
Recipient previous upper abdominal surgery	Recipient previous upper abdominal surgery prior to	Yes No	Inpatient/outpatient notes	No	Recipient condition at enrollment

	enrollment	Unknown			
(If Yes to Previous Upper Abdominal Surgery) Type of Upper Abdominal Surgery	What type(s) of upper abdominal surgery has the patient had prior to enrollment?	Cholescystectomy Gastric Resection Ulcer Operation Small Bowel Resection Other	Inpatient/outpatient notes Transplant Evaluation	N	Recipient Condition at enrollment
Recipient spontaneous bacterial peritonitis	Recipient spontaneous bacterial peritonitis prior to enrollment	Yes No Unknown	Inpatient/outpatient notes	No	Recipient condition at enrollment
Recipient history of TIPSS	Recipient history of TIPSS (Transjugular intrahepatic portacava stent shunt) prior to enrollment	Yes No Unknown	Inpatient/outpatient notes	No	Recipient condition at enrollment
Recipient diabetes mellitus	Recipient diabetes mellitus at time of enrollment	No Insulin-dependent Non-insulin dependent Yes, type unknown Unknown diabetes mellitus status	Inpatient/outpatient notes	No	Recipient condition at enrollment
(If “insulin-dependent”, “non-insulin dependent”, or “Yes, type unknown) answered on previous question) Diabetes Treatment	What diabetic treatment is the patient receiving?	Insulin Oral Agent Both insulin and oral agent No Medications	Inpatient/outpatient Notes Transplant Evaluation Drug Orders	No	Recipient Condition at enrollment
Recipient dialysis	Recipient receiving dialysis at time of enrollment	No Hemodialysis/CVVHD Peritoneal dialysis Dialysis – unknown type was performed Unknown	Inpatient/outpatient notes	No	Recipient condition at enrollment
Recipient angina/coronary artery disease	Documented signs/symptoms of Angina or CAD prior to enrollment	Yes No Unknown	Inpatient/outpatient notes. Cardiology stress test, EKG, functional tests.	No	Recipient condition at enrollment
Recipient drug treated systemic hypertension	Recipient drug treated systemic hypertension at enrollment	Yes No Unknown	Inpatient/outpatient notes	No	Recipient condition at enrollment
Recipient serum creatinine at listing	Recipient serum creatinine closest to enrollment (mg/dL)	0.0	Laboratory	No	Recipient condition at enrollment
Recipient total serum albumin	Recipient total serum albumin closest to enrollment (g/dL)	0.0	Laboratory	No	Recipient condition at enrollment
Recipient total serum	Recipient total serum	0.0	Laboratory	No	Recipient condition at

bilirubin	bilirubin closest to enrollment (mg/dL)				enrollment
Recipient INR	Recipient INR closest to enrollment	0.0	Laboratory	No	Recipient condition at enrollment

N.B. Not included, but present in SRTR (from TCR): Citizenship, life support modalities other than ventilator (mostly cardiac), previous transplant other than liver, source of payment data, liver medical factors: marked muscle wasting, history of portal vein thrombosis, symptomatic cerebrovascular disease, symptomatic peripheral vascular disease, drug treated COPD, pulmonary embolism within last 6 months, any previous transfusion, any previous malignancy, PRA>10%

* See appendix A (LiverDGNFormatList.xls).

Recipient Condition at Transplant

Revised 04/25/2003

Data element	Definition	Answer format	Location in chart	SRTR validation	Data module
Recipient medical condition immediately prior to transplant	Recipient medical condition immediately prior to transplant	Patient in ICU Hospitalized, not in ICU Not Hospitalized	Inpatient/outpatient notes Transplant admission note	Yes	Recipient condition at transplant
Recipient on life support immediately prior to transplant	Recipient on life support immediately prior to transplant	Yes No	Inpatient/outpatient notes Transplant admission note	Yes	Recipient condition at transplant
(If yes to life support) Recipient on ventilator immediately prior to transplant	Recipient on ventilator immediately prior to transplant	Yes No	Inpatient/outpatient notes Transplant admission note	Yes	Recipient condition at transplant
Recipient functional status immediately prior to transplant	At the time of transplant how well did patient perform activities of daily living?	No activity limitations. (NYHA Class I or Class II) Performs activities of daily living with some assistance. (NYHA Class III) Performs activities of daily living with total assistance. (NYHA Class IV) N/A Patient hospitalized Unknown	Inpatient/outpatient notes Transplant admission note	Yes	Recipient condition at transplant
Recipient employment status immediately prior to transplant	Select the one choice that best describes the Recipient employment status at time transplant. **Working** indicates that patient is employed inside/outside the home or attending school. **Not Working** indicates that patient is unemployed and not attending school.	Working full time Working part time by choice Working part time due to disease Working part time reason unknown Not working by choice Not working due to disease Not working, unable to find employment Not working, reason unknown Retired Employment status unknown	Inpatient/outpatient notes Transplant admission note/discharge summary	Yes	Recipient condition at transplant
Recipient weight immediately prior to transplant	Recipient weight immediately prior to transplant	0.0	Inpatient/outpatient notes Transplant admission note/anesthesia	Yes	Recipient condition at transplant

			prepop note		
Recipient weight units immediately prior to transplant	Recipient weight units	Pounds Kilograms	Inpatient/outpatient notes	Yes	Recipient condition at transplant
Recipient primary diagnosis at enrollment	Pre-populated from Recipient Condition at Enrollment form	OPTN diagnosis codes*	N/A	N/A	Recipient condition at enrollment
Recipient secondary diagnosis at enrollment	Pre-populated from Recipient Condition at Enrollment form	OPTN diagnosis codes*	N/A	N/A	Recipient condition at enrollment
Recipient tertiary diagnosis at enrollment	Pre-populated from Recipient Condition at Enrollment form	OPTN diagnosis codes*	N/A	N/A	Recipient condition at enrollment
Recipient diagnoses changed between enrollment and transplant	Recipient diagnoses changed between enrollment and transplant	Yes No	Inpatient/outpatient notes	Yes	Recipient condition at transplant
Recipient primary diagnosis at transplant (only if changed)	Recipient diagnosis 1 at the time of transplant (order does not matter)	OPTN diagnosis codes*	N/A Transplant admission note	N/A	Recipient condition at transplant
Recipient secondary diagnosis at transplant (only if changed)	Recipient diagnosis 2 at the time of transplant (order does not matter)	OPTN diagnosis codes*	N/A Transplant admission note	N/A	Recipient condition at transplant
Recipient tertiary diagnosis at transplant (only if changed)	Recipient diagnosis 3 at the time of transplant (order does not matter)	OPTN diagnosis codes*	N/A Transplant admission note	N/A	Recipient condition at transplant
Recipient hepatocellular carcinoma diagnosis at the time of transplant	Recipient hepatocellular carcinoma diagnosis at the time of transplant	Yes No	Inpatient/outpatient notes Transplant admission note	No	Recipient condition at transplant
Recipient hepatitis C diagnosis at the time of transplant	Recipient hepatitis C diagnosis at the time of transplant	Yes No	Inpatient/outpatient notes Transplant admission note	No	Recipient condition at transplant
Recipient grade III or IV encephalopathy at transplant	Recipient grade III or IV encephalopathy at the time of transplant	Yes No Unknown	Inpatient/outpatient notes	Yes	Recipient condition at transplant
Recipient uncontrollable variceal bleeding at transplant	Recipient uncontrollable variceal bleeding at the time of transplant	Yes No Unknown	Inpatient/outpatient notes	Yes	Recipient condition at transplant
Recipient ascites	More than one pint (500 ml) of fluid in recipient abdominal cavity at the time of transplant	Yes No Unknown	Inpatient/outpatient notes	Yes	Recipient condition at transplant

Recipient previous abdominal surgery at Transplant	Any Recipient previous upper abdominal surgery prior to transplant	Yes No Unknown	Inpatient/outpatient notes Transplant admission note	No	Recipient condition at transplant
(If Yes to Previous Upper Abdominal Surgery) Type of Upper Abdominal Surgery	What type(s) of upper abdominal surgery has the patient had prior to transplant	Cholescystectomy Gastric Resection Ulcer Operation Small Bowel Resection Other	Inpatient/outpatient notes Transplant Evaluation	N	Recipient Condition at transplant
Recipient spontaneous bacterial peritonitis	Recipient spontaneous bacterial peritonitis at the time of transplant	Yes No Unknown	Inpatient/outpatient notes Transplant admission note	Yes	Recipient condition at transplant
Recipient history of TIPSS	Recipient history of TIPSS (Transjugular intrahepatic portacava stent shunt) at the time of transplant	Yes No Unknown	Inpatient/outpatient notes Transplant admission note	Yes	Recipient condition at transplant
Recipient diabetes mellitus	Recipient diabetes mellitus at transplant	No Insulin-dependent Non-insulin dependent Yes, type unknown Unknown diabetes mellitus status	Inpatient/outpatient notes Transplant admission note	No	Recipient condition at transplant
(If “insulin-dependent”, “non-insulin dependent”, or “Yes, type unknown) answered on previous question) Diabetes Treatment	What diabetic treatment is the patient receiving?	Insulin Oral Agent Both insulin and oral agent No Medications	Inpatient/outpatient Notes Transplant Evaluation Drug Orders	No	Recipient Condition at transplant
Recipient dialysis	Recipient receiving dialysis at transplant	Yes No Unknown	Inpatient/outpatient notes Transplant admission note	Yes	Recipient condition at transplant
Recipient angina/coronary artery disease	Documented signs/symptoms of Angina or CAD prior to transplant	Yes No Unknown	Inpatient/outpatient notes. Cardiology stress test, EKG, functional tests. Transplant admission note Medication Orders Procedure Notes (US, angiogram)	No	Recipient condition at transplant
Recipient drug treated systemic hypertension	Recipient drug treated systemic hypertension at transplant	Yes No Unknown	Inpatient/outpatient notes Transplant	No	Recipient condition at transplant

			admission note Medication Orders		
Recipient serum creatinine immediately prior to transplant	Recipient serum creatinine immediately prior to transplant (mg/dL)	0.0	Laboratory	Yes	Recipient condition at transplant
Recipient total serum albumin	Recipient total serum albumin immediately prior to transplant (g/dL)	0.0	Laboratory	Yes	Recipient condition at transplant
Recipient total serum bilirubin	Recipient total serum bilirubin immediately prior to transplant (mg/dL)	0.0	Laboratory	Yes	Recipient condition at transplant
Recipient INR	Recipient INR (prothrombin) immediately prior to transplant	0.0	Laboratory	Yes	Recipient condition at transplant

N.B. Not included, but present in SRTR (from TRR): Risk factors (marked muscle wasting, incidental tumor found at time of transplant, inotropes for blood pressure support, portal vein thrombosis), pre-transplant serum lab data (SGOT/AST, SGPT/ALT, alkaline phosphatase)

* See appendix A (LiverDGNFormatList.xls).

HCC Data at Listing

Revised 04/25/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Lobar Staging	Is HCC located in the right lobe, left lobe, or both lobes of the liver?	Right Lobe Only Left Lobe Only Bilobar	Transplant evaluation Imaging Studies	N
Number of HCC Nodules in the liver	How many HCC nodules were identified in the subject's liver immediately prior to or at listing? If there is a conflict between reports, record maximum number.	1 2 3 4 5 >5	Transplant evaluation Imaging Studies	N
Size of each Nodule	What was the maximum diameter of each nodule identified?	Nodule 1 = ___cm Nodule 2 = ___cm Nodule 3 = ___cm Nodule 4 = ___cm Nodule 5 = ___cm Nodule 6 = ___cm	Transplant evaluation Imaging Studies	N
Vascular Invasion	Was there HCC tumor invasion into vascular structures?	N Y, portal vein Y, other vascular structures	Transplant Evaluation Imaging Studies	N
(if Yes, portal vein) What are the location(s) of tumor invasion on the portal vein?	What are the location(s) of tumor invasion on the portal vein?	Main Portal Vein Right Portal Vein Left Portal Vein Right-sided Branches Left-sided Branches	Transplant Evaluation Imaging Studies	N
Primary Tumor Classification	Based on the number and size of HCC nodules, and the presence or absence of vascular invasion, the classification stages are as follows: T0: Not found T1: one nodule < 1.9cm T2: one nodule 2.0-5.0cm OR 2-3 nodules all < 3.0cm,.	T0 T1 T2 T3 T4a T4b TX	Transplant Evaluation Imaging Studies	N

	T3: one nodule >5.0cmOR 2-3 nodules at least one >3.0cm. T4a: 4 or more nodules, any size. T4b: T2, T3 or T4a plus gross intrahepatic portal or hepatic vein involvement as indicated by CT, MRI or ultrasound. TX: not assessed				
Nodal Status	Was there evidence of HCC found in the regional lymph nodes? Record: N0 : no regional (porta hepatitis) nodes involved N1: regional (porta hepatitis) nodes involved or NX: not assessed.	N0 N1 NX		Transplant Evaluation Imaging Studies	N
Metastatic Status	Has the cancer spread beyond the liver? Record: M0: no metastatic disease including extrahepatic portal or hepatic vein involvement. M1 metastatic disease including extrahepatic portal or hepatic vein involvement. MX not assessed	M0 M1 MX		Transplant Evaluation Imaging Studies	N
TNM Stage	Record the TNM Stage of the HCC immediately prior to or at listing. The TNM classification is based on the following: Table 1. pTNM staging for HCC		Stage I Stage II Stage III Stage IVA1 Stage IVA2 Stage IVB	Transplant Evaluation Imaging Studies	N

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
Stage IVA1	T4a		
Stage IVA2	T4b		
Stage IVB	Any T	Any N1	M1

American Joint Committee on Cancer

1. HCC PREOPERATIVE ASSESSMENT FORM

This form is completed with pre-operative data.

1. C. Preoperative HCC Diagnosis

The data used to complete this section is derived from the last CT scan, MRI or biopsy obtained for the patient prior to transplantation. The TNM classification is based on the following:

Table 1. pTNM staging for HCC

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1	N1	M0
	T2	N1	M0
	T3	N0	M0
	T3	N1	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

American Joint Committee on Cancer

Primary tumor (T)

- T0: No evidence of primary tumor
- T1: Solitary tumor 2 cm or less, no vascular invasion
- T2: Solitary tumor 2 cm or less with vascular invasion OR
  - Multiple tumors, one lobe, </= 2 cm, without vascular invasion, OR
  - Solitary tumor > 2cm without vascular invasion
- T3: Solitary tumor > 2 cm with vascular invasion OR
  - Multiple tumors, one lobe, </= 2 cm with vascular invasion, OR
  - Multiple tumors, one lobe, >2 cm with / without vascular invasion
- T4: Multiple tumors, more than one lobe, OR
  - Any tumor(s) invading major branch of portal or hepatic veins

Regional lymph nodes (N)

- N0: No regional lymph nodes
- N1: Regional lymph node

Distant metastases (M)

- M1: No distant metastases
- M2: Distant metastases

1. HCC IMMEDIATE POSTPERATIVE ASSESSMENT

This form is completed with immediate post-operative data within the first two weeks after transplantation.

1. C. Post-operative HCC Diagnosis

Post operative findings are documented from the histopathologic report obtained from the explanted liver.

HCC Data at Enrollment

Revised 04/25/2003

Data element	Definition	Answer format	Location in chart	SRTR validation	Data module
Lobar Staging	Is HCC located in the right lobe, left lobe, or both lobes of the liver?	Right Lobe Only Left Lobe Only Bilobar	Transplant evaluation Imaging Studies	N	HCC Data at Enrollment
Number of HCC Nodules in the liver	How many HCC nodules were identified in the subject's liver at the time of study enrollment? If there is a conflict between reports, record maximum number.	1 2 3 4 5 >5	Transplant evaluation Imaging Studies	N	HCC Data at Enrollment
Size of each Nodule	What was the maximum diameter of each nodule identified?	Nodule 1 = ___cm Nodule 2 = ___cm Nodule 3 = ___cm Nodule 4 = ___cm Nodule 5 = ___cm Nodule 6 = ___cm	Transplant evaluation Imaging Studies	N	HCC Data at Enrollment
Vascular Invasion	Was there HCC tumor invasion into vascular structures?	N Y, portal vein Y, other vascular structures	Transplant Evaluation Imaging Studies	N	HCC Data at Enrollment
(if Yes, portal vein) What are the location(s) of tumor invasion on the portal vein?	What are the location(s) of tumor invasion on the portal vein?	Main Portal Vein Right Portal Vein Left Portal Vein Right-sided Branches Left-sided Branches	Transplant Evaluation Imaging Studies	N	HCC Data at Enrollment
Primary Tumor Classification	Based on the number and size of HCC nodules, and the presence or absence of vascular invasion, the classification stages are as follows: T0: Not found T1: one nodule < 1.9cm T2: one nodule 2.0-5.0cm OR 2-3 nodules all < 3.0cm,.	T0 T1 T2 T3 T4a T4b TX	Transplant Evaluation Imaging Studies	N	HCC Data at Enrollment

