LAPS

Leukocyte Antibodies Prevalence Study

Operations Manual
Version 2: September 2006

Sponsored by:
The National Hearth, Lung, and Blood Institute (NHLBI)
National Institutes of Health (NIH)

Blood Center Participants:
Blood Center of Wisconsin
Blood Centers of the Pacific
American Red Cross Blood Services - Southern Region
Hoxworth Blood Center
Institute for Transfusion Medicine
American Red Cross Blood Services - New England Region

Coordinating Center:
Westat

Central Repository:
SeraCare

Central Laboratory:
Blood Systems Research Institute

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RESEARCH CORPORATION

MEMORANDUM

TO: List* September 19, 2006

FROM: Sunitha Mathew

SUBJECT: LAPS Manual of Operations - Version 2

Attached please find Version 2 of the Leukocyte Antibodies Prevalence Study (LAPS) Manual of Operations (MOP). This version replaces MOP Version 1, June 2006 that you received during the training session conducted at Westat. This MOP is also available for download in PDF format on the REDS-II website under Documents/MOP.

From here on, small changes to the MOP will be documented in the form of field memos that will be sent to you. In the event of major changes, a new version of the MOP will be made available.

A brief summary of the major changes to LAPS MOP Version 1 is listed below. Please consult the appropriate chapters and its accompanying exhibits for more detailed explanations and directions.

- **Eligible Donors**
  All donors making an allogeneic whole blood donation or an apheresis donation are eligible to participate in LAPS provided they meet all remaining inclusion criteria.

- **Specimen Processing**
  Specimen refrigeration and processing times have been changed. Specimens should be refrigerated within 4-6 hours of collection and fully processed within 48 -72 hours of collection.

- **Shipping Schedule**
  Given the delay in starting LAPS, a new monthly shipping schedule has been added. See chapter 5 and Exhibit 8 for details.

- **Shipping Notification**
  The shipment notification procedures have changed per BSRI's request. Prior to shipment the new Shipping Notification Form (Exhibit 11) should be faxed (hard copy or using STS) to Simon Ng at BSRI. This should be followed by an email to the CC. For your convenience faxes/emails to SeraCare can now be sent using STS. For details please refer to chapter 5, section 5.4 and 5.5.

- **Questionnaire**
  OMB clearance number and expiration date have been added to the upper right hand corner of the questionnaire.

- **SMS Reports Cheat Sheet**
  An additional cheat sheet (flow chart) for running SMS reports has been added.

- **Cheat sheets, Shipping schedule, Barcode aid sheet**
  Laminated versions of all cheat sheets, shippin g schedule and barc ode aid sheet are provided for your convenience.

- **Contact List**
  A list of LAPS contacts is provided at the back of the binder.

- **SMS and STS User's Guides**
  New versions of SMS and STS User's guides are under development. These will be uploaded on the SMS and STS websites and the REDS-II websit e shortly. Please print out and place them under appropriate tabs of your MOP.

*

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1. INTRODUCTION

1.1 REDS-II Overview

The Retrovirus Epidemiology Donor Study – II (REDS-II) is a research program sponsored by the National Heart, Lung, and Blood Institute (NHLBI) to study the safety and availability of the blood supply. Six Blood Centers, a coordinating center, a central laboratory, and a central repository participate in the program. Below is a list of the participants and their role.

- Blood Centers
  - Blood Centers of the Pacific (BCP), San Francisco, CA;
  - Blood Center of Wisconsin (BCW), Milwaukee, WI;
  - Southern Region, American Red Cross (SARC), Atlanta, GA;
  - Hoxworth Blood Center (HBC), Cincinnati, OH;
  - Institute for Transfusion Medicine (ITxM), Pittsburgh, PA; and
  - New England Region, American Red Cross (NEARC), Dedham, MA
- Coordinating Center
  - Westat, Rockville, MD
- Central Laboratory
  - Blood Systems Research Institute (BSRI), San Francisco, CA
- Central Repository
  - SeraCare, Gaithersburg, MD

Under the umbrella of REDS-II several protocols will be developed and implemented. The Leukocyte Antibodies Prevalence (LAP) Study is one such protocol being implemented.

1.2 LAP Study Background and Overview

Transfusion Related Acute Lung Injury (TRALI) is a life threatening complication of transfusion. TRALI is a significant cause of transfusion associated morbidity and mortality and has been reported as the second most common cause of a fatal transfusion reaction[1]. It has been previously reported that 1:5000 transfusions result in TRALI [2]. A review of transfusion related fatalities from 1976 through 1986 has shown that acute pulmonary injury was responsible for 15 percent of all deaths.[1] In this study TRALI was the second most common cause of death after acute hemolysis, which was responsible for 51 percent of the deaths. TRALI is thought to result from the interaction of specific leukocyte antibodies with leukocytes. This study is designed to examine the prevalence of leukocyte antibodies in blood donors.