	T3: one nodule >5.0cmOR 2-3 nodules at least one >3.0cm. T4a: 4 or more nodules, any size. T4b: T2, T3 or T4a plus gross intrahepatic portal or hepatic vein involvement as indicated by CT, MRI or ultrasound. TX: not assessed				
Nodal Status	Was there evidence of HCC found in the regional lymph nodes? Record: N0 : no regional (porta hepatitis) nodes involved N1: regional (porta hepatitis) nodes involved or NX: not assessed.	N0 N1 NX	Transplant Evaluation Imaging Studies	N	HCC Data at Enrollment
Metastatic Status	Has the cancer spread beyond the liver? Record: M0: no metastatic disease including extrahepatic portal or hepatic vein involvement. M1 metastatic disease including extrahepatic portal or hepatic vein involvement. MX not assessed	M0 M1 MX	Transplant Evaluation Imaging Studies	N	HCC Data at Enrollment
TNM Stage	Record the TNM Stage of the HCC at enrollment. The TNM classification is based on the following: Table 1. pTNM staging for HCC Stage I T1 N0 M0 Stage II T2 N0 M0 Stage III T3 N0 M0 Stage IVA1 T4a Stage IVA2 T4b Stage IVB Any T Any N1 M1 American Joint Committee on Cancer	Stage I Stage II Stage III Stage IVA1 Stage IVA2 Stage IVB	Transplant Evaluation Imaging Studies	N	HCC Data at Enrollment
Ablations	How many ablations has the	0-10	Procedure	N	HCC Data at

	patient prior to enrollment? (record 0 for none)		reports		Enrollment
(if 1-10 ablations performed) Type of Ablations	What type of ablative procedures were performed? Choose as many as apply and note the number performed for each type of intervention	Radiofrequency Ablation Cryotherapy Alcohol Ablation Chemoembolization Chemoinfusion Surgical Resection	Procedure reports	N	HCC Data at Enrollment
(if yes to surgical resection) Type of Surgical Resection	What type of surgical resection was performed?	Wedge Segment Lobe	Procedure Reports Operative Reports		
Chemotherapy/Radiotherapy	Has the patient received chemotherapy or radiation treatment to treat HCC prior to enrollment?	Y, systemic Y, regional N	Transplant Evaluation Pharmacy Orders	N	HCC Data at Enrollment
(If Yes to Chemotherapy/Radiotherapy) Chemotherapeutic Agent(s) used.	Identify the chemotherapeutic agents used to treat the patient prior to enrollment. Include the chemotherapeutic agent utilized if chemoinfusion/chemoembolization ablative treatment was used.	Adriamycin Cisplatin 5FU Radiotherapy Unknown Other	Transplant Evaluation Pharmacy Orders	N	HCC Data at Enrollment
AFP	Record the alpha feta protein result closest to enrollment. If no value, record N/A	ng/ml N/A	Lab Results	N	HCC Data at Enrollment

HCC Data Immediately Prior to Transplant

Revised 04/25/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Date of last abdominal CT scan or MRI prior to transplantation that was used to stage HCC	Record the date of the last abdominal CT scan or MRI that occurred prior to transplantation. All answers regarding the tumor staging/description will come from this imaging study.	mmddyyyyy	Imaging Studies	N
Lobar Staging	Is HCC located in the right lobe, left lobe, or both lobes of the liver?	Right Lobe Only Left Lobe Only Bilobar	Transplant evaluation Imaging Studies	N
Number of HCC Nodules in the liver	How many HCC nodules were identified in the subject's liver? If there is a conflict between reports, record maximum number.	1 2 3 4 5 >5	Transplant evaluation Imaging Studies	N
Size of each Nodule	What was the maximum diameter of each nodule identified?	Nodule 1 = ___cm Nodule 2 = ___cm Nodule 3 = ___cm Nodule 4 = ___cm Nodule 5 = ___cm Nodule 6 = ___cm	Transplant evaluation Imaging Studies	N
Vascular Invasion	Was there HCC tumor invasion into vascular structures?	N Y, portal vein Y, other vascular structures	Transplant Evaluation Imaging Studies	N
(if Yes, portal vein) What are the location(s) of tumor invasion on the portal vein?	What are the location(s) of tumor invasion on the portal vein?	Main Portal Vein Right Portal Vein Left Portal Vein Right-sided Branches Left-sided Branches	Transplant Evaluation Imaging Studies	N
Primary Tumor Classification	Based on the number and size of HCC nodules, and the presence or absence of vascular invasion, the classification stages are as follows: T0: Not found T1: one nodule < 1.9cm T2: one nodule 2.0-5.0cm OR 2-3 nodules all < 3.0cm,.	T0 T1 T2 T3 T4a T4b TX	Transplant Evaluation Imaging Studies	N

	T3: one nodule >5.0cmOR 2-3 nodules at least one >3.0cm. T4a: 4 or more nodules, any size. T4b: T2, T3 or T4a plus gross intrahepatic portal or hepatic vein involvement as indicated by CT, MRI or ultrasound. TX: not assessed			
Nodal Status	Was there evidence of HCC found in the regional lymph nodes? Record: N0 : no regional (porta hepatitis) nodes involved N1: regional (porta hepatitis) nodes involved or NX: not assessed.	N0 N1 NX	Transplant Evaluation Imaging Studies	N
Metastatic Status	Has the cancer spread beyond the liver? Record: M0: no metastatic disease including extrahepatic portal or hepatic vein involvement. M1 metastatic disease including extrahepatic portal or hepatic vein involvement. MX not assessed	M0 M1 MX	Transplant Evaluation Imaging Studies	N
TNM Stage	Record the TNM Stage of the HCC immediately prior to transplant. The TNM classification is based on the following: Table 1. pTNM staging for HCC Stage I T1 N0 M0 Stage II T2 N0 M0 Stage III T3 N0 M0 Stage IVA1 T4a Stage IVA2 T4b Stage IVB Any T Any N1 M1 American Joint Committee on Cancer	Stage I Stage II Stage III Stage IVA1 Stage IVA2 Stage IVB	Transplant Evaluation Imaging Studies	N
Ablations	How many ablations has the patient received prior to transplant? (record 0 for none)	0-10	Procedure reports	N
(if 1-10 ablations performed) Type of Ablations	What type of ablative procedures were performed? Choose as many as apply and note the number performed for each type of intervention	Radiofrequency Ablation Cryotherapy Alcohol Ablation Chemoembolization Chemoinfusion Surgical Resection	Procedure reports	N
(if yes to surgical resection) Type of Surgical Resection	What type of surgical resection was performed?	Wedge Segment	Procedure Reports	

		Lobe	Operative Reports	
Chemotherapy/Radiotherapy	Has the patient received chemotherapy and/or radiation treatment to treat HCC prior to transplant?	Y, systemic Y, regional/local N	Transplant Evaluation Pharmacy Orders	N
(If Yes to Chemotherapy/Radiotherapy) Chemotherapeutic Agent(s) used	Identify the chemotherapeutic agents used to treat the patient between enrollment and transplant. Include the chemotherapeutic agent utilized if chemoinfusion/chemoembolization ablative treatment was used.	Adriamycin Cisplatin 5FU Radiotherapy Unknown Other	Transplant Evaluation Pharmacy Orders	N
AFP	Record the alpha feta protein result closest to transplant. If no value, record N/A	ng/ml N/A	Lab Results	N

HCV Data at Enrollment

Revised 04/30/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
HCV RNA	Record last available test closest to enrollment	Positive Negative Indeterminate Not done	Lab reports	No
Date of HCV RNA	Record the date of the test	mmddyyyy	Lab reports	No
Serum Aspartate Transaminase (AST)	Record value closest to date of enrollment	IU/L	Lab reports	No
Serum Alanine Aminotransferase (ALT)	Record value closest to date of enrollment	IU/L	Lab reports	No
Serum Alkaline Phosphate (ALK)	Record value closest to date of enrollment	u/L	Lab reports	No
Serum Total Bilirubin	Record value closest to date of enrollment	mg/dl	Lab reports	No
HCV Treatment	Was the patient receiving anti-viral treatment at time of enrollment?	Y N	Transplant Evaluation	No
(If yes to HCV Treatment) HCV Treatment Method	What type of HCV treatment(s) was the patient receiving at time of enrollment? (Note answer may be one of the interferons + ribavirin)	Standard Interferon PEG Interferon Ribavirin	Transplant Evaluation	No
Start Date of HCV Treatment	Record the date of initiation of HCV treatment?	mmddyyyy	Transplant Evaluation	No
Stop date of HCV treatment	Record the date of completion of HCV treatment? (Note stop date should be after enrollment)	mmddyyyy	Transplant Evaluation	No
Prior HCV Treatment	Did the patient complete a course of HCV treatment prior to enrollment (do not count ongoing treatment that was occurring at the time of enrollment)?	Y N	Transplant Evaluation	NO
(if Yes to Prior HCV Treatment)	What was the length of HCV treatment course prior to enrollment?	< 3 months 3-6 months > 6 months	Transplant Evaluation	No
(if Yes to Prior HCV Treatment) Prior HCV Treatment Method	What type of HCV treatment(s) was the patient receiving at time of enrollment? (Note answer may be one of the interferons + ribavirin)	Standard Interferon PEG Interferon Ribavirin	Transplant Evaluation	No

HCV Data at Transplant

Revised 04/21/2003

Data element	Definition	Answer format	Location in chart	SRTR validation	Data module
HCV RNA	Record last available test prior to transplant	Positive Negative Indeterminate Not available	Lab reports	No	HCV pre-op data at transplant
Date of HCV RNA	Record the date of the test	mmddyyyy	Lab reports	No	HCV pre-op data at transplant
HCV genotype	Record(s) result obtained at any time prior to transplant	Genotype 1, subtype unspecified or mixed 1a 1b 2 3 4 5 6 others not available	Lab reports	No	HCV pre-op data at transplant
Serum Aspartate Transaminase (AST)	Record value closest to date of transplant	IU/L	Lab reports	Yes	HCV pre-op data at transplant
Serum Alanine Aminotransferase (ALT)	Record value closest to date of transplant	IU/L	Lab reports	Yes	HCV pre-op data at transplant
Serum Alkaline Phosphate (ALK)	Record value closest to date of transplant	u/L	Lab reports	Yes	HCV pre-op data at transplant
Serum Total Bilirubin	Record value closest to date of transplant	mg/dl	Lab reports	Yes	HCV pre-op data at transplant
HCV Treatment	Was the patient **initiated** on anti-viral treatment after enrollment?	Y N	Transplant Evaluation	No	HCV pre-op data at transplant
(If yes to HCV Treatment) HCV Treatment Method	What type of HCV treatment did the patient receive after enrollment? (Note may be interferon + ribavirin)	Standard Interferon PEG Interferon Ribavirin	Transplant Evaluation	No	HCV pre-op data at transplant
Start Date of HCV Treatment	Record the date of initiation of HCV treatment after enrollment	mmddyyyy	Transplant Evaluation	No	HCV pre-op data at transplant
Stop Date of HCV Treatment	Record the date of completion of HCV treatment after enrollment?	mmddyyyy	Transplant Evaluation	No	HCV pre-op data at transplant

Recipient Intraoperative Data

Revised 04/30/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Date of Surgery	Record the date of the transplant surgery.	mmddyyyy	Operative Notes	Y
Procedure Aborted	Was the transplant procedure aborted before completion?	Y N	Recipient Intraoperative Notes Donor Intraoperative Notes	N
(if yes to Procedure Aborted) Reason(s) for Procedure Abortion	Why was the procedure aborted? Check all that apply.	Quality of donor liver Insufficient liver mass Technical difficulties in donor Donor Instability Unexpected medical findings in recipient Recipient Instability Recipient Death on table Other (specify)	Recipient Intraoperative Notes Donor Intraoperative Notes	N
Graft Type	What graft type did the recipient receive?	1. Cadaveric Whole 2. Cadaveric Split 3. Cad Other 4. Right lobe living donor 5. Living Donor Other	Recipient Intraoperative Notes Donor Intraoperative Notes	Y
(If cadaveric whole graft) Whole cadaveric arterial anatomy	Describe the donor whole cadaveric arterial anatomy	1. Normal 2. Total Replaced L 3. Total Replaced R 4. Replaced L and R 5. Accessory L 6. Accessory R 7. Accessory L and R 8. Other (specify):	Recipient Intraoperative Notes Donor Intraoperative Notes	Y
Back-table arterial reconstruction for whole cadaveric donor	Describe the back-table arterial reconstruction for whole cadaveric donor	1. Not required 2. Celiac to superior mestenteric artery 3. Accessory or replaced R to splenic 4. Accessory or replaced R to gastroduodenal artery 5. Other (specify):	Recipient Intraoperative Notes Donor Intraoperative Notes	N
Cold Ischemia Time	What was the cold ischemia time (from time of donor cross clamp to the time the liver was	00 minutes	Recipient Intraoperative Notes Donor	Y

	taken out of ice) in minutes?		Intraoperative Notes	
Portal and Arterial Reperfusion Information	Are portal and arterial reperfusion performed separately or simultaneously?	Separately Simultaneously Unknown	Recipient Intraoperative Notes Donor Intraoperative Notes	N
(if previous answer is separately) Warm Ischemia Time	Time (in minutes) from when the liver is taken out of ice until portal reperfusion.	00 minutes	Recipient Intraoperative Notes Donor Intraoperative Notes	N
(if previous answer is separately) Time to Arterialization	Time (in minutes) from portal reperfusion to time of arterial reperfusion	00 minutes	Recipient Intraoperative Notes Donor Intraoperative Notes	N
(if portal & arterial perfusion are performed simultaneously) Warm ischemia time	Time (in minutes) from when the liver is taken out of ice to portal and arterial reperfusion.	00 minutes	Recipient Intraoperative Notes Donor Intraoperative Notes	N
Total Time of Surgery	What was the total time of surgery? (from entering into OR until departure from OR)	____ hours ____ minutes	Recipient Intraoperative Notes Donor Intraoperative Notes	N
(if yes to Living Donor) Number of Living Donor Hepatic Venous Anastomoses	How many hepatic venous anastomoses were perfomed?	1 2 3 4	Recipient Intraoperative Notes Donor Intraoperative Notes	N
Site(s) of Living Donor to Recipient Anastomoses	Describe each donor and corresponding recipient anastomotic site utilizing the following codes. Donors: 1 = Right hepatic vein (RHV) 2 = Middle hepatic vein (MHV) 3 = Inferior right hepatic vein (IHV) 4 = Other (specify):	Donor Site _____ to Recipient Site _____	Recipient Intraoperative Notes Donor Intraoperative Notes	N

	Recipients: 1 = Hepatic venous confluence 2 = RHV 3 = IHV 4 = MHV 5 = Other (specify)			
Back-Table Hepatic Venous Reconstruction	Did back-table venous reconstruction occur?	Y N	Recipient Intraoperative Notes Donor Intraoperative Notes	N
(if yes to back-table hepatic venous reconstruction) Type of Back-Table Hepatic Venous Reconstruction	Describe the type of back-table hepatic venous reconstruction.	1. Venoplasty 2. Graft venous anastomosis 3. Other (specify):		
(if Graft Venous Anastomosis Chosen) Type of Graft Venous Anastomosis	What type of graft was utilized to achieve hepatic venous reconstruction (e.g. donor iliac vein)?	Text field		
(if yes to cadaveric donor) Cadaveric Donor Piggy Back	Was the cadaveric graft done as a piggy back?	Y N	Recipient Intraoperative Notes Donor Intraoperative Notes	N
Number of Cadaveric Donor Portal Anastomoses	How many portal venous anastomoses were performed?	1 2 3 4 5	Recipient Intraoperative Notes Donor Intraoperative Notes	N
Site(s) of Cadaveric Donor to Recipient Antastomoses	Describe each donor and corresponding recipient portal anastomotic site utilizing the following codes. Donors: 1= Main portal vein 2 = Right portal vein 3 = Other (specify): Recipients: 1 = Main portal vein 2 = Right portal vein 3 = Superior Mesenteric Artery 4 = Other (specify):	Donor Site _____ to Recipient Site _____	Recipient Intraoperative Notes Donor Intraoperative Notes	N

Back-Table Portal Reconstruction	Did back-table portal reconstruction occur?	Y N	Recipient Intraoperative Notes Donor Intraoperative Notes	N
(if yes to back-table portal venous reconstruction) Type of Back-Table Portal Venous Reconstruction	Describe the type of back-table portal venous reconstruction.	1. Venoplasty 2. Graft venous anastomosis 3. Other (specify):		
(if Graft Venous Anastomosis Chosen) Type of Graft Venous Anastomosis	What type of graft was utilized to achieve portal venous reconstruction (e.g. donor ileac vein)?	Text field		
Number of Arterial Anastomoses	How many arteries were connected?	1 2 3		
Arterial Anastomosis Graft Utilization	Was a graft used to complete arterial anastomosis?	Y (specify type) N		
Arcuate Ligament	Was the arcuate ligament released?	Y N		
(If LDLT) Number of biliary Anastomoses	How many biliary anastomoses were performed?	1 2 3 4 5		
Site(s) Biliary Antastomoses	Describe each donor and corresponding recipient biliary reconstructive anastomotic site utilizing the following codes. Donors: 1= Right main duct 2 = Right accessory duct 3 = Other (specify): Recipeints: 1 = common bile duct 2 = Roux limb 3 = Cystic Duct 4 = Other (specify):	Donor Site _____ to Recipient Site _____	Recipient Intraoperative Notes Donor Intraoperative Notes	N
Back-Table Hepatic Biliary Reconstruction	Was there back-table biliary reconstruction?	Y N		

(If Yes to Back- Table Hepatic Biliary Reconstruction) Description of Back-Table Biliary Reconstruction	Describe the back-table biliary reconstruction.	1. Ductoplatsty 2. Graft Anastomosis 3. Other (specify):
Other Non-Transplant Procedures	Were there other non-transplant procedures performed?	Y (specify): N
Intra-abdominal Fluid	How much ascites, (in cc's) was suctioned out during the operation? If none, record 0.	0-0000 cc Unknown
Fluid Requirements	How many units of packed red blood cells did the recipient receive during the transplant? Mark 0 for none.	0-00
Total Length of Operative Procedure	What was the total length of the operative procedure? (incision to skin closure and dressing)	_____ hours _____ minutes
Total Anesthesia Time	How long was the patient under anesthesia? (induction to skin closure and dressing)	_____ hours _____ minutes

HCC Explant Assessment

Revised 04/21/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Immediate Post-operative HCC findings (explant pathology)	Was HCC found on explant pathology?	Y N	Explant Pathology Report	N
(If yes to HCC found at explant pathology) Geographic Staging	Is HCC located in the right lobe, left lobe, or both lobes of the liver?	Right Lobe Only Left Lobe Only Bilobar	Explant Pathology Report	N
Number of HCC Nodules in the liver	How many HCC nodules were identified in the subject's liver at the time of study enrollment?	1 2 3 4 5 >5	Explant Pathology Report	N
Size of each Nodule	What was the maximum diameter of each nodule identified?	Nodule 1 = ___cm Nodule 2 = ___cm Nodule 3 = ___cm Nodule 4 = ___cm Nodule 5 = ___cm	Explant Pathology Report	N
Vascular Invasion	Was there HCC tumor invasion into vascular structures? Micro Invasion = micrometer tumor invasion into the portal or hepatic vein. Macro Invasion = millimeter tumor invasion into the portal or hepatic vein.	N Y, micro invasion Y, macro invasion	Explant Pathology Report	N
Primary Tumor Classification	Based on the number and size of HCC nodules, and the presence or absence of vascular invasion, the classification stages are as follows: T0: Not found T1: one nodule < 1.9cm T2: one nodule 2.0-5.0cm OR 2-3 nodules all < 3.0cm, T3: one nodule >5.0cmOR 2-3 nodules at least one >3.0cm. T4a: 4 or more nodules, any size. T4b: T2, T3 or T4a plus gross intrahepatic portal or hepatic vein involvement as indicated by explant pathology. TX: not assessed	T0 T1 T2 T3 T4a T4b TX	Explant Pathology Report	N
Nodal Status	Was there evidence of HCC found in the regional lymph nodes? Record: N0 : no	N0	Explant Pathology Report	N

<table>
<tr><td></td><td>regional (porta hepatitis) nodes involved
N1: regional (portahepatitis) nodes involved or NX: not assessed.</td><td>N1
NX</td><td></td><td></td></tr>
<tr><td>Metastatic Status</td><td>Has the cancer spread beyond the liver?
Record: M0: no metastatic disease including extrahepatic portal or hepatic vein involvement.
M1 metastatic disease including extrahepatic portal or hepatic vein involvement.
MX not assessed</td><td>M0
M1
MX</td><td>Explant Pathology Report</td><td>N</td></tr>
<tr><td>TNM Stage</td><td>Record the TNM Stage of the HCC immediately at transplant. The TNM classification is based on the following:
Table 1. pTNM staging for HCC
<table><tr><td>Stage I</td><td>T1</td><td>N0</td><td>M0</td></tr><tr><td>Stage II</td><td>T2</td><td>N0</td><td>M0</td></tr><tr><td>Stage III</td><td>T3</td><td>N0</td><td>M0</td></tr><tr><td>Stage IVA1</td><td>T4a</td><td></td><td></td></tr><tr><td>Stage IVA2</td><td>T4b</td><td></td><td></td></tr><tr><td>Stage IVB</td><td>Any T</td><td>Any N1</td><td>M1</td></tr></table>American Joint Committee on Cancer</td><td>Stage I
Stage II
Stage III
Stage IVA1
Stage IVA2
Stage IVB</td><td>Explant Pathology Report</td><td>N</td></tr>
<tr><td>Grade</td><td>What was the tumor grade?
G1 = well-differentiated
G2 = moderatey differentiated
G3 = poorly differentiated</td><td>G1
G2
G3
Unknown</td><td>Explant Pathology Report</td><td>N</td></tr>
<tr><td>Mitosis</td><td>What level of mitosis was observed on microscopic analysis?</td><td>< 10 HPF
≥ 10 HPF
Unknown</td><td>Explant Pathology Report</td><td>N</td></tr>
<tr><td>Tumor Necrosis</td><td>What was the proportion of tumor necrosis?</td><td>0%
1%-25%
26%-50%
51%-75%
76%-100%
Unknown</td><td>Explant Pathology Report</td><td>N</td></tr>
</table>

Recipient Baseline Immunosuppression and Rejection Episodes

Revised 04/16/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Baseline Immunosuppression Information during the transplant hospital stay	What was the baseline immunosuppression regimen given to this patient during the transplant hospital stay?	Prednisone Methylprednisolone Cyclosporine Neoral FK506 Rapamycin Gengraf Certican Azathioprine Mycophenolate Mofetil ATG OKT3 Thymoglobulin Zenapax Simulect	Post Transplant Medical Record Pharmacy Orders Nursing Notes	Y
Antibody Induction	Was antibody induction used?	Y N	Post Transplant Medical Record Pharmacy Orders Nursing Notes	Y
Prednisone at 3 months	What was the daily steroid dose at 3 months post-transplant? If none, enter 0. If on an every other day regimen, divide the bi-daily dose by half and enter that amount.	000.00 mg/day	Post Transplant Medical Record Pharmacy Orders Nursing Notes	N
Rejection Episode	Did the patient have a treated rejection episode from time of transplant to 1 year post transplant?	Y N	Post Transplant Medical Record	N*
(if Yes to Rejection Episode) Number of Rejection Episodes	How many treated rejection episodes did the patient have between time of transplant and 1 year post transplant? In order to count as a separate episode, the incident must occur at least 22 days from the end of treatment to the start of a subsequent round of treatment.	1-10	Post Transplant Medical Record Pharmacy Orders Nursing Notes	Y?

Date of Rejection Episode	Provide the date of each treated rejection episode. Record this as the day the rejection treatment begins.	mmddyyyy	Post Transplant Medical Record Pharmacy Orders Nursing Notes	Y?
Maintenance Immunosuppression Regimen in use immediately prior to treatment of this rejection episode	What was the baseline immunosuppression regimen in use at the time of the treated rejection episode?	Prednisone Methylprednisolone Cyclosporine Neoral FK506 Rapamycin Gengraf Certican Azathioprine	Post Transplant Medical Record Pharmacy Orders Nursing Notes	Y?
Antibody Induction	Was antibody induction used?	Y N	Post Transplant Medical Record Pharmacy Orders Nursing Notes	Y
Rejection Treatment	What medications were used to treat this rejection episode? Check all that apply.	Recycling Oral Steroids IV Steroids Switch Maintenance Immunosuppression Cyclosporine Neoral FK506 Rapamycin Gengraf Certican Azathioprine	Post Transplant Medical Record Pharmacy Orders Nursing Notes	Y
Biopsy Confirmation	Was the rejection episode confirmed by biopsy?	Y N Unknown	Pathology Report	Y?
(If Yes to Biopsy Confirmation) Rejection Severity	What was the acute rejection severity as recorded in the pathology reading of the biopsy that confirmed the rejection episode?	No Rejection Indeterminate Mild Moderate Severe Not Stated	Pathology Report	Y?

Multiple Rejection Episodes and Treatment

Revised 05/07/03

Data element	Definition	Answer format	Location in chart	SRTR validation
Date of Rejection Episode	Provide the date of each treated rejection episode. Record this as the day the rejection treatment begins.	mmddyyyy	Post Transplant Medical Record Pharmacy Orders Nursing Notes	Y
Maintenance Immunosuppression Regimen in use immediately prior to treatment of this rejection episode	What was the baseline immunosuppression regimen in use at the time of the treated rejection episode?	Prednisone Methylprednisolone Cyclosporine Neoral FK506 Rapamycin Gengraf Certican Azathioprine	Post Transplant Medical Record Pharmacy Orders Nursing Notes	Y
Antibody Induction	Was antibody induction used?	Y N	Post Transplant Medical Record Pharmacy Orders Nursing Notes	Y
Rejection Treatment	What medications were used to treat this rejection episode? Check all that apply.	Recycling Oral Steroids IV Steroids Switch Maintenance Immunosuppression Cyclosporine Neoral FK506 Rapamycin Gengraf Certican Azathioprine	Post Transplant Medical Record Pharmacy Orders Nursing Notes	Y
Biopsy Confirmation	Was the rejection episode confirmed by biopsy?	Y N Unknown	Pathology Report	Y
(If Yes to Biopsy Confirmation) Rejection Severity	What was the acute rejection severity as recorded in the pathology reading of the biopsy that confirmed the rejection episode?	No Rejection Indeterminate Mild Moderate Severe Not Stated	Pathology Report	N

Recipient Hospitalizations (for all potential recipients): Revised 04/25/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Date of Admission	Date that the subject was admitted into the hospital	mmddyyyy	Inpatient Discharge Summary	Y
Date of Discharge	Date that the subject was discharged from the hospital	mmddyyyy	Inpatient Discharge Summary	Y
Discharge Destination	Where was the patient discharged to?	Home Hospital-affiliated Transitional Residence Transfer to another hospital Rehabilitation Facility Other	Discharge Summary	N
Number of ICU days	How many days did the patient stay in ICU during this hospital admission? Use 0 for none	000	ICU Flow Chart Progress Notes Discharge Summary	Y
Type of hospital	Was the patient admitted to the transplant center or an outside hospital?	A2ALL Transplant Center Non-A2ALL Hospital	Progress Notes Discharge Summary Admission Note	N
Reason for hospital admission	Why was the patient admitted to the hospital?	Pre-transplant Encephalopathy Pre-transplant Infection Pre-transplant Variceal Bleeding Pre-transplant Ascites Pre-transplant HCC Treatment Hepatorenal Syndrome Pre-transplant Cardiac Pre-transplant Other Liver Transplant Operation Post Transplant Encephalopathy Post Transplant Infection Post Transplant Variceal Bleeding Post Transplant Ascites Post Transplant Cardiac Malignancy Biliary Tract Rejection Other	Progress Notes Discharge Summary Admission Note Nursing Notes Laboratory Procedure Reports	Y
Discharge Diagnosis	What was the primary discharge diagnosis?	(pick from list of diagnoses – form 17a	Discharge summary	N

4100	4100: AHN: DRUG OTHER SPECIFY	AHN: DRUG OTHER SPECIFY
4101	4101: AHN: TYPE A	AHN: TYPE A
4102	4102: AHN: TYPE B- HBSAG+	AHN: TYPE B- HBSAG+
4103	4103: AHN: NON A- NON B	AHN: NON A- NON B
4104	4104: AHN: TYPE C	AHN: TYPE C
4105	4105: AHN: TYPE D	AHN: TYPE D
4106	4106: AHN: TYPE B AND C	AHN: TYPE B AND C
4107	4107: AHN: TYPE B AND D	AHN: TYPE B AND D
4108	4108: AHN: ETIOLOGY UNKNOWN	AHN: ETIOLOGY UNKNOWN
4110	4110: AHN: OTHER SPECIFY	AHN: OTHER SPECIFY
4200	4200: CIRRHOSIS: DRUG/INDUST EXPOSURE OT	CIRRHOSIS: DRUG/INDUST EXPOSURE OT
4201	4201: CIRRHOSIS: POSTNECROTIC- TYPE A	CIRRHOSIS: POSTNECROTIC- TYPE A
4202	4202: CIRRHOSIS: POSTNECROTIC- TYPE B- H	CIRRHOSIS: POSTNECROTIC- TYPE B- H
4203	4203: CIRRHOSIS: POSTNECROTIC- TYPE NON	CIRRHOSIS: POSTNECROTIC- TYPE NON
4204	4204: CIRRHOSIS: POSTNECROTIC- TYPE C	CIRRHOSIS: POSTNECROTIC- TYPE C
4205	4205: CIRRHOSIS: POSTNECROTIC- TYPE D	CIRRHOSIS: POSTNECROTIC- TYPE D
4206	4206: CIRRHOSIS: POSTNECROTIC- TYPE B AN	CIRRHOSIS: POSTNECROTIC- TYPE B AN
4207	4207: CIRRHOSIS: POSTNECROTIC- TYPE B AN	CIRRHOSIS: POSTNECROTIC- TYPE B AN
4208	4208: CIRRHOSIS: CRYPTOGENIC- IDIOPATHIC	CIRRHOSIS: CRYPTOGENIC- IDIOPATHIC
4210	4210: CIRRHOSIS: POSTNECROTIC- OTHER SPE	CIRRHOSIS: POSTNECROTIC- OTHER SPE
4212	4212: CIRRHOSIS: POSTNECROTIC-AUTOIMMUNE	CIRRHOSIS: POSTNECROTIC-AUTOIMMUNE
4215	4215: LAENNEC'S CIRRHOSIS (ALCOHOLIC)	LAENNEC'S CIRRHOSIS (ALCOHOLIC)
4216	4216: LAENNEC'S CIRRHOSIS AND POSTNECROT	LAENNEC'S CIRRHOSIS AND POSTNECROT
4220	4220: PRIMARY BILIARY CIRRHOSIS (PBC)	PRIMARY BILIARY CIRRHOSIS (PBC)
4230	4230: SEC BILIARY CIRRHOSIS: CAROLI'S DI	SEC BILIARY CIRRHOSIS: CAROLI'S DI
4231	4231: SEC BILIARY CIRRHOSIS: CHOLEDOCHOL	SEC BILIARY CIRRHOSIS: CHOLEDOCHOL
4235	4235: SEC BILIARY CIRRHOSIS: OTHER SPECI	SEC BILIARY CIRRHOSIS: OTHER SPECI
4240	4240: PSC: CROHN'S DISEASE	PSC: CROHN'S DISEASE
4241	4241: PSC: ULCERATIVE COLITIS	PSC: ULCERATIVE COLITIS
4242	4242: PSC: NO BOWEL DISEASE	PSC: NO BOWEL DISEASE
4245	4245: PSC: OTHER SPECIFY	PSC: OTHER SPECIFY
4250	4250: FAMILIAL CHOLESTASIS: BYLER'S DISE	FAMILIAL CHOLESTASIS: BYLER'S DISE
4255	4255: FAMILIAL CHOLESTASIS: OTHER SPECIF	FAMILIAL CHOLESTASIS: OTHER SPECIF
4260	4260: CHOLES LIVER DISEASE: OTHER SPECIF	CHOLES LIVER DISEASE: OTHER SPECIF
4265	4265: NEONATAL HEPATITIS OTHER SPECIFY	NEONATAL HEPATITIS OTHER SPECIFY
4270	4270: BILIARY ATRESIA: EXTRAHEPATIC	BILIARY ATRESIA: EXTRAHEPATIC
4271	4271: BILIARY ATRESIA: HYPOPLASIA	BILIARY ATRESIA: HYPOPLASIA
4272	4272: BILIARY ATRESIA: ALAGILLE'S SYNDRO	BILIARY ATRESIA: ALAGILLE'S SYNDRO
4275	4275: BILIARY ATRESIA: OTHER SPECIFY	BILIARY ATRESIA: OTHER SPECIFY
4280	4280: CONGENITAL HEPATIC FIBROSIS	CONGENITAL HEPATIC FIBROSIS
4285	4285: CYSTIC FIBROSIS	CYSTIC FIBROSIS
4290	4290: BUDD-CHIARI SYNDROME	BUDD-CHIARI SYNDROME
4300	4300: METDIS: ALPHA-1-ANTITRYPSIN DEFIC	METDIS: ALPHA-1-ANTITRYPSIN DEFIC
4301	4301: METDIS: WILSON'S DISEASE	METDIS: WILSON'S DISEASE
4302	4302: METDIS: HEMOCHROMATOSIS - HEMOSIDE	METDIS: HEMOCHROMATOSIS - HEMOSIDE
4303	4303: METDIS: GLYC STOR DIS TYPE I (GSD-	METDIS: GLYC STOR DIS TYPE I (GSD-
4304	4304: METDIS: GLYC STOR DIS TYPE II (GSD	METDIS: GLYC STOR DIS TYPE II (GSD
4305	4305: METDIS: HYPERLIPIDEMIA-II- HOMOZGY	METDIS: HYPERLIPIDEMIA-II- HOMOZGY
4306	4306: METDIS: TYROSINEMIA	METDIS: TYROSINEMIA
4307	4307: METDIS: PRIMARY OXALOSIS/OXALURIA-	METDIS: PRIMARY OXALOSIS/OXALURIA-
4315	4315: METDIS: OTHER SPECIFY	METDIS: OTHER SPECIFY
4400	4400: PLM: HEPATOMA - HEPATOCELLULAR CAR	PLM: HEPATOMA - HEPATOCELLULAR CAR
4401	4401: PLM: HEPATOMA (HCC) AND CIRRHOSIS	PLM: HEPATOMA (HCC) AND CIRRHOSIS
4402	4402: PLM: FIBROLAMELLAR (FL-HC)	PLM: FIBROLAMELLAR (FL-HC)
4403	4403: PLM: CHOLANGIOCARCINOMA (CH-CA)	PLM: CHOLANGIOCARCINOMA (CH-CA)

4404	4404: PLM: HEPATOBLASTOMA (HBL)	PLM: HEPATOBLASTOMA (HBL)			
4405	4405: PLM: HEMANGIOENDOTHELIOMA-HEMANGIO	PLM: HEMANGIOENDOTHELIOMA-HEMANGIO			
4410	4410: PLM: OTHER SPECIFY	PLM: OTHER SPECIFY			
4420	4420: BILE DUCT CANCER (CHOLANGIOMA-BILI	BILE DUCT CANCER (CHOLANGIOMA-BILI			
4430	4430: SECONDARY HEPATIC MALIGNANCY OTHER	SECONDARY HEPATIC MALIGNANCY OTHER			
4450	4450: BENIGN TUMOR: HEPATIC ADENOMA	BENIGN TUMOR: HEPATIC ADENOMA			
4451	4451: BENIGN TUMOR: POLYCYSTIC LIVER DIS	BENIGN TUMOR: POLYCYSTIC LIVER DIS			
4455	4455: BENIGN TUMOR: OTHER SPECIFY	BENIGN TUMOR: OTHER SPECIFY			
4500	4500: TPN/HYPERALIMENTATION IND LIVER DI	TPN/HYPERALIMENTATION IND LIVER DI			
4510	4510: GRAFT VS. HOST DIS SEC TO NON-LI T	GRAFT VS. HOST DIS SEC TO NON-LI T			
4520	4520: TRAUMA OTHER SPECIFY	TRAUMA OTHER SPECIFY			
Other Specify					