The two current hypotheses for pathogenesis of TRALI include the development of acute pulmonary insufficiency from immune and non-immune causes. The immune mediated mechanism postulates that passively transferred anti-leukocyte antibodies from blood donors are responsible for TRALI. The donor antibodies implicated in TRALI include antibodies directed towards Human Leukocyte Antigen (HLA) class I and class II antigens, and anti-neutrophil antibodies. The LAP Study is a cross-sectional multi-center study to measure the prevalence of HLA and neutrophil antibodies in blood donors with or without a history of blood transfusion or pregnancy to determine the risk of HLA antibody elevation associated with each factor, and to develop a repository of blood samples obtained from these donors. Specifically, 7,900 adult blood donors from the six Blood Centers participating in the Retrovirus Epidemiology Donor Study II (REDS-II) will be enrolled in the study. Eligible donors will be asked to complete a short questionnaire on their transfusion history (ever, number, date of last transfusion) and, for female donors, questions on pregnancy history (ever, number and outcome of pregnancies, and date of last pregnancy). Each donor will also be asked to provide a sample of blood which will be tested for the presence of HLA class I and class II antibodies. These data will help us evaluate variations in HLA antibody prevalence based on blood transfusion and pregnancy history and time since the last immunizing event. Further, neutrophil specific antibodies will be measured in those blood donors who have HLA antibodies. Also, donors with neutrophil antibodies will be tested to determine their neutrophil phenotype using routine serologic and DNA methods, since individuals homozygous for certain neutrophil antigens are more prone to develop certain neutrophil antibodies. The results from testing HLA positive donors for neutrophil antibodies in this primary study could be used to develop an optimal testing strategy for large numbers of donors using the stored repository samples. These data will provide the basis for developing a testing strategy and calculating donor loss in the event that a TRALI prevention strategy is implemented

that includes deferring donors with a history of transfusion or pregnancy or those with HLA or neutrophil antibodies. The second major goal of this study is to develop a repository of blood samples from well characterized blood donors whose detailed transfusion and pregnancy histories are known. Repository samples will be stored indefinitely. Although future research on repository samples is yet to be determined, they may be used for studies designed to help transfusion safety and transfusion biology.

1. Sazama K. Reports of 355 transfusion-associated deaths: 1976 through 1985. Transfusion 1990; 30:583-90.

2. Engelfriet CP and Reesnik HW. Transfusion-related acute lung injury (TRALI): International Forum. Vox Sang 2001; 81:269-283.

1.3 Computer Systems

For collecting a variety of types of study data and monitoring the overall progress of the study, three systems will be used by REDS-II study staff.

Study Management System (SMS). The SMS is designed for tracking enrollment of study participants and monitoring recruitment progress. No personally identifying information such as name or address will be stored in this system. Instead, the system will record the unique subject identifiers assigned to enrolled donors, along with their donor ID and blood unit identifier. Study Coordinators will record subject enrollment information such as consent status; gender; transfusion status; for females, parity information; and whether a questionnaire and specimen have been collected. As needed, the coordinator may also use the system's scheduler function to appoint study visits. Several report functions are included to assist in monitoring enrollment numbers by gender, transfusion status, and parity, and a few additional reports that will be needed for the day-to-day management of the study.

The SMS is a web-based system developed and hosted by Westat. Each Blood Center will be provided with a username and password that will allow them to access the Westat hosted system. See SMS Users Guide for specific instructions on how to use the SMS.

Specimen Tracking System (STS). The STS is designed to track specimen collection, processing, and shipping activities. Descriptive information about the specimens collected (e.g. material, volume, etc.) will be stored in the STS along with the status and location of each specimen from the point

of creation until the specimen is exhausted or received at the final repository location. It includes several validation features and reporting features that can be used for specimen management and reconciliation. Like the SMS, no personally identifying subject information will be stored here. The STS is a web-based system that will require the same username and password assigned for the SMS access. While data will be exported from the SMS and imported into the STS for the purposes of updating specific information, the STS does not directly interface with the SMS. STS Users Guide provides instructions on how to use the STS.

Questionnaire Data Entry (QDE) Website. The QDE website allows Study Coordinators to enter all information collected from consented donors on the paper questionnaire into a central data location. It is an easy and efficient method for entering study data. See QDE Users Guide for specific instructions on how to use the data capture form.

1.4 Study Timeline

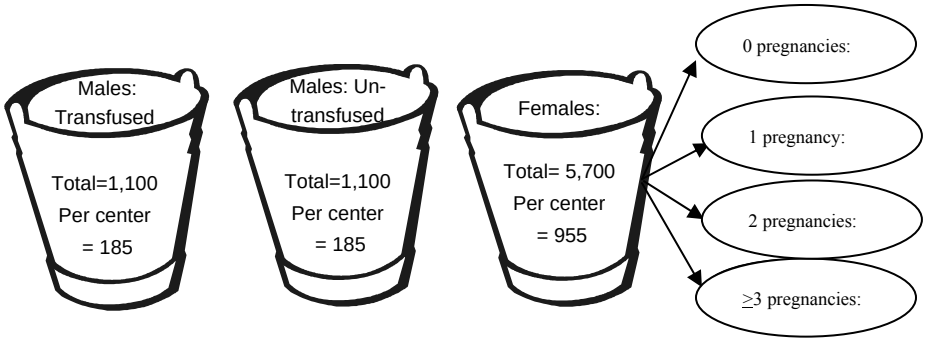
Recruitment for this study is scheduled to run for 8 months. The actual study start date, however, is dependent on the receipt of approval from Office of Management and Budgets (OMB). Currently, we are anticipating that the earliest recruitment start date will be August 1, 2006, however, it could be as late as November 2006. All HLA antibody prevalence testing will be conducted on an ongoing basis throughout the study recruitment period by the central laboratory, BSRI. However, those specimens identified for further testing due to positive HLA screening results will not be tested until one month subsequent to the close of recruitment. These additional tests to further type HLA and neutrophil antibodies will be performed at BCW. An overview of the current timeline is provided below.