Recipient Morbidity

Revised 05/07/03

Data element	Definition	Answer format	Location in chart	SRTR validation	Data module
Bile Leak/Biloma	Did the patient experience persistent bilious drainage beyond 7 days post surgery or have a diagnosis of an intra-abdominal bile collection?	Y (complete complication severity form) N	Nursing Notes Radiologic Studies CT Scan Report Interventive Operative Report	N	Recipient Post-Surgical Morbidity
Biliary Stricture	Did the patient develop a biliary stricture? A biliary stricture is defined as the presence of narrowing of the intrahepatic or extrahepatic bile ducts.	Y (complete complication severity form) N	Nursing Notes ERCP Report Transhepatic Cholangiography Report Post transplant medical record	N	Recipient Post-Surgical Morbidity
Intra-abdominal Bleeding	Did the patient have episode(s) of intra-abdominal bleeding? If the patient experiences a series of bleeds over several days, but never fully recovers between them, this constitutes one episode.	Y (complete complication severity form) N	Nursing Notes Blood Bank Records Lab (Hematology) Reports Imaging Studies Interventive Operative Reports	N	Recipient Post-Surgical Morbidity
(if yes to intra-abdominal bleeding) Number of Units of RBC's Transfused	How many units of transfused PRBC's did the patient receive during this bleeding episode? Answer 0 if not transfused.	0-000 units of PRBC's	Nursing Notes Blood Bank Records Lab (Hematology) Reports Interventive Operative Reports	N	Recipient Post-Surgical Morbidity
GI Bleeding	Did the patient have episode(s) of upper or lower GI bleeding? If the patient experiences a series of bleeds over several days, but never fully recovers between them, this constitutes one episode.	Y, Upper GI Bleeding (complete complication severity form) Y, Lower GI Bleeding (complete complication severity form) N	Nursing Notes Blood Bank Records Lab (Hematology) Reports Imaging Studies Interventive Operative Reports	N	Recipient Post-Surgical Morbidity
(if Yes to GI Bleeding) Cause of GI Bleeding	What caused the upper or lower GI bleeding?	Ulcers Varices Other (specify)	Nursing Notes Imaging Studies Interventive Operative Reports Progress Notes	N	Recipient Post-Surgical Morbidity

(if yes to intra-abdominal bleeding) Number of Units of RBC's Transfused	How many units of transfused RBC's did the patient receive during this bleeding episode? Answer 0 if not transfused.	0-000 units of PRBC's	Nursing Notes Blood Bank Records Lab (Hematology) Reports Interventive Operative Reports	N	Recipient Post-Surgical Morbidity
Localized Intra-abdominal Abscess	Did the patient develop any localized intra-abdominal abscesses that were treated with antibiotics, surgical or radiologic intervention?	Y (complete complication severity form) N	Nursing Notes Progress Notes Imaging Studies Lab Reports Procedure Reports Pathology Reports (cultures) Drug Orders	N	Recipient Post-Surgical Morbidity
Prolonged Ileus	Did the patient experience a delay in return of bowel function beyond 7 days post-op?	Y (complete complication severity form) N	Nursing notes I/O records	N	Recipient Post-Surgical Morbidity
(if yes to prolonged ileus) Length of Ileus	How long did the prolonged ileus last? Count from the day of surgery to the day of resumed oral intake.	0-000 days	Nursing notes I/O records	N	Recipient Post-Surgical Morbidity
Bowel Obstruction	Did the patient experience a bowel obstruction documented by imaging study or identified at re-exploration?	Y (complete complication severity form) N	Nursing Notes I/O Records Imaging Study Reports Procedure Reports Bedside Interventions Surgical Intervention Reports	N	Recipient Post-Surgical Morbidity
Re-Exploration	Did the patient experience an unplanned return to the operating room following the transplant procedure?	Y , upper abdominal (complete complication severity form) Y, lower abdominal (complete complication severity form) N	Operative Notes Lab Reports	N	Recipient Post-Surgical Morbidity
(if Yes to Re-exploration) Results of Re-Exploration	Did the surgeons identify any surgical complications arising from the transplant procedure during re-exploratory surgery?	Y N	Operative Notes Lab Reports	N	Recipient Post-Surgical Morbidity
Myocardial Infarction	Did the patient experience a myocardial infarction post-transplant, during the perioperative period (transplant hospitalization)?	Y N	EKG Results Lab Reports (elevated troponin) Autopsy Report	N	Recipient Post-Surgical Morbidity

(if Yes to Myocardial Infarction) Date	Record the date the Myocardial Infarction occurred	mmddyyyy	EKG Results Lab Reports (elevated troponin) Autopsy Report	N	Recipient Post-Surgical Morbidity
Congestive Heart Failure	Did the patient develop congestive heart failure post transplant, during the perioperative period (transplant hospitalization)?	Y N	Cardiac Imaging Studies Chest X-Ray Report Cardiac Function Tests Progress Notes Drug Orders Autopsy Records	N	Recipient Post-Surgical Morbidity
(if Yes to CHF) Date	Record the date the CHF was diagnosed.	mmddyyyy	Cardiac Imaging Studies Chest X-Ray Report Cardiac Function Tests Progress Notes Drug Orders Autopsy Records	N	Recipient Post-Surgical Morbidity
Pneumothorax	Did the patient develop a pneumothorax requiring placement of a chest tube?	Y N	Progress Notes Procedure Notes Imaging Studies	N	Recipient Post-Surgical Morbidity
(if Yes to pnemothorax) Date	Record the date the pneumothorax was diagnosed.	mmddyyyy	Progress Notes Procedure Notes Imaging Studies	N	Recipient Post-Surgical Morbidity
Pleural Effusion	Did the patient develop a pleural effusion severe enough to require either chest tube placement or thoracocentesis (tapping of fluid from the pleural space)?	Y N	Progress Notes Procedure Notes Imaging Studies	N	Recipient Post-Surgical Morbidity
(if Yes to pleural effusion) Date	Record the date the pleural effusion was diagnosed.	mmddyyyy	Progress Notes Procedure Notes Imaging Studies	N	Recipient Post-Surgical Morbidity
Pulmonary Edema	Did the patient experience accumulations of fluid in the interstitial lung tissues, confirmed by x-ray in the absence of congestive heart failure?	Y N	Progress Notes Procedure Notes Chest X-Ray Drug Orders	N	Recipient Post-Surgical Morbidity
(if Yes to pulmonary edema) Date	Record the date the pulmonary edema was diagnosed.	mmddyyyy	Progress Notes Procedure Notes Chest X-Ray Drug Orders	N	Recipient Post-Surgical Morbidity
Cardiopulmonary Arrest	Did the patient's heartbeat and breathing suddenly stop? Answer Yes only if the episode required resuscitation.	Y N	Progress Notes Autopsy Report	N	Recipient Post-Surgical Morbidity
(if Yes to	Record the date the cardiopulmonary arrest	mmddyyyy	Progress Notes	N	Recipient

cardiopulmonary arrest) Date	occurred		Procedure Notes Chest X-Ray Drug Orders		Post-Surgical Morbidity
Respiratory Arrest	Did the patient experience respiratory arrest requiring intubation and not accompanied by cardiac arrest?	Y N	Progress Notes Procedure Notes Nursing Notes Respiratory Therapy Notes Autopsy Report	N	Recipient Post-Surgical Morbidity
(if Yes to respiratory arrest) Date	Record the date the to respiratory arrest occurred	mmddyyyy	Progress Notes Procedure Notes Chest X-Ray Drug Orders	N	Recipient Post-Surgical Morbidity
Aspiration	Did the patient experience sudden respiratory distress that required intubation, associated with the appearance of a new focal infiltrate on a chest x-ray or suctioning of gastric contents from an endotracheal tube?	Y N	Progress Notes Procedure Notes Nursing Notes Respiratory Therapy Notes Chest X-Ray Report	N	Recipient Post-Surgical Morbidity
(if Yes aspiration) Date	Record the date the to aspiration occurred	mmddyyyy	Progress Notes Procedure Notes Chest X-Ray Drug Orders	N	Recipient Post-Surgical Morbidity
Pulmonary Embolism	Did the patient have a sudden onset of dyspnea associated with tachypnea and tachycardia documented as a probable pulmonary embolism by V/Q scan or a spiral CT?	Y N	Imaging Study Reports Progress Notes	N	Recipient Post-Surgical Morbidity
(if Yes to PE) Date	Record the date the PE occurred	mmddyyyy	Progress Notes Procedure Notes Chest X-Ray Drug Orders	N	Recipient Post-Surgical Morbidity
Dehiscence	Did the patient's sutures/staples come apart, causing the wound to open?	Y N	Progress Notes Operative Notes Procedure Notes	N	Recipient Post-Surgical Morbidity
(if Yes to dehisence) Date	Record the date the dehisence occurred	mmddyyyy	Progress Notes Operative Notes Procedure Notes	N	Recipient Post-Surgical Morbidity
Hernia Development	Did the patient develop a hernia post-transplant?	Y N	Progress Notes Operative Notes Procedure Notes	N	Recipient Post-Surgical Morbidity
(if Yes to hernia development) Date	Record the date the hernia development occurred	mmddyyyy	Progress Notes Operative Notes Procedure Notes	N	Recipient Post-Surgical Morbidity
Encephalopathy/Hepatic Coma	Did the patient experience post-tranplant liver-induced altered mental status or disturbed level of consciousness necessitating treatment	Y (complete complication severity form) N	Progress Notes Nursing Notes Drug Orders	N	Recipient Post-Surgical Morbidity

	with lactulose, neomycin or metronizadole?				
Ascites	Did the patient develop ascites post-transplant? Answer yes if ascites was treated with diuretics (furosemide, spironolactone, bumetanide, metalazone) or paracentesis	Y (complete complication severity form) N	Imaging Studies Physical Exam Notes Procedure Notes Drug Orders	N	Recipient Post-Surgical Morbidity
Hepatic Artery Thrombosis	Did the patient experience hepatic artery thrombosis?	Y (complete complication severity form) N	Imaging Studies Operative Notes Autopsy Report	N	Recipient Post-Surgical Morbidity
Portal Vein Thrombosis	Did the patient experience portal vein thrombosis?	Y (complete complication severity form) N	Imaging Studies Operative Notes Autopsy Report	N	Recipient Post-Surgical Morbidity
Inferior Vena Cava Thrombosis	Did the patient experience inferior vena cava thrombosis?	Y (complete complication severity form) N	Imaging Studies Operative Notes Autopsy Report	N	Recipient Post-Surgical Morbidity
Chronic Rejection	Did the patient develop chronic rejection? Answer yes if there is histological evidence of chronic rejection. The process does not necessarily have to be treated in order to qualify as chronic rejection.	Y (complete complication severity form) N	Imaging Studies Operative Notes Autopsy Report	N	Recipient Post-Surgical Morbidity
Recurrence of Original Liver Disease	Did the patient's original liver disease recur post transplant (with the exception of HCC and HCV)?	Y (complete complication severity form) N	Imaging Studies Operative Notes Autopsy Report	N	Recipient Post-Surgical Morbidity
Re-Transplantation	Did the patient receive another liver graft due to liver failure after this transplant?	Y (complete complication severity form) N	Imaging Studies Operative Notes Autopsy Report	Y	Recipient Post-Surgical Morbidity
Deep Vein Thrombosis	Did the patient experience deep vein thrombosis that was treated with anticoagulants?	Y (complete complication severity form) N	Imaging Studies Drug Orders Nursing Notes Lab Reports	N	Recipient Post-Surgical Morbidity
Neuropraxia	Did the patient experience sensory or motor peripheral nerve dysfunction that resulted in altered sensations or loss of motor function in the absence of central nervous system disorder?	Y (complete complication severity form) N	Progress Notes Nursing Notes Physical Therapy Orders	N	Recipient Post-Surgical Morbidity
Infections	Did the patient experience post transplant infection(s) requiring intervention?	Y N		N	Recipient Post-Surgical Morbidity

<table>
<tr>
<td>(If yes to Infections) Site and Type of Infection</td>
<td>Specify the type and site of infection. For example: a fungal pulmonary</td>
<td>
<table>
<tr><th>Site/Type</th><th>Bacterial</th><th>Viral</th><th>Fungal</th></tr>
<tr><td>Wound</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td></tr>
<tr><td>Bile Ducts</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td></tr>
<tr><td>Blood</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td></tr>
<tr><td>Liver</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td></tr>
<tr><td>Pulmonary</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td></tr>
<tr><td>CNS</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td></tr>
<tr><td>Urinary Tract</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td><td>❑ Yes
❑ No</td></tr>
</table>
</td>
<td>Lab Reports
Pathology Reports
Drug Orders
Nursing Notes
Imaging Studies
Progress Notes</td>
<td>N</td>
<td>Recipient Post-Surgical Morbidity</td>
</tr>
<tr>
<td>If Yes to Infections Date</td>
<td>What date was the infection(s) diagnosed?</td>
<td>mmddyyyy</td>
<td>Lab Reports
Pathology Reports
Drug Orders
Nursing Notes
Imaging Studies
Progress Notes</td>
<td>N</td>
<td>Recipient Post-Surgical Morbidity</td>
</tr>
<tr>
<td>Other Complications</td>
<td>Did other complications occur to this patient post-transplant?</td>
<td>Y
N</td>
<td>Variable</td>
<td>N</td>
<td>Recipient Post-Surgical Morbidity</td>
</tr>
<tr>
<td>If Yes to Other Complications) Date</td>
<td>What date was the other complication(s) diagnosed?</td>
<td>mmddyyyy</td>
<td>Variable</td>
<td>N</td>
<td>Recipient Post-Surgical Morbidity</td>
</tr>
</table>

Recipient Complication Severity

Revised 04/30/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Date of Onset	When did the complication begin?	mmddyyyy	Variable	N
Resolution	Did the complication resolve within 3 months post-operatively? This does not apply to complications that are self-limiting acute events.	Y N Unknown Not applicable	Variable	N
(If No or N/A to Resolution) Progression	Did the complication get worse? (requiring frequent/varied/continued intervention in an effort to control the complication or its sequelae)	Y N		
Medications Required for Treatment	Was it necessary to treat the complication with medications?	Y N	Variable	N
(if yes to Medications Required for Treatment) Type of Medications	What medication was used to treat the complication? Routine = anti-pyretics, antiemetics, antibiotics for superficial wound infection or UTI, prophylactic ulcer therapy	1. Routine Medications 2. Medications for bacterial, viral or fungal infections other than prophylaxis 3. Ulcer Therapy other than prophylaxis 4. Other (specify):	Variable	N
Interventions/Procedures	Did the complication require a procedure or intervention?	Y N	Variable	N
(if yes to Interventions/Procedures) Type of Intervention or Procedure	What type(s) of intervention or procedure was required to treat the complication?	1. bedside therapeutic procedure (e.g. evacuation of pneumothorax, pleural effusion or monitoring lines) 2. surgical intervention 3. endoscopic intervention	Variable	N

		4. radiologic intervention		
Blood Transfusion	Did the patient receive a blood transfusion associated with this complication?	Y N	Variable	N
(if yes to Blood Transfusion) Units of RBC's	How many units of blood did the patient receive?	0-000 units of PRBC's	Variable	N
ICU Admission	Was the patient admitted to ICU as a result of this complication, or if already in the ICU was the patient's stay in the ICU prolonged due to this complication?	Y N	Variable	N
(if Yes to ICU Admission **AND** this is the transplant surgery hospitalization) Length of ICU Stay	Was the patient's stay in the ICU prolonged ≥ 5 days?	Y N	Variable	N
Extended Hospital Stay	Did management of this complication require the patient's hospital stay to be longer than 4 weeks (if initial transplant surgery admission) or 14 days (if subsequent post transplant admission) total?	Y N	Variable	N
Residual Disability/Disease	Did the complication cause the patient to experience residual disability or persistent disease?	Y N	Variable	N
Re-Listing	Did the complication result in liver complications that caused the patient to be listed for another liver transplant?	Y N	Variable	Y
(If Yes to Re-Listing) Date of Re-Listing	What date was the patient placed on the waiting list for subsequent liver transplantation?	mmddyyyy	Variable	Y

Re-Transplantation	Did the complication result in liver failure that led to re-transplantation?	Y N	Variable	N
Death	Did the patient die as a result of this complication?	Y N	Variable	N

2. DEFINITIONS OF RECIPIENT ADVERSE EVENTS

The following is a guide for identification of complications. In general adverse events that are considered to be a deviation from normal postoperative course and have required some type of intervention are considered as complications. Intervention is defined as a requirement of treatment by medications, endoscopic, radiologic, and/or surgical approaches. Endoscopic intervgentions are defined as endoscopic procedures that are performed for purposes other than diagnosis. These include procedures such as banding or injection of varices, placement of stents or dilatation of strictures, and/or drainage of collections. Intervention radiological procedures may include drainage of thoracic or abdominal collections, placements of drains, stents or dilatation of strictures and/ or embolization for bleeding. For all complications, the date of the event is recorded. The severity of the complication is also recorded as outlined in the severity grading system.

B. Biliary complications

B1. A bile leak is defined as a persistant bilious driange beyond 7 days after surgery that may occur from the cut surface of the liver, from the donor's oversawn bile duct stump, or an unidentified accessory duct. The presence of bile leak is identified by the presence of bilious drainage beyond 7 days in the drain, outlined by a radiological study such as ERCP or transhepatic cholangiograph, or identified during surgical exploration. Additionally a bile leak may manifest as a fuid colloection of bile (biloma), which is identified on CT scan and may require either radilological or surgical intervention.

B2. Biliary stricture: Presence of defined narrowing of the intrahepatic or extrahepatic bile ducts as radiologically identified by ERCP or transhepatic cholangiography. A bile stricture may occur at any time after donation.

C. Abdominal/ GI

C1. Intra-abdominal bleeding. Any bleeding within the abdomen. If a patient experiences a series of bleeds over several days, but never fully recovers between them, this constitutes only "one" episode. Also record the total number of packed red blood cell units transfused.

C2. GI Bleeding. Bleeding communicating with the GI tract. This may be originating from the upper (esophagus, stomach, duodenum) or lower (small intestine distal to the duodenum, colon or rectum). If a patient experiences a series of bleeds over several days, but never fully recovers between them, this constitutes only "one" episode. Also record the total number of packed red blood cell units transfused. The cause of GI bleeding should be also recorded.

C3. Localized intra-abdominal abscess/fluid. These are collection that contain pus and are accompanied by peritonitis and or manifestations of infection such as fever or elevated white count. They are identified by CT scan, ultrasonography or during reoperation and require treatment such as antibiotic therapy, surgical or radiolodic intervention. Clinically insignificant collections that are detected during routine radiologic studies, but do not require treatment, should not be documented as complications. If an intraabdominal collection contains bile, it should be classified under B1, as a bile leak.

C4. Prolonged ileus. This is defined by delayed return of bowel function for > 7 days after surgery. This is manifested by the delay in oral intake, bowel movements, and/or prolonged nasogastric suctioning. Please recored the length of ileus defined as the time from surgery to the day of resumed oral intake.

C5. Bowel obstruction. This is manifested by the delay in oral intake, bowel movements, and/or prolonged nasogastric suctioning beyond 7 days after the initial operation in the presence of radilogic study documenting the absence of continuity of the GI tract. This may be treated by conservative measures (GI suctioning, IV fluids) or by surgical intervention.

C6. Re-exploration. This is defined as unplanned return to the operating room following the initial procedure. The findings during the second procedure should be documented as negative if the surgeon did not identify any findings that required additional treatment or surgical procedures. If findings were identified that required additional therapy or operative procedure, this exploration should be documented as a positive exploration. Findings of a positive exploration should be documentd as an additional complication. Example: If a patient undergoes a laparotomy for increasing abdominal pain and no new findings were documented during this surgrery, this is documents as a negative laparotomy. If a bile leak that requires additional surgery was encountered, this is documents as a positive laparotomy. Additionall, a bile leak complication should be checked under B1. If an abcess is found, this is documentd as a positive laparotomy and an additional complication is marked under C3.

D. Cardiopulmonary

1. Myocardial infarction. Interruption of the blood supply to an area of the myocardium causing necrosis. Diagnosis is made by new ST-segment elevation or Q waves on EKG or with a ratio of CKMB:CK $\geq$ 2.5 or elevated troponin levels.

2. Congestive Heart failure (CHF). The inability of the heart to maintain an adequate blood flow. This results in congestion of the blood in certain veins and organs with an inadequate blood supply to bodu tissues. Diagnosis is made by the presence of acute pulmonary edema or cardiomegaly on chest X-ray. If performed, an echocardiogram should demonstrate one or more of the following findings, depressed left or right ventricular systolic function on echocardiography, any regional wall motion abnormality, or left or right ventricular hypertrophy.

3. Pneumothorax. Air or gas in the pleural space. Document only those resulting in chest tube placement

4. Pleural effusion. Fluid in the pleural space. Pleural effusion is commonin both living donors and recipients following donation or transplantation. Document only those resulting in chest tube placement or tapping of fluid.

5. Pulmonary edema. Accumulation of fluid in the interstitial lung tissues. Diagnosis is confirmed by a chest Xray that is reported to show pulmonary edema, without other findings to suggest congestive heart failure (number 2).

6. Cardiopulmonary Arrest. A sudden cessation of the heart with lack of respiration. Document only complete cardiopulmonary arrests that require CPR. If CPR is not successful and the patient died, please complete a death form. If the patient suffered from a respiratory arrest that was not accompanied by cardiac arrythmias or cardiac stanstill, do not check here.

7. Respiratory Arrest. Respiratory arrest that required reintubation and was not accompanied by cardiac arrythmias or cardiac stanstill. If CPR is not successful and the patient died, please complete a death form.

8. Aspiration. Aspiration of a sufficient volume of gastric acid produces a chemical pneumonitis with or without a secondary infection. Document the occurrence of sudden respiratory distress that may require intubation associated with the appearance of a new, focal infiltrate on a chest Xray or suctioning of gastric contents from an endotracheal tube should intubation occur.

9. Pulmonary embolus. Patients should have sudden onset of dyspnea associated with tachypnea and tachycardia in the presence of a normal chest Xray. Document those with a high probability for embolus V/Q scan or a spiral CT of the chest that demonstrates an embolus.

E. Wound Complications

19. Dehiscence

20. Hernia development

F. Liver specific events

Defined as events specifically related to the function of the liver. These events correlate with worsening liver function and should be recorded as yes or no.

1. Encephalopathy defined as liver-induced altered mental status or disturbed level of consciousness. This is based Definition based on diagnosis listed by examining physician, and treatment is required in form of lactulose, neomycin or metronidazole therapy. This category includes hepatic coma.

2. Ascites. Defined as the use of diuretics (typically furosemide, spironolactone, bumetanide or metalazone) or paracentesis to manage ascites. Physical examination or imaging study such as ultrasound/abdominal CT or MRI should describe free intraperitoneal fluid or presence of ascites.

3. Liver Failure. Defined as generalized deterioration of the hepatic function as manifested by the development of encephalopathy, renal insufficiency (serum creatinine >2), abnormal prothrombin time that is progressive and ultimately leads to listing for transplant.

4. Hepatic artery thrombosis. Defined as loss of flow in the hepatic artery as determinjed by ultrasonography, angiography, CT angiography or MRA or or intraoperative assessment of vessel. This should be recorded even if it did not lead to retransplant.

5. Portal vein thrombosis as proven by ultrasonography, angiography, CT angiography or MRA or detected during a surgical procedure. . This should be recorded even if it did not lead to transplantation.

6. Primary graft non-function: Progressive worsening of liver function as measured by elevated prothrombin time, with no explanation on a technical basis (no vascular thrombosis by ultrasound), and need for re-transplant.

7. Retransplantation. Defined as having received a liver graft for liver failure. Cause or retransplantation should be recorded.

8. Acute rejection: Histologic evidence of features of rejection that lead to adjustment of immunosuppressive therapy or treatment with pulse steroids or antibody agents.

9. HCV recurrence: Histologic evidence of graft damage secondary to hepatitis C and evidence of viremia.

10. HCC recurrence: Imaging of lesion either within the liver or other extrahepatic site that is suspicious for recurrent or metastatic disease. Tissue diagnosis is not necessary.

11. Chronic rejection : Histologic evidence of features of chronic rejection. This process does not necessarily need to be treated to qualify as a complication.

G. General

1. Deep venous thrombosis. Presence of thrombosis of the lower extremities as verified by an imaging study such as ultrasound/Doppler with the rquirement of post-operative anti-coagulation therapy.

2. Neuropraxia. Sensory or motor peripheral nerve dysfunction that results in altered sensations or loss of motor function in the absence of a central nervous system disorder. This mostly occurs in the upper extremity, but can also occur in lower extremity.

3. Infections. Defined in general as a body fluid or tissue sample with a positive laboratory culture result that is treated with an intervention. This may include hospitalization, antibiotics, bedside wound opening, or formal surgical intervention. Exceptions to a positive culture are noted below. In addition to whether infection was present , the specific site should be recorded using the definitions below:

Wound: Surgical wound infection or deep intrabdominal abscess which requires intervention

Biliary Tree: Episode of cholangitis defined as blood borne organisms which are cultured in the setting of abnormal liver function tests or imaging study revealing biliary tract disease. Also included are fluid collection which contain bile and are believed to be in communication with the biliary tree.

Blood: Blood borne organsim is cultured with no other defined source. This would include bactermia or fungemia presumed secondary to an indwelling line infection

Liver: Intrahepatic fluid collections which are determined to be an abscess as evidenced by positive culture of aspirated or drained fluid.

Pulmonary: Diagnosis is made by the presence of new or progressive focal pulmonary infiltrates on chest x-ray or CT scan and some degree of pulmonary compromise (clinical symptoms of shortness of breath, signs of tachypnea, abnormal blood gas, ventilator requirement) and may be accompanied by purulent tracheobronchial secretions, fever, leukocytosis, and/or a positive culture from sputum. A positive culture is not needed for this type of infection.

CNS: Mental status changes or neurologic findings and an abnormal exam of cerebral spinal fluid. In the case of fungal infection, characteristic mass lesions on imaging are adequate.

Urinary tract: Urine is culture positive for an organism and treatment is started.

H. Other Complications

This includes complications that were not outlined in the above categories that have required intervention.

HCV Post-op Recurrence and Rx Data Revised 04/21/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Quantitative HCV RNA level post-transplant	Record first quantitative HCV RNA level post-transplant	Value	Lab reports	No
Units for HCV RNA quantification	Record units for HCV RNA	Copies/ml Equiv/ml IU/ml Unknown	Lab reports	No
Date of quantitative HCV RNA test	Record date of quantitative HCV RNA test	mmddyyyy	Lab reports	No
HCV RNA at 3 months post-transplant	Record test result 3 months post-transplant	Positive Negative Indeterminate Not available	Lab reports	No
HCV RNA at 12 months post-transplant	Record test result 3 months post-transplant	Positive Negative Indeterminate Not available	Lab reports	No
Serum AST	Record value at 1 week, months 1,3, 6, and then at 6-month intervals. At one month intervals, values obtained at ± 1 week are acceptable. At the 6 month intervals, values obtained at ± 1 month are acceptable. Record N/A for no data	1 week: ___IU/L 1 month: ___IU/L 3 month: ___IU/L 6 month: ___IU/L 12 month: ___IU/L 18 month: ___IU/L 24 month: ___IU/L 30 month: ___IU/L	Lab reports	No
Serum ALT	Record value at 1 week, months 1,3, 6, and then at 6-month intervals. At one month intervals, values obtained at ± 1 week are acceptable. At the 6 month intervals, values obtained at ± 1 month are	1 week: ___IU/L 1 month: ___IU/L 3 month: ___IU/L 6 month: ___IU/L 12 month: ___IU/L 18 month: ___IU/L 24 month: ___IU/L 30 month: ___IU/L	Lab reports	No

	acceptable. Record N/A for no data			
Serum ALK	Record value at 1 week, months 1,3, 6, and then at 6-month intervals. At one month intervals, values obtained at ± 1 week are acceptable. At the 6 month intervals, values obtained at ± 1 month are acceptable. Record N/A for no data	1 week: ___IU/L 1 month: ___IU/L 3 month: ___IU/L 6 month: ___IU/L 12 month: ___IU/L 18 month: ___IU/L 24 month: ___IU/L 30 month: ___IU/L	Lab reports	No
Serum Total Bilirubin	Record value at 1 week, months 1,3, 6, and then at 6-month intervals. At one month intervals, values obtained at ± 1 week are acceptable. At the 6 month intervals, values obtained at ± 1 month are acceptable. Record N/A for no data	1 week: ___mg/dl 1 month: ___mg/dl 3 month: ___ mg/dl 6 month: ___ mg/dl 12 month: ___ mg/dl 18 month: ___ mg/dl 24 month: ___ mg/dl 30 month: ___ mg/dl	Lab reports	No
Date of Liver Biopsy at one year post transplant (± 3 months)	Record the date of the liver biopsy performed at one year post transplant.	mmddyyyy	Pathology reports based on review by local pathologist	No
Knodell Score – Periportal +/- bridging Necrosis	Record the Knodell score for periportal +/- bridging necrosis for the liver biopsy that occurred one year post-transplant.	Knodell score __ Not available	Pathology reports based on review by local pathologist	No
Knodell Score – Lobular Inflammation and focal necrosis	Record the Knodell score for lobular inflammation and focal necrosis for the liver biopsy that occurred one year post	Knodell score __ Not available	Pathology reports based on review by local pathologist	No
Knodell Score – Portal Inflammation	Record the Knodell score for portal inflammation for the liver biopsy that occurred one year post	Knodell score __ Not available	Pathology reports based on review by local pathologist	No
Ishak Fibrosis Score	Record the Ishak Fibrosis Score for fibrosis for the	0 1	Pathology reports based on review by	No

	liver biopsy that occurred one year post-transplant.	2 3 4 5 6 Not available	local pathologist	
Date of Liver Biopsy at last available post transplant follow-up	Record the date of the liver biopsy performed at last available post transplant follow-up	mmddyyyy	Pathology reports based on review by local pathologist	No
Knodell Score – Periportal +/- bridging Necrosis	Record the Knodell score for periportal +/- bridging necrosis for the liver biopsy that occurred at last available follow-up	Knodell score __ Not available	Pathology reports based on review by local pathologist	No
Knodell Score – Lobular Inflammation and focal necrosis	Record the Knodell score for lobular inflammation and focal necrosis for the liver biopsy that occurred at last available follow-up	Knodell score __ Not available	Pathology reports based on review by local pathologist	No
Knodell Score – Portal Inflammation	Record the Knodell score for portal inflammation for the liver biopsy that occurred at last available follow-up	Knodell score __ Not available	Pathology reports based on review by local pathologist	No
Ishak Fibrosis Score	Record the Ishak Fibrosis Score for fibrosis for the liver biopsy at last available follow-up.	0 1 2 3 4 5 6 Not available	Pathology reports based on review by local pathologist	No
HCV Treatment	Did the patient receive anti-viral treatment post transplant?	Y N	Post Transplant Medical Records	No
(If yes to HCV Treatment) Start Date and Stop Date of HCV Treatment(s)	Record the start and stop dates of HCV treatment(s) post transplant	Start Date: mmddyyyy Stop Date: mmddyyyy	Post Transplant Medical Records	No
HCV Treatment Method	What type of HCV treatment did the patient	Standard Interferon PEG Interferon	Post Transplant Medical Records	No

	receive post transplant? (Can be one of the interferon + ribavirin)	Ribavirin		
Pre HCV Treatment Liver Biopsy	Was a Liver Biopsy done immediately prior to initiation of HCV treatment?	Y N	Post Transplant Medical Records	No
(if yes to HCV Treatment Liver Biopsy) Date of Liver Biopsy immediately prior to HCV Treatment	Record the date of the liver biopsy performed immediately prior to HCV treatment	mmddyyyy	Pathology Reports	No
Knodell Score – Periportal +/- bridging Necrosis	Record the Knodell score for periportal +/- bridging necrosis for the liver performed immediately prior to HCV treatment	Knodell score __ Not available	Pathology reports based on review by local pathologist	No
Knodell Score – Lobular Inflammation and focal necrosis	Record the Knodell score for lobular inflammation and focal necrosis for the liver biopsy performed immediately prior to HCV treatment	Knodell score __ Not available	Pathology reports based on review by local pathologist	No
Knodell Score – Portal Inflammation	Record the Knodell score for portal inflammation for the liver biopsy performed immediately prior to HCV treatment	Knodell score __ Not available	Pathology reports based on review by local pathologist	No
Ishak Fibrosis Score	Record the Ishak Fibrosis Score for fibrosis for the liver biopsy performed immediately prior to HCV treatment.	0 1 2 3 4 5 6 Not available	Pathology reports based on review by local pathologist	No

HCC Postoperative Recurrence and Treatment Data

Revised 04/15/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Cancer Recurrence	Did the patient develop cancer post transplant?	Y N	Post transplant medical record Imaging Studies Lab Reports	N
(if Yes to cancer recurrence) Date of Recurrence	Date first diagnosed?	mmddyyyy	Post transplant medical record Imaging Studies Lab Reports	N
Location of recurrence	Where was the initial site of recurrence?	Intrahepatic Extrahepatic	Post transplant medical record Imaging Studies Lab Reports	
(If extrahepatic) Location of extrahepatic recurrence	In what site, external to the liver did cancer initially recur?	Bone Lungs Incision or Abdominal Wall Other	Post transplant medical record Imaging Studies Lab Reports	
Ablations	How many ablations has the patient received after the liver transplant, after diagnosis of recurrent cancer or as adjunct therapy after transplant? (record 0 for none)	0-10	Procedure reports	N
(if 1-10 ablations performed) Date of Ablation	Record the date of the ablative treatment.	mmddyyyy	Procedure reports	N
Type of Ablations	What type of ablative procedures were performed? Choose as many as apply and note the number performed for each type of intervention	Radiofrequency Ablation Cryotherapy Alcohol Ablation Chemoembolization Chemoinfusion Surgical Resection	Procedure reports	N
(if yes to surgical resection) Type of Surgical Resection	What type of surgical resection was performed?	Wedge Segment Lobe	Procedure Reports Operative Reports	
Chemotherapy and Radiation treatment	Has the patient received chemotherapy and/or radiation to treat HCC since the liver transplant?	Y, Systemic Y, Regional/local N	Post transplant medical record Pharmacy Orders	N

(If Yes to Chemotherapy/Radiation) Dates of Cycle	Record the Start and Stop Dates of chemotherapeutic cycle	Start Date: mmddyyyy Stop Date: mmddyyyy N/A: Ablative Therapy	Post transplant medical record Pharmacy Orders	N
Chemotherapeutic Agent(s) used.	Identify the chemotherapeutic agent(s) used to treat the patient since transplant. Include chemotherapeutic agents used for chemoinfusion /chemoembolization ablative treatments.	Adriamycin Cisplatin 5FU Radiotherapy Unknown Other	Post transplant medical record Pharmacy Orders	N
Post-transplant AFP done?	Were there any post-transplant alpha fetal protein levels done?	Y N Unknown	Lab Reports	N
(if yes to post-transplant AFP) Results of post-transplant AFP at 3 months, 6 months, 1 year, 2 years and 3 years	Record the results for the given time intervals. Record N/A if not done.	3 months: ng/ml 6 months: ng/ml 1 year: ng/ml 2 year: ng/ml 3 year: ng/ml	Lab Reports	N

Graft Outcomes

Revised 04/16/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Date of Transplant	What date did this transplant occur?	mmddyyyy	Intraoperative Notes	Y
Source of donation	What type of donor provided the liver for Retransplantation?	Cadaveric Living donor	Post Transplant medical records Re-transplant operative notes	Y
Graft Loss	Did the liver graft stop functioning?	Y N	Post transplant medical records	Y
(If Yes) Date of graft failure	On what date was graft failure documented?	mmddyyyy	Post Transplant medical records	Y
(If Yes to Graft Loss) Primary Cause of graft loss	What was the primary reason for graft failure?	Primary Graft Failure Vascular Thrombosis Biliary Tract Complication Hepatitis: DeNovo Hepatitis: Recurrent Recurrent Disease: Non-Hepatitis Rejection: Acute Infection Other (chronic rejection)/other	Post Transplant medical records Explant Pathology Report Autopsy Report Pathology Reports Laboratory Reports Procedure Reports Imaging Studies	Y
(If Yes to Graft Loss) Secondary Cause of graft loss	What was the secondary cause of graft failure?	Primary Graft Failure Vascular Thrombosis Biliary Tract Complication Hepatitis: DeNovo Hepatitis: Recurrent Recurrent Disease: Non-Hepatitis Rejection: Acute Infection Other (chronic rejection)/other	Post Transplant medical records Explant Pathology Report Autopsy Report Pathology Reports Laboratory Reports Procedure Reports Imaging Studies	Y
(If Yes to Graft Loss) Retransplantation?	Did the subject receive another liver transplant?	Y N	Post Transplant medical records Re-transplant operative notes	Y

Patient Survival - Recipients

Revised 04/09/2003

(survival status)

Data element	Definition	Answer format	Location in chart	SRTR validation
Last known patient status	What was the patient's status at last contact?	Alive Dead	Post Transplant Medical Record Autopsy Report	Y
If alive, date last known alive.	If alive, date last known alive.	mmddyyyy	Post Transplant Medical Record Visit Record	N
If dead, date of death	When did the patient die?	mmddyyyy	Post Transplant Medical Record Autopsy Report	Y
If dead, primary cause of death	Select the primary cause of death from the list	Code – derive from Form 23a – Recipient Cause of Death Codes	Autopsy Report Discharge Summary	Y
If dead, secondary cause of death.	Select the secondary cause of death from the list	Code – derive from Form 23a – Recipient Cause of Death Codes	Autopsy Report Discharge Summary	N
If dead, tertiary cause of death	Select the tertiary cause of death from the list	Code – derive from Form 23a – Recipient Cause of Death Codes	Autopsy Report Discharge Summary	N

998: UNKNOWN
999: OTHER SPECIFY
4600: GRAFT FAILURE:PRIMARY
4601: GRAFT FAILURE:VASCULAR THROMBOSIS
4602: GRAFT FAILURE:BILIARY TRACT COMPLI
4603: GRAFT FAILURE:HEPATITIS
4604: GRAFT FAILURE:RECURRENT DISEASE (N
4605: GRAFT FAILURE:REJECTION
4606: GRAFT FAILURE:INFECTION (NON-HEPAT
4610: GRAFT FAILURE:OTHER SPECIFY
4615: GRAFT VS. HOST DISEASE
4620: CARDIO: ARRYTHMIA
4621: CARDIO: ARTERIAL OR PULMONARY EMBO
4622: CARDIO: HYPERKALEMIC ARREST
4623: CARDIO: CONGESTIVE FAILURE (CHF)
4624: CARDIO: MYOCARDIAL INFARCTION
4625: CARDIO: OTHER SPECIFY
4626: CARDIAC ARREST
4630: CEREBROVASCULAR: EMBOLIC STROKE
4631: CEREBROVASCULAR: HEMORRHAGIC STROK
4635: CEREBROVASCULAR: OTHER SPECIFY
4640: PULM INSUFF OR EDEMA (EXC PNEUMONI
4645: RESPIRATORY FAILURE: OTHER SPECIFY
4650: RENAL FAILURE
4660: MULTIPLE ORGAN SYSTEM FAILURE
4700: HEMORRHAGE: LOWER GASTROINTESTINAL
4701: HEMORRHAGE: NEUROLOGICAL (BRAIN)
4702: HEMORRHAGE: VARICEAL
4705: HEMORRHAGE: OTHER SPECIFY
4706: HEMORRHAGE
4800: INF: BACTERIAL PERITONITIS
4801: INF: PNEUMONIA LEGIONELLA PNEUMO
4802: INF: GENERALIZED SEPSIS
4803: INF: FUNGAL ASPERGILLUS CRYPTOCO
4804: INF: MIXED OTHER SPECIFY
4805: INF: OPPORTUNISTIC
4806: INF: VIRAL
4810: INF: OTHER SPECIFY
4811: INFECTION
4850: MALIGNANCY: PRIMARY OTHER SPECIFY
4851: MALIGNANCY: METASTATIC OTHER SPECI
4855: MALIGNANCY: OTHER SPECIFY
4856: MALIGNANCY
4860: POST-TX LYMPHOPROLIFERATIVE DISORD
4900: OPERATIVE: OTHER SPECIFY
4910: BRAIN DEAD:NEVER RECOVERED FROM SU
4920: SUICIDE:ATTEMPTED SUICIDE - DIED L
4930: TRAUMA: MOTOR VEHICLE
4935: TRAUMA: OTHER SPECIFY
4940: DIABETES MELLITUS
4945: ACUTE PANCREATITIS
4950: AIDS

Retrospective Study Donor Eligibility Checklist

Name: _____ **Study ID** _____

☐ Patient is age 18 or older at enrollment

☐ Was evaluated as a donor between 1/1/98 and 2/28/03.

- *The Study ID for donors is a 7-character code.*
  - *Character 1,2 = Center Number (assigned by DCC)*
  - *Character 3 = D*
  - *Character 4,5,6 = Last 3 digits of recipient's Study ID*
  - *Character 7 = Chronologic order that this donor was evaluated for the recipient (1 = first donor evaluated, 2 = 2nd donor evaluated)*

Donor Enrollment

Revised 04/09/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Donor Study ID Number	Record the donor's study ID Number from the Enrollment Checklist	00D0001	Enrollment Checklist	N
Donor last name	Donor surname	Text	Face sheet	Y
Donor first name	Donor first name	Text	Face sheet	Y
Donor middle initial	Donor middle initial	Text	Face sheet	Y
Donor date of birth	Donor date of birth	mmddyyyy	Face sheet	Y
Donor SSN	Donor SSN	000000000	Face sheet	Y
Donor gender	Donor gender	Male Female	Face sheet	Y
Donor H&P Date	Record the date of this donor's history and physical.	mmddyyyy	Exam Notes	N

Donor Demographics

Revised 04/09/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Donor state of permanent residence at the time of enrollment	Record the donor's state of permanent residence at time of enrollment	Two-character state abbreviation	Face sheet	Yes
Donor ethnicity	Donor ethnicity	Hispanic/Latino Non-Hispanic/Non-Latino	Face sheet	Yes
Donor race	Donor race	White Black or African-American American Indian or Alaskan Native Asian Native Hawaiian or Other Pacific Islander Mid-east or Arabian Indian sub-continent	Face sheet	Yes
Donor ABO blood type	Donor ABO blood type	A B O AB	Laboratory	Yes
Donor highest education level at time of enrollment	Donor highest education level at time of enrollment	None Grade school (0-8) High school (9-12) Attended college/Technical school Associate/Bachelor degree Post-college graduate degree Unknown	Social history	Yes
Living Donor relationship to recipient	Describe the relationship of the living donor to the recipient	Living, Biologically Related Parent Child Identical Twin Full Sibling (Not Identical Twin) Half Sibling Other Relative, specify: Living, Biologically Unrelated Spouse Other	Social History Donor Evaluation	Yes

Donor Evaluation

Revised 04/142003

Data element	Definition	Answer format	Location in chart	SRTR validation
Height	Donor Height	0.0	Inpatient/outpatient notes Exam Records	Yes
Donor Height Units	Donor Height Units	Inches Centimeters	Inpatient/outpatient notes Exam Records	No
Donor weight at enrollment	Donor weight	0.0	Inpatient/outpatient notes Exam Records	Yes
Donor weight units at enrollment	Recipient weight units	Pounds Kilograms	Inpatient/outpatient notes Exam Records	No
Serum Alkaline Phosphate (ALK)	Record value done closest to date donor evaluation	u/L	Lab reports	No
Serum Total Bilirubin	Record value done closest to date donor evaluation	mg/dl	Lab reports	No
CMV	What was the result of the donor's CMV IgG at evaluation?	Positive Negative Unknown Not done Indeterminate	Lab Reports	Yes
Donor Acceptance	Was the donor accepted for transplant	Y N	Inpatient/outpatient notes Exam Records	No
(if no) Rejection reason	Select the reason(s) why the donor was rejected.	Declined to donate Medical contraindications Donor Liver Steatosis Anatomical contraindications Psychosocial contraindications Recipient died Recipient too sick/removed from transplant consideration Recipient got cadaveric transplant	Inpatient/outpatient notes Exam Records Lab Reports Imaging Studies Social Work Notes Progress Notes	No
Date of Rejection	What is the date of the decision to reject this	mmddyyyy	Inpatient/outpatient notes	No

	donor?	Exam Records Lab Reports Imaging Studies Social Work Notes Progress Notes

Donor Intraoperative Data

Revised 04/30/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Date of Surgery	Record the date of the liver donation surgery.	mmddyyyy	Operative Report	Y
Left Lobe Volume	What was the weight of the left lobe of the donor liver according to preoperative imaging?	000 gm	Imaging Studies Operative Report	N
Right Lobe Volume	What was the weight of the right lobe of the donor liver according to preoperative imaging?	000 gm	Imaging Studies Operative Report	N
Procedure Aborted	Was the donation procedure aborted before completion?	Y N	Intraoperative Notes Anesthesia Records	Y
(if yes to Procedure Abortion) Reason(s) for Procedure Abortion	Why was the procedure aborted? Check all that apply.	Quality of donor liver Insufficient liver mass Technical difficulties in donor Donor Instability Recipient Instability Unexpected medical findings in recipient Recipient Death on table Other (specify)	Recipient Intraoperative Notes Donor Intraoperative Notes Anesthesia Records	N
Graft Transplanted	Was the resected graft transplanted into the recipient?	Y N	Donor Operative Notes Recipient Operative Notes	Y
(if No to graft transplanted) Reason(s) for Nontransplantation	Why wasn't the resected graft transplanted into the recipient? Check all that apply	Quality of donor liver Insufficient liver mass Recipient Instability Unexpected medical findings in recipient Recipient Death on table Other (specify):	Donor Operative Notes Recipient Operative Notes Anesthesia Records	N
Right Lobe Volume post-resection in OR	What was the weight of the right lobe of the donor liver after resection in the OR?	000 gm	Operative Report	N
% Residual Volume in Donor	What was the percentage of residual volume in the donor?	00.0%	Operative Report	N
Preoperative/Intraoperative	Was a preoperative or	Y	Operative Report	N

Biopsy	intraoperative biopsy performed on the donor liver?	N	Pathology Report	
(if yes to Preoperative/Intraoperative Biopsy) % Fat	What was the percentage of microvesicular and macrovesicular fat noted on the biopsy report?	Macrovesicular _____% fat Microvesicular _____% fat Other findings (specify)	Operative Report Pathology Report	N
Epidural Anesthesia	Did the patient receive epidural anesthesia?	Y N	Operative Notes Anesthesia Records	N
Epidural Analgesia	Did the patient receive epidural analgesia (e.g. Duramorph)?	Y N	Operative Notes Anesthesia Records	N
Total Number of Hepatic Veins From the Right Lobe Preserved for Anastomosis	What was the total number of hepatic veins from the right lobe preserved for anastomosis?	0	Operative Notes	N
Site of Vein Preserved	What was the site of each vein preserved for anastomosis?	1. RHV 2. MHV 3. IRHV 4. Vein from Segment 5 5. Other (specify):	Operative Notes	N
Size of Vein Preserved	What was the size of each vein preserved for anastomosis?	___ mm	Operative Notes	N
Portal vein/veins to Right Lobe	How many portal vein/veins to right lobe?	0	Operative Notes	N
Hepatic arteries to Right Lobe	How many hepatic arteries to right lobe?	0	Operative Notes	N
Bile Ducts From Right Lobe	How many bile ducts from the right lobe?	0	Operative Notes	N
Post-resection cholangiogram	Was a post-resection cholangiogram performed?	Y N	Operative Notes Imaging Report	N
(if yes to Cholangiogram) Cholangiogram Results	What were the results of the post-resection cholangiogram?	Normal Stricture Leak	Operative Notes Imaging Report	N
Units of Transfused RBC's	How many units of packed red blood cells were transfused to the donor during the donation surgery?	0-00 units PRBC's	Operative Notes Blood Bank Records Nursing Notes Anesthesia Records	N
Hypotension	Did the donor experience episode(s) of hypotension (<100 mm Hg) during the surgery?	Y N	Anesthesia Records Nursing Notes Operative Notes	N
(if Yes to Hypotension)	What was the total	0-000 minutes	Anesthesia	N

Duration of Hypotensive Episode(s)	duration of the hypotensive episodes (if more than one episode occurred, add them together)?		Records Nursing Notes Operative Notes	
Intraoperative Injury	Did an intraoperative injury occur?	Y N	Operative Notes Procedure Notes Imaging Studies	N
(if Yes to Intraoperative Injury) Intraoperative Injury Description	What structure(s) was injured?	Bile Duct Hepatic Artery Portal Vein Other (specify):	Operative Notes Procedure Notes Imaging Studies	N
Other Complications	Did other complications occur during the surgery?	Y (specify): N	Operative Notes	N
Other Intraoperative Surgical Procedures	Were other intraoperative surgical procedures performed at the time of the donation surgery?	Y N	Operative Notes	N
Total Length of Operative Procedures	How long did the donation surgery last?	____ hours ____ minutes	Operative Notes Anesthesia Records	N
Total Anesthesia Time	How long was the donor under anesthesia?	____ hours ____ minutes	Operative Notes Anesthesia	N

Donor Hospitalizations

Revised 04/25/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Date of Admission	Date that the subject was admitted into the hospital	mmddyyyy	Inpatient Discharge Summary	Y
Date of Discharge	Date that the subject was discharged from the hospital	mmddyyyy	Inpatient Discharge Summary	Y
Discharge Destination	Where was the patient discharged to?	Home Hospital-affiliated Transitional Residence Transfer to another hospital Rehabilitation Facility Other	Discharge Notes Face Sheet	N
Number of ICU days	How many days did the patient stay in ICU during this hospital admission? Use 0 for none	000	ICU Flow Chart Progress Notes Discharge Summary	N
Type of hospital	Was the patient admitted to the transplant center or an outside hospital?	A2ALL Transplant Center Non-A2ALL Hospital	Progress Notes Discharge Summary Admission Note	N
Reason for hospital admission	Why was the patient admitted to the hospital?	Pre-donation Other Liver Donation Operation Post Donation Complication Post Donation Other	Progress Notes Discharge Summary Admission Note Nursing Notes Laboratory Procedure Reports	N
(If Post Donation Complication or Post Donation Other answered on previous question) Primary Discharge Diagnosis	Record the primary discharge diagnosis from the list.	(List of diagnoses)	Discharge Summary	N

4100	4100: AHN: DRUG OTHER SPECIFY	AHN: DRUG OTHER SPECIFY
4101	4101: AHN: TYPE A	AHN: TYPE A
4102	4102: AHN: TYPE B- HBSAG+	AHN: TYPE B- HBSAG+
4103	4103: AHN: NON A- NON B	AHN: NON A- NON B
4104	4104: AHN: TYPE C	AHN: TYPE C
4105	4105: AHN: TYPE D	AHN: TYPE D
4106	4106: AHN: TYPE B AND C	AHN: TYPE B AND C
4107	4107: AHN: TYPE B AND D	AHN: TYPE B AND D
4108	4108: AHN: ETIOLOGY UNKNOWN	AHN: ETIOLOGY UNKNOWN
4110	4110: AHN: OTHER SPECIFY	AHN: OTHER SPECIFY
4200	4200: CIRRHOSIS: DRUG/INDUST EXPOSURE OT	CIRRHOSIS: DRUG/INDUST EXPOSURE OT
4201	4201: CIRRHOSIS: POSTNECROTIC- TYPE A	CIRRHOSIS: POSTNECROTIC- TYPE A
4202	4202: CIRRHOSIS: POSTNECROTIC- TYPE B- H	CIRRHOSIS: POSTNECROTIC- TYPE B- H
4203	4203: CIRRHOSIS: POSTNECROTIC- TYPE NON	CIRRHOSIS: POSTNECROTIC- TYPE NON
4204	4204: CIRRHOSIS: POSTNECROTIC- TYPE C	CIRRHOSIS: POSTNECROTIC- TYPE C
4205	4205: CIRRHOSIS: POSTNECROTIC- TYPE D	CIRRHOSIS: POSTNECROTIC- TYPE D
4206	4206: CIRRHOSIS: POSTNECROTIC- TYPE B AN	CIRRHOSIS: POSTNECROTIC- TYPE B AN
4207	4207: CIRRHOSIS: POSTNECROTIC- TYPE B AN	CIRRHOSIS: POSTNECROTIC- TYPE B AN
4208	4208: CIRRHOSIS: CRYPTOGENIC- IDIOPATHIC	CIRRHOSIS: CRYPTOGENIC- IDIOPATHIC
4210	4210: CIRRHOSIS: POSTNECROTIC- OTHER SPE	CIRRHOSIS: POSTNECROTIC- OTHER SPE
4212	4212: CIRRHOSIS: POSTNECROTIC-AUTOIMMUNE	CIRRHOSIS: POSTNECROTIC-AUTOIMMUNE
4215	4215: LAENNEC'S CIRRHOSIS (ALCOHOLIC)	LAENNEC'S CIRRHOSIS (ALCOHOLIC)
4216	4216: LAENNEC'S CIRRHOSIS AND POSTNECROT	LAENNEC'S CIRRHOSIS AND POSTNECROT
4220	4220: PRIMARY BILIARY CIRRHOSIS (PBC)	PRIMARY BILIARY CIRRHOSIS (PBC)
4230	4230: SEC BILIARY CIRRHOSIS: CAROLI'S DI	SEC BILIARY CIRRHOSIS: CAROLI'S DI
4231	4231: SEC BILIARY CIRRHOSIS: CHOLEDOCHOL	SEC BILIARY CIRRHOSIS: CHOLEDOCHOL
4235	4235: SEC BILIARY CIRRHOSIS: OTHER SPECI	SEC BILIARY CIRRHOSIS: OTHER SPECI
4240	4240: PSC: CROHN'S DISEASE	PSC: CROHN'S DISEASE
4241	4241: PSC: ULCERATIVE COLITIS	PSC: ULCERATIVE COLITIS
4242	4242: PSC: NO BOWEL DISEASE	PSC: NO BOWEL DISEASE
4245	4245: PSC: OTHER SPECIFY	PSC: OTHER SPECIFY
4250	4250: FAMILIAL CHOLESTASIS: BYLER'S DISE	FAMILIAL CHOLESTASIS: BYLER'S DISE
4255	4255: FAMILIAL CHOLESTASIS: OTHER SPECIF	FAMILIAL CHOLESTASIS: OTHER SPECIF
4260	4260: CHOLES LIVER DISEASE: OTHER SPECIF	CHOLES LIVER DISEASE: OTHER SPECIF
4265	4265: NEONATAL HEPATITIS OTHER SPECIFY	NEONATAL HEPATITIS OTHER SPECIFY
4270	4270: BILIARY ATRESIA: EXTRAHEPATIC	BILIARY ATRESIA: EXTRAHEPATIC
4271	4271: BILIARY ATRESIA: HYPOPLASIA	BILIARY ATRESIA: HYPOPLASIA
4272	4272: BILIARY ATRESIA: ALAGILLE'S SYNDRO	BILIARY ATRESIA: ALAGILLE'S SYNDRO
4275	4275: BILIARY ATRESIA: OTHER SPECIFY	BILIARY ATRESIA: OTHER SPECIFY
4280	4280: CONGENITAL HEPATIC FIBROSIS	CONGENITAL HEPATIC FIBROSIS
4285	4285: CYSTIC FIBROSIS	CYSTIC FIBROSIS
4290	4290: BUDD-CHIARI SYNDROME	BUDD-CHIARI SYNDROME
4300	4300: METDIS: ALPHA-1-ANTITRYPSIN DEFIC	METDIS: ALPHA-1-ANTITRYPSIN DEFIC
4301	4301: METDIS: WILSON'S DISEASE	METDIS: WILSON'S DISEASE
4302	4302: METDIS: HEMOCHROMATOSIS - HEMOSIDE	METDIS: HEMOCHROMATOSIS - HEMOSIDE
4303	4303: METDIS: GLYC STOR DIS TYPE I (GSD-	METDIS: GLYC STOR DIS TYPE I (GSD-
4304	4304: METDIS: GLYC STOR DIS TYPE II (GSD	METDIS: GLYC STOR DIS TYPE II (GSD
4305	4305: METDIS: HYPERLIPIDEMIA-II- HOMOZGY	METDIS: HYPERLIPIDEMIA-II- HOMOZGY
4306	4306: METDIS: TYROSINEMIA	METDIS: TYROSINEMIA
4307	4307: METDIS: PRIMARY OXALOSIS/OXALURIA-	METDIS: PRIMARY OXALOSIS/OXALURIA-
4315	4315: METDIS: OTHER SPECIFY	METDIS: OTHER SPECIFY
4400	4400: PLM: HEPATOMA - HEPATOCELLULAR CAR	PLM: HEPATOMA - HEPATOCELLULAR CAR
4401	4401: PLM: HEPATOMA (HCC) AND CIRRHOSIS	PLM: HEPATOMA (HCC) AND CIRRHOSIS
4402	4402: PLM: FIBROLAMELLAR (FL-HC)	PLM: FIBROLAMELLAR (FL-HC)
4403	4403: PLM: CHOLANGIOCARCINOMA (CH-CA)	PLM: CHOLANGIOCARCINOMA (CH-CA)

4404	4404: PLM: HEPATOBLASTOMA (HBL)	PLM: HEPATOBLASTOMA (HBL)			
4405	4405: PLM: HEMANGIOENDOTHELIOMA-HEMANGIO	PLM: HEMANGIOENDOTHELIOMA-HEMANGIO			
4410	4410: PLM: OTHER SPECIFY	PLM: OTHER SPECIFY			
4420	4420: BILE DUCT CANCER (CHOLANGIOMA-BILI	BILE DUCT CANCER (CHOLANGIOMA-BILI			
4430	4430: SECONDARY HEPATIC MALIGNANCY OTHER	SECONDARY HEPATIC MALIGNANCY OTHER			
4450	4450: BENIGN TUMOR: HEPATIC ADENOMA	BENIGN TUMOR: HEPATIC ADENOMA			
4451	4451: BENIGN TUMOR: POLYCYSTIC LIVER DIS	BENIGN TUMOR: POLYCYSTIC LIVER DIS			
4455	4455: BENIGN TUMOR: OTHER SPECIFY	BENIGN TUMOR: OTHER SPECIFY			
4500	4500: TPN/HYPERALIMENTATION IND LIVER DI	TPN/HYPERALIMENTATION IND LIVER DI			
4510	4510: GRAFT VS. HOST DIS SEC TO NON-LI T	GRAFT VS. HOST DIS SEC TO NON-LI T			
4520	4520: TRAUMA OTHER SPECIFY	TRAUMA OTHER SPECIFY			
Other Specify					

Donor Morbidity

Revised 04/30/2003

Data element	Definition	Answer format	Location in chart	SRTR validation	Data module
Bile Leak/Biloma	Did the patient experience persistent bilious drainage beyond 7 days post surgery, or have a diagnosis of an intra-abdominal bile collection?	Y (complete complication severity form) N	Nursing Notes Radiologic Studies CT Scan Report Interventive Operative Report	N	Donor Morbidity
Biliary Stricture	Did the patient develop a biliary stricture? A biliary stricture is defined as the presence of narrowing of the intrahepatic or extrahepatic bile ducts.	Y (complete complication severity form) N	Nursing Notes ERCP Report Transhepatic Cholangiography Report Post transplant medical record	N	Donor Morbidity
Intra-abdominal Bleeding	Did the patient have episode(s) of intra-abdominal bleeding? If the patient experiences a series of bleeds over several days, but never fully recovers between them, this constitutes one episode.	Y (complete complication severity form) N	Nursing Notes Blood Bank Records Lab (Hematology) Reports Imaging Studies Interventive Operative Reports	N	Donor Morbidity
(if yes to intra-abdominal bleeding) Number of Units of RBC's Transfused	How many units of transfused RBC's did the patient receive during this bleeding episode? Answer 0 if not transfused.	0-000 units of PRBC's	Nursing Notes Blood Bank Records Lab (Hematology) Reports Interventive Operative Reports	N	Donor Morbidity
GI Bleeding	Did the patient have episode(s) of upper or lower GI bleeding? If the patient experiences a series of bleeds over several days, but never fully recovers between them, this constitutes one episode.	Y, Upper GI Bleeding (complete complication severity form) Y, Lower GI Bleeding (complete complication severity form) N	Nursing Notes Blood Bank Records Lab (Hematology) Reports Imaging Studies Interventive Operative Reports	N	Donor Morbidity
(if Yes to GI Bleeding) Cause of GI Bleeding	What caused the upper or lower GI bleeding?	Ulcers Other (specify)	Nursing Notes Imaging Studies Interventive Operative Reports Progress Notes	N	Donor Morbidity
(if yes to intra-abdominal	How many units of transfused RBC's did the	0-000 units of PRBC's	Nursing Notes	N	Donor

bleeding) Number of Units of RBC's Transfused	patient receive during this bleeding episode? Answer 0 if not transfused.		Blood Bank Records Lab (Hematology) Reports Interventive Operative Reports		Morbidity
Localized Intra-abdominal Abscess	Did the patient develop any localized intra-abdominal abscesses that were treated with antibiotics, surgical or radiologic intervention?	Y (complete complication severity form) N	Nursing Notes Progress Notes Imaging Studies Lab Reports Procedure Reports Pathology Reports (cultures) Drug Orders	N	Donor Morbidity
Prolonged Ileus	Did the patient experience a delay in return of bowel function beyond 7 days post-op?	Y (complete complication severity form) N	Nursing notes I/O records	N	Donor Morbidity
(if yes to prolonged ileus) Length of Ileus	How long did the prolonged ileus last? Count from the day of surgery to the day of resumed oral intake.	0-000 days	Nursing notes I/O records	N	Donor Morbidity
Bowel Obstruction	Did the patient experience a bowel obstruction documented by imaging study or identified at re-exploration?	Y (complete complication severity form) N	Nursing Notes I/O Records Imaging Study Reports Procedure Reports Bedside Interventions Surgical Intervention Reports	N	Donor Morbidity
Re-Exploration	Did the patient experience an unplanned return to the operating room following the initial donation procedure?	Y , upper abdominal (complete complication severity form) Y, lower abdominal (complete complication severity form) N	Operative Notes Lab Reports	Y	Donor Morbidity
(if Yes to Re-exploration) Results of Re-Exploration	Did the surgeons identify any surgical complications arising from the donation procedure during re-exploratory surgery?	Y N	Operative Notes Lab Reports	N	Donor Morbidity
Myocardial Infarction	Did the patient experience a myocardial infarction post-donation, during the perioperative period?	Y (complete complication severity form) N	EKG Results Lab Reports (elevated troponin) Autopsy Report	N	Donor Morbidity
Congestive Heart Failure	Did the patient develop congestive heart failure	Y (complete complication	Cardiac Imaging	N	Donor

	post operatively, during the perioperative period?	severity form) N	Studies Chest X-Ray Report Cardiac Function Tests Progress Notes Drug Orders Autopsy Records		Morbidity
Pneumothorax	Did the patient develop a pneumothorax requiring placement of a chest tube?	Y (complete complication severity form) N	Progress Notes Procedure Notes Imaging Studies	N	Donor Morbidity
Pleural Effusion	Did the patient develop a pleural effusion severe enough to require either chest tube placement or thoracocentesis (tapping of fluid from the pleural space)?	Y (complete complication severity form) N	Progress Notes Procedure Notes Imaging Studies	N	Donor Morbidity
Pulmonary Edema	Did the patient experience accumulations of fluid in the interstitial lung tissues, confirmed by xray in the absence of congestive heart failure?	Y (complete complication severity form) N	Progress Notes Procedure Notes Chest X-Ray Drug Orders	N	Donor Morbidity
Cardiopulmonary Arrest	Did the patient's heartbeat and breathing suddenly stop? Answer Yes only if the episode required resuscitation.	Y (complete complication severity form) N	Progress Notes Autopsy Report	N	Donor Morbidity
Respiratory Arrest	Did the patient experience respiratory arrest requiring intubation and not accompanied by cardiac arrest?	Y (complete complication severity form) N	Progress Notes Procedure Notes Nursing Notes Respiratory Therapy Notes Autopsy Report	N	Donor Morbidity
Aspiration	Did the patient experience sudden respiratory distress that required intubation, associated with the appearance of a new focal infiltrate on a chest x-ray or suctioning of gastric contents from an endotracheal tube?	Y (complete complication severity form) N	Progress Notes Procedure Notes Nursing Notes Respiratory Therapy Notes Chest X-Ray Report	N	Donor Morbidity
Pulmonary Embolism	Did the patient have a sudden onset of dyspnea associated with tachypnea and tachycardia documented as a probable pulmonary embolism by V/Q scan or a spiral CT?	Y (complete complication severity form) N	Imaging Study Reports Progress Notes	N	Donor Morbidity
Dehiscence	Did the patient's sutures/staples come apart, causing the wound to open?	Y (complete complication severity form) N	Progress Notes Operative Notes Procedure Notes	N	Donor Morbidity
Hernia Development	Did the patient develop a hernia post-operatively?	Y (complete complication severity form) N		N	Donor Morbidity
Encephalopathy/Hepatic	Did the patient experience post-operative liver-	Y (complete complication	Progress Notes	N	Donor

Coma	induced altered mental status or disturbed level of consciousness necessitating treatment with lactulose, neomycin or metronizadole?	severity form) N	Nursing Notes Drug Orders		Morbidity
Ascites	Did the patient develop ascites post-operatively? Answer yes if ascites was treated with diuretics (furosemide, spironolactone, bumetanide, metalazone) or paracentesis	Y (complete complication severity form) N	Imaging Studies Physical Exam Notes Procedure Notes Drug Orders	N	Donor Morbidity
Liver Failure	Did the patient experience a generalized deterioration of hepatic function after donation?	Y (complete complication severity form) N	Imaging Studies Lab Reports Progress Notes Drug Orders Procedure Notes Autopsy Report	N	Donor Morbidity
Hepatic Artery Thrombosis	Did the patient experience hepatic artery thrombosis?	Y (complete complication severity form) N	Imaging Studies Operative Notes Autopsy Report	N	Donor Morbidity
Portal Vein Thrombosis	Did the patient experience portal vein thrombosis?	Y (complete complication severity form) N	Imaging Studies Operative Notes Autopsy Report	N	Donor Morbidity
Inferior Vena Cava Thrombosis	Did the patient experience inferior vena cava thrombosis?	Y (complete complication severity form) N	Imaging Studies Operative Notes Autopsy Report	N	Donor Morbidity
Transplantation	Did the patient receive a liver graft due to liver failure after donation?	Y (complete complication severity form) N	Imaging Studies Operative Notes Autopsy Report	N	Donor Morbidity
Deep Vein Thrombosis	Did the patient experience deep vein thrombosis that was treated with anticoagulants?	Y (complete complication severity form) N	Imaging Studies Drug Orders Nursing Notes Lab Reports	N	Donor Morbidity
Neuropraxia	Did the patient experience sensory or motor peripheral nerve dysfunction that resulted in altered sensations or loss of motor function in the absence of central nervous system disorder?	Y (complete complication severity form) N	Progress Notes Nursing Notes Physical Therapy Orders	N	Donor Morbidity
Infections	Did the patient experience post operative infection(s) requiring intervention?	Y (complete complication severity form) N		Y	Donor Morbidity

(If yes to Infections) Site and Type of Infection	Specify the type and site of infection.	**Site/Type** / **Bacterial** / **Viral** / **Fungal** Wound: ❑ Yes ❑ No / ❑ Yes ❑ No / ❑ Yes ❑ No Bile Ducts: ❑ Yes ❑ No / ❑ Yes ❑ No / ❑ Yes ❑ No Blood: ❑ Yes ❑ No / ❑ Yes ❑ No / ❑ Yes ❑ No Liver: ❑ Yes ❑ No / ❑ Yes ❑ No / ❑ Yes ❑ No Pulmonary: ❑ Yes ❑ No / ❑ Yes ❑ No / ❑ Yes ❑ No CNS: ❑ Yes ❑ No / ❑ Yes ❑ No / ❑ Yes ❑ No Urinary Tract: ❑ Yes ❑ No / ❑ Yes ❑ No / ❑ Yes ❑ No	Lab Reports Pathology Reports Drug Orders Nursing Notes Imaging Studies Progress Notes	N	Donor Morbidity
Psychological Difficulties	Did the patient experience psychological difficulties requiring intervention postoperatively?	Y (complete complication severity form) N	Nursing Notes Social Work Notes Drug Orders	N	Donor Morbidity
(if yes to Psychological Difficulties)	Describe the psychological problem that occurred.	Depression Suicide Attempt Other(specify):	Nursing Notes Social Work Notes Drug Orders	N	Donor Morbidity

Donor Complication Severity

Revised 04/30/2003

Data element	Definition	Answer format	Location in chart	SRTR validation
Date of Onset	When did the complication begin?	mmddyyyy	Variable	N
Resolution	Did the complication resolve within 3 months post-operatively? This does not apply to complications that are self-limiting acute events.	Y N Unknown Not applicable	Variable	N
(If No or N/A to Resolution) Progression	Did the complication get worse? (requiring frequent/varied/continued intervention in an effort to control the complication or its sequelae)	Y N		
Medications Required for Treatment	Was it necessary to treat the complication with medications?	Y N	Variable	N
(if yes to Medications Required for Treatment) Type of Medications	What medication was used to treat the complication? Routine = anti-pyretics, antiemetics, antibiotics for superficial wound infection or UTI, prophylactic ulcer therapy	1. Routine Medications 2. Medications for bacterial, viral or fungal infections other than prophylaxis 3. Ulcer Therapy other than prophylaxis 4. Other (specify):	Variable	N
Interventions/Procedures	Did the complication require a procedure or intervention?	Y N	Variable	N
(if yes to Interventions/Procedures) Type of Intervention or Procedure	What type(s) of intervention or procedure was required to treat the complication?	1. bedside therapeutic procedure (e.g. evacuation of pneumothorax, pleural effusion or monitoring lines) 2. surgical intervention 3. endoscopic intervention	Variable	N

		4. radiologic intervention		
Blood Transfusion	Did the patient receive a blood transfusion associated with this complication?	Y N	Variable	N
(if yes to Blood Transfusion) Units of RBC's	How many units of blood did the patient receive?	0-000 units of PRBC's	Variable	N
ICU Admission	Was the patient admitted to ICU as a result of this complication?	Y N	Variable	N
Hospital Stay >14 Days	Was the patient required to stay in the hospital for more than 14 days as a result of this complication?	Y N	Variable	N
Residual Disability/Disease	Did the complication cause the patient to experience residual disability or disease?	Y N	Variable	N
Transplant Wait Listing	Did the complication result in liver complications that caused the patient to be listed as a candidate for liver transplant?	Y N	Variable	Y
(if Yes to Transplant Wait Listing) Date of Listing	What date was the patient placed on the list of liver transplant candidates	mmddyyyy	Variable	Y
Transplantation	Did the complication result in liver failure that led to transplantation?	Y N	Variable	N
Death	Did the patient die as a result of this complication?	Y N	Variable	N

DEFINITIONS OF DONOR ADVERSE EVENTS

The following is a guide for identification of complications. In general adverse events that are considered to be a deviation from normal postoperative course and have required some type of intervention are considered as complications. Intervention is defined as a requirement of treatment by medications, endoscopic, radiologic, and/or surgical approaches. Endoscopic intervgentions are defined as endoscopic procedures that are performed for purposes other than diagnosis. These include procedures such as banding or injection of varices, placement of stents or dilatation of strictures, and/or drainage of collections. Intervention radiological procedures may include drainage of thoracic or abdominal collections, placements of drains, stents or dilatation of strictures and/ or embolization for bleeding. For all complications, the date of the event is recorded. The severity of the complication is also recorded as outlined in the severity grading system.

A. Intraoperative Injury

These are injuries that occur during the operative procedure and refer to the donor structures. If a right hepatectomy procedure is performed any injury to the donor structures, namely the common bile duct, the left hepatic duct, the left hepatic artery, common hepatic artery, left branch of the portal vein, and the main trunk of the portal vein should be recorded. If a left lobe hepatectomy is performed, injury to the common bile duct, the right hepatic duct, the right hepatic artery, common hepatic artery, right branch of the portal vein, and the main trunk of the portal vein should be recorded.

Injury to these structures may be detected and reported at the time of the primary operation or documented by diagnostic testing or surgical re-exploration during hospitalization. For example, an injury to the bile duct may manifest as a persistent bile duct leak in the post-operative period that is detected by ERCP or a bile leak that requires surgical exploration, repair or drainage. Donor hepatic arterial injury may be detected during the initial procedure or manifest by donor arterial thrombosis, bleeding, or pseudoanuerym formation as evidenced by a doppler study, hepatic angiography, or CT angiography. Portal vein injuries may be manifesated by bleeding in the primary procedure, or by portal vein thrombosis as documented postoperatively by a doppler study, hepatic angiography, or CT angiography.

B. Biliary complications

B1. A bile leak is defined as a persistant bilious driange beyond 7 days after surgery that may occur from the cut surface of the liver, from the donor's oversawn bile duct stump, or an unidentified accessory duct. The presence of bile leak is identified by the presence of bilious drainage beyond 7 days in the drain, outlined by a radiological study such as ERCP or transhepatic cholangiograph, or identified during surgical exploration. Additionally a bile leak may manifest as a fuid colloection of bile (biloma), which is identified on CT scan and may require either radilological or surgical intervention.

B2. Biliary stricture: Presence of defined narrowing of the intrahepatic or extrahepatic bile ducts as radiologically identified by ERCP or transhepatic cholangiography. A bile stricture may occur at any time after donation.

C. Abdominal/ GI

C1. Intra-abdominal bleeding. Any bleeding within the abdomen. If a patient experiences a series of bleeds over several days, but never fully recovers between them, this constitutes only "one" episode. Also record the total number of packed red blood cell units transfused.

C2. GI Bleeding. Bleeding communicating with the GI tract. This may be originating from the upper (esophagus, stomach, duodenum) or lower (small intestine distal to the duodenum, colon or rectum). If a patient experiences a series of bleeds over several days, but never fully

recovers between them, this constitutes only “one” episode. Also record the total number of packed red blood cell units transfused. The cause of GI bleeding should be also recorded.

C3. Localized intra-abdominal abscess/fluid. These are collection that contain pus and are accompanied by peritonitis and or manifestations of infection such as fever or elevated white count. They are identified by CT scan, ultrasonography or during reoperation and require treatment such as antibiotic therapy, surgical or radiolodic intervention. Clinically insignificant collections that are detected during routine radiologic studies, but do not require treatment, should not be documented as complications. If an intraabdominal collection contains bile, it should be classified under B1, as a bile leak.

C4. Prolonged ileus. This is defined by delayed return of bowel function for > 7 days after surgery. This is manifested by the delay in oral intake, bowel movements, and/or prolonged nasogastric suctioning. Please recored the length of ileus defined as the time from surgery to the day of resumed oral intake.

C5. Bowel obstruction. This is manifested by the delay in oral intake, bowel movements, and/or prolonged nasogastric suctioning beyond 7 days after the initial operation in the presence of radilogic study documenting the absence of continuity of the GI tract. This may be treated by conservative measures (GI suctioning, IV fluids) or by surgical intervention.

C6. Re-exploration. This is defined as unplanned return to the operating room following the initial procedure. The findings during the second procedure should be documented as negative if the surgeon did not identify any findings that required additional treatment or surgical procedures. If findings were identified that required additional therapy or operative procedure, this exploration should be documented as a positive exploration. Findings of a positive exploration should be documentd as an additional complication. Example: If a patient undergoes a laparotomy for increasing abdominal pain and no new findings were documented during this surgrery, this is documents as a negative laparotomy. If a bile leak that requires additional surgery was encountered, this is documents as a positive laparotomy. Additionall, a bile leak complication should be checked under B1. If an abcess is found, this is documentd as a positive laparotomy and an additional complication is marked under C3.

D. Cardiopulmonary

1. Myocardial infarction. Interruption of the blood supply to an area of the myocardium causing necrosis. Diagnosis is made by new ST-segment elevation or Q waves on EKG or with a ratio of CKMB:CK $\geq$ 2.5 or elevated troponin levels.

2. Congestive Heart failure (CHF). The inability of the heart to maintain an adequate blood flow. This results in congestion of the blood in certain veins and organs with an inadequate blood supply to bodu tissues. Diagnosis is made by the presence of acute pulmonary edema or cardiomegaly on chest X-ray. If performed, an echocardiogram should demonstrate one or more of the following findings, depressed left or right ventricular systolic function on echocardiography, any regional wall motion abnormality, or left or right ventricular hypertrophy.

3. Pneumothorax. Air or gas in the pleural space. Document only those resulting in chest tube placement

4. Pleural effusion. Fluid in the pleural space. Pleural effusion is commonin both living donors and recipients following donation or transplantation. Document only those resulting in chest tube placement or tapping of fluid.

5. Pulmonary edema. Accumulation of fluid in the interstitial lung tissues. Diagnosis is confirmed by a chest Xray that is reported to show pulmonary edema, without other findings to suggest congestive heart failure (number 2).

6. Cardiopulmonary Arrest. A sudden cessation of the heart with lack of respiration. Document only complete cardiopulmonary arrests that require CPR. If CPR is not successful

and the patient died, please complete a death form. If the patient suffered from a respiratory arrest that was not accompanied by cardiac arrythmias or cardiac stanstill, do not check here.

7. Respiratory Arrest. Respiratory arrest that required reintubation and was not accompanied by cardiac arrythmias or cardiac stanstill. If CPR is not successful and the patient died, please complete a death form.

8. Aspiration. Aspiration of a sufficient volume of gastric acid produces a chemical pneumonitis with or without a secondary infection. Document the occurrence of sudden respiratory distress that may require intubation associated with the appearance of a new, focal infiltrate on a chest Xray or suctioning of gastric contents from an endotracheal tube should intubation occur.

9. Pulmonary embolus. Patients should have sudden onset of dyspnea associated with tachypnea and tachycardia in the presence of a normal chest Xray. Document those with a high probability for embolus V/Q scan or a spiral CT of the chest that demonstrates an embolus.

E. Wound Complications

19. Dehiscence

20. Hernia development

UF. Liver specific events

Defined as events specifically related to the function of the liver. These events correlate with worsening liver function and should be recorded as yes or no.

1. Encephalopathy defined as liver-induced altered mental status or disturbed level of consciousness. This is based Definition based on diagnosis listed by examining physician, and treatment is required in form of lactulose, neomycin or metronidazole therapy. This category includes hepatic coma.

2. Ascites. Defined as the use of diuretics (typically furosemide, spironolactone, bumetanide or metalazone) or paracentesis to manage ascites. Physical examination or imaging study such as ultrasound/abdominal CT or MRI should describe free intraperitoneal fluid or presence of ascites.

3. Liver Failure. Defined as generalized deterioration of the hepatic function as manifested by the development of encephalopathy, renal insufficiency (serum creatinine >2), abnormal prothrombin time that is progressive and ultimately leads to listing for transplant.

4. Hepatic artery thrombosis. Defined as loss of flow in the hepatic artery as determinjed by ultrasonography, angiography, CT angiography or MRA or or intraoperative assessment of vessel. This should be recorded even if it did not lead to transplantation.

5. Portal vein thrombosis as proven by ultrasonography, angiography, CT angiography or MRA or detected during a surgical procedure. . This should be recorded even if it did not lead to transplantation.

6. Inferior vena caval thrombosis as proven by ultrasonography, angiography, CT angiography or MRA or detected during a surgical procedure.

7. Transplantation. Defined as having received a liver graft for liver failure.

G. General

1. Deep venous thrombosis. Presence of thrombosis of the lower extremities as verified by an imaging study such as ultrasound/Doppler with the rquirement of post-operative anti-coagulation therapy.

2. Neuropraxia. Sensory or motor peripheral nerve dysfunction that results in altered sensations or loss of motor function in the absence of a central nervous system disorder. This mostly occurs in the upper extremity, but can also occur in lower extremity.

3. Infections. Defined in general as a body fluid or tissue sample with a positive laboratory culture result that is treated with an intervention. This may include hospitalization,

antibiotics, bedside wound opening, or formal surgical intervention. Exceptions to a positive culture are noted below. In addition to whether infection was present, the specific site should be recorded using the definitions below:

Wound: Surgical wound infection or deep intrabdominal abscess which requires intervention

Biliary Tree: Episode of cholangitis defined as blood borne organisms which are cultured in the setting of abnormal liver function tests or imaging study revealing biliary tract disease. Also included are fluid collection which contain bile and are believed to be in communication with the biliary tree.

Blood: Blood borne organsim is cultured with no other defined source. This would include bactermia or fungemia presumed secondary to an indwelling line infection

Liver: Intrahepatic fluid collections which are determined to be an abscess as evidenced by positive culture of aspirated or drained fluid.

Pulmonary: Diagnosis is made by the presence of new or progressive focal pulmonary infiltrates on chest x-ray or CT scan and some degree of pulmonary compromise (clinical symptoms of shortness of breath, signs of tachypnea, abnormal blood gas, ventilator requirement) and may be accompanied by purulent tracheobronchial secretions, fever, leukocytosis, and/or a positive culture from sputum. A positive culture is not needed for this type of infection.

CNS: Mental status changes or neurologic findings and an abnormal exam of cerebral spinal fluid. In the case of fungal infection, characteristic mass lesions on imaging are adequate.

Urinary tract: Urine is culture positive for an organism and treatment is started.

4. Psychological. Major psychological issues that have required treatment or hospitalizations such as depression or suicidal attempts.

H. Other Complications

This includes complications that were not outlined in the above categories that have required intervention.

Donor Patient Survival

Revised 04/09/2003

(survival status)

Data element	Definition	Answer format	Location in chart	SRTR validation
Last known patient status	What was the patient's status at last contact?	Alive Dead	Post Transplant Medical Record Autopsy Report	Y
If alive, date last known alive.	If alive, date last known alive.	mmddyyyy	Post Transplant Medical Record Visit Record	N
If dead, date of death	When did the patient die?	mmddyyyy	Post Transplant Medical Record Autopsy Report	Y
If dead, primary cause of death	Select the primary cause of death from the list		Autopsy Report Discharge Summary	Y
If dead, secondary cause of death.	Select the secondary cause of death from the list		Autopsy Report Discharge Summary	N
If dead, tertiary cause of death	Select the tertiary cause of death from the list		Autopsy Report Discharge Summary	N

Data Module and Element Definitions and Code Lists

Most of the data entry forms are self-explanatory within the form itself. Below you will find references to the data Modules that correspond to each form and some notes to keep in mind when completing certain forms. The data Modules are very useful in deciphering just what type of data and the data format that is required on each form. Please be sure to refer to these data Modules at any time you are unsure of the question being asked.

Form 1: Recipient Enrollment Checklist-Core Module

Purpose: To determine the eligibility of patient for study and assign the subject ID number.

General Instructions: Refer to data Module 1 for further assistance.

Form 2: Recipient Study Enrollment-Core Module

General Instructions: This form is to be completed after the recipient and donor enrollment checklist form.
The date that the recipient's potential donor had their History and Physical is defined as the study enrollment for the recipient. The date must be entered in the following format: mm/dd/yyyy. Follow the instructions in the section titled: Assigning subject numbers. Refer to data Module 2 for further assistance.

Form 3: Recipient Demographics-Core Module

General Instructions: Refer to data Module 3 for further assistance.

Form 4: Listing and Transplant Information-Core Module

General Instructions: If you answered "yes" to transplant surgery in this form, you will need to complete the following forms: Recipient Condition at Transplant Form, the Recipient Intraoperative form, Recipient Morbidity Form, Graft Outcomes Form and the Baseline Immunosuppression and Rejection Episodes Form. If this patient has had a previous transplant, please see the instructions at the end of the code lists.

Form 5: Recipient Condition at Listing-Core Module

General Instructions: Refer to data Module 5 for further assistance. If the subject has HCC at the time of listing, you will need to complete the HCC at Listing Form.

Form 6: Recipient Condition at Enrollment-Core Module

General Instructions: Refer to data Module 6 for further assistance. This forms covers the period from listing to enrollment. If the subject has HCC at the time of enrollment, you will need to complete the HCC at Enrollment Form. If the subject also has HCV at the time of enrollment, you will need to complete the HCV at Enrollment Form.

Form 7: Recipient Condition at Transplant

General Instructions: Refer to data Module 7 for further assistance. This form covers the period from enrollment to transplantation. If the subject has HCC at transplant,

complete the HCC at Transplant Form. If the subject has HCV at transplant, complete the HCV at Transplant Form.

Form 8: HCC at Listing

General Instructions: Refer to data Module 8 for further assistance. This form is to be completed if you answered "yes" to the subject having HCC at listing on the Recipient Condition at Listing Form.

Note: For HCC assesment refer to- Form 8a.

Form 9: HCC at Enrollment

General Instructions: Refer to data Module 9 for further assistance. This form covers the period from listing to enrollment. This form is to be completed if you answered "yes" to the subject having HCC at the time of enrollment on the Recipient Condition at Enrollment Form.

Form 10: HCC at Transplant

General Instructions: Refer to data Module 10 for further assistance. This form covers the period from enrollment to transplantation. This form is to be completed if you answered "yes" to the subject having HCC at the time of transplant from the Recipient Condition at Transplant Form.

Form 11: HCV at Enrollment

General Instructions: Refer to data Module 11 for further assistance. This form covers the period from listing to enrollment. This form is to be completed if you answered "yes" to the subject having HCV at enrollment from the Recipient Condition at Enrollment Form. The Knodell score to be entered on this form should be taken directly from the pathologist's report. If it's not available, enter none.

Note: For Knodell score refer to - Form 11a.

Form 12: HCV at Transplant

General Instructions: Refer to Module 12 for further assistance. This form covers the period from enrollment to transplant. This from is to be completed if you answered "yes" to the subject having HCV at transplant from the Recipient Condition at Transplant Form. The Knodell score to be entered on this form should be taken directly from the pathologist's report. If it's not available, enter none.

Form 13: Recipient Intraoperative Data

General Instructions: Refer to data Module 13 for further assistance.

Form 14: HCC at Explant Assessment

General Instructions: Refer to data Module 14 for further assistance. This form is to be completed if you answer "yes" to HCC at transplant from the Recipient Condition at Transplant Form and answered "yes" to liver transplant performed on the Listing and Transplant Information Form. Refer to the explant assessment form for tumor grading.

Form 15: Recipient Baseline Immunosuppression and Rejection Episodes

General Instructions: Refer to data Module 15 for further assistance. Baseline refers to the time immediately post-transplant. For the immunosuppressive regimen at baseline, check all that apply this will also include any antibody induction treatment used at the time of the transplant procedure.

Note: For more than one treated rejection episode you will need to complete the Multiple Rejection Episodes and Treatment Form.

Form 16: Multiple Rejection Episodes and Treatment

General Instructions: Refer to data Module 16 for further assistance.

Note: For each treated episode of rejection you must complete individual Rejection Episodes and Treatment Form.

Form 17: Recipient Hospitalizations-Core Module

General Instructions: Refer to data module 17 for further assistance. More than one hospitalization will require completion of individual Recipient Hospitalization Forms.

Note: For primary discharge diagnosis refer to the pick list of diagnoses - Form 17a.

Form 18: Recipient Morbidity

General Instructions: Refer to data Module 18 for further assistance.

Note: Each post surgical complication (where indicated) that you answer "yes" must have its own Complication Severity form completed.

Form 19: Recipient Complication Severity

General Instructions: Refer to data Module 19 for further assistance.

Note: This form is to be completed if you have answered yes to any of the complications on the Recipient Morbidity Form (one form per complication). Each Severity Form is named for the complication it describes (i.e. "Biloma Severity Form").

Note: For definitions of recipient adverse events refer to - Form 19a.

Form 20: HCV Post-op Recurrence and Rx Data

General Instructions: Refer to data Module 20 for further assistance. This form is to be completed if you answered "yes" to HCV on the Recipient Condition at Transplant Form. The Knodell score to be entered on this form should be taken directly from the pathologist's report. If it's not available, enter none.

Form 21: HCC Post-op Recurrence and Rx Data

General Instructions: Refer to data Module 21 for further assistance. This form is to be completed if you answered "yes" to HCC at transplant on the Recipient Condition at Transplant.

Form 22: Graft Outcomes

General Instructions: Refer to data Module 22 for further assistance. If you answered "yes" to the recipient receiving a liver transplant on the Listing and Transplant Information Form, you will need to complete this form. If you answered "yes" to recipient being re-transplanted on the Recipient Patient Survival Form you will need to complete this form.

Form 23: Recipient Patient Survival-Core Module

General Instructions: Refer to data Module 23 for further assistance.

Note: For recipient cause of death refer to the code list - Form 23a.

Form 24: Donor Enrollment Checklist-Core Module

Purpose: To determine the eligibility of patient for study and assign the subject ID number.

General Instructions: Refer to data Module 24 for further assistance. Follow the instructions in the section titled: Assigning subject numbers.

Form 25: Donor Study Enrollment-Core Module

General Instructions: Refer to data Module 25 for further assistance. If the donor is accepted, you will complete the Donor Intraoperative Form.

Form 26: Donor Demographics-Core Module

General Instructions: Refer to data Module 26 for further assistance.

Form 27: Donor Evaluation-Core Module

General Instructions: Refer to data Module 27 for further assistance.

***Note*:** Donor evaluation is equal to donor history and physical.

Form 28: Donor Intraoperative Data

General Instructions: Refer to data Module 28 for further assistance. If the donor has been accepted and transplant was performed, this form will need to be completed.

Form 29: Donor Hospitalizations

General Instructions: Refer to data Module 29 for further assistance. Each hospitalization reported for the donor will require completion of individual Donor Hospitalization Forms.

Note: For list of liver diagnosis codes refer to the pick list of diagnoses - Form 17a or 29a.

Form 30: Donor Morbidity

General Instructions: Refer to data Module 30 for further assistance. From this form you will complete the Donor Complications and Severity Form if the donor experienced any complications. Each complication will require completion of individual Donor Complications and Severity Form.

Form 31: Donor Complications and Severity

General Instructions: Refer to data Module 31 for further assistance. Each complication reported for the donor will require individual completion of the Donor Complication and Severity Form.

Note: For definitions of donor adverse events refer to - Form 31a.

Form 32: Donor Patient Survival-Core Module

General Instructions: Refer to data Module 32 for further assistance.

Things to remember:

1. You must hit "save" to save your data.
2. Partial saves are allowed, so you can come back later and continue to enter the remainder of the form.
3. Always check the top of the form page to be sure you are entering data on the correct form.