June 2006	IRB Submission
June 20 & 21, 2006	Training
August 2006	OMB Approval
September 2006	Recruitment Start Date
May 2007	Recruitment End Date
June 2007	Final Phase of Laboratory Testing
November 2007	Data Compilation & Analysis

2. ON-SITE DONOR RECRUITMENT

2.1 Target Numbers

Following the LAPS protocol, each center is required to enroll donors in three different categories - 185 transfused male donors, 185 non-transfused male donors, and 995 female donors.



All donors who present for donation at specific recruitment sites and are eligible to donate will be approached to participate. Recruitment into a particular donor category will stop once the enrollment for that category is met. For example, it is anticipated that the recruitment target for un-transfused males will likely be satisfied approximately 1 month after the study begins. Thus, after the first month of the study, centers will likely no longer be enrolling un-transfused males but focusing recruitment efforts on females and transfused males. Transfused males typically only represent around 4% of a center's blood donor population. Thus, limiting to on-site recruitment alone for this category in an 8 month period would not yield the goal of 185 transfused males per center. Being cognizant of this, two options have been designed for targeted enrollment of transfused male donors. These are described in **Section 3**.

2.2 Selection of Sites

Blood Centers should select sites for on-site recruitment with the following goals in mind:

1. Racial/ethnic distribution is representative of your center's donor pool; and
2. Adequate representation of first time and repeat donors.

Most centers have chosen to recruit study participants at fixed sites (30 – 50 donors per day). However, centers can also choose to recruit at a combination of fixed and mobile sites to meet their targets in the event that fixed sites alone will not be able to provide necessary donor diversity and/or enough operational hours to meet recruitment targets. The CC will not specify the fixed/mobile sites from which to recruit donors. Instead, it is each Blood Center's responsibility to select sites that will best represent their overall donor population over the course of the study. To achieve this, different fixed and/or mobile sites may need to be designated weekly for the LAP study recruitment in order to collect a representative sample of that center's donor population. The CC will periodically compare demographic and other donation data information of LAPS participants with the overall monthly donation data collected on donors for REDS-II to monitor enrollment racial/ethnic distributions, as well as donor status (first time versus repeat).

2.3 Donor Recruitment Supplies

Blood Centers are responsible for supplying their designated fixed/mobile sites with the items listed in this section. Blood Centers should not estimate on a given day how many of the donors presenting to make a donation may decide to enroll in the LAP study. Instead, Blood Centers should anticipate enrolling 100% of all donors presenting to the site and ensure that the designated fixed/mobile site is amply supplied. Thus, if you are recruiting at a site that generally collects from 30 donors a day, the Study Coordinator should come with the necessary quantity of supplies to recruit 30 donors a day. Procedures for using each of the supplies listed in **Box 2A** below are detailed further in the sections indicated.

Box 2A
LAPS Recruitment Supplies

For each donor recruited for the LAP Study, the following supplies are needed:

- One (1) sheet of Subject ID labels per donor (see Section 2.4).
- One (1) LAPS information sheet – to be included in donor information packet (see Section 2.6).
- Two (2) informed consent documents – one form to be signed by the donor for the Blood Center to retain and one copy for the consenting donor to keep for his/her records (see Section 2.7).
- One (1) LAPS Questionnaire – to be completed by each donor consenting to participate in the LAP study. Donors consenting for repository alone need not complete the questionnaire (see Section 2.12).
- One (1) 7ml purple-top (EDTA) tube (see Section 2.8).
- One (1) 7ml red-top tube (no additives) – optional depending on your center's plans to collect serum (see section 2.8).
- Three (3) extra blood unit ID (BUI) labels to be placed on the 2 specimen tubes and on the log form. (see Sections 2.8 and 2.9).

2.4 Subject ID labels

For uniformity as well as a pricing discount for each of the individual Blood Centers, the CC has placed a central order for the Subject ID labels. Each Blood Center will receive center specific Subject ID labels which will be used to identify and link different study components to an enrolled donor. These labels will be placed in the designated areas on the signed Informed Consent document that the Blood Center retains, the Informed Consent document that the donor retains, the Log Form, the Questionnaire, the EDTA purple-top tube (see Section 4.5.4 for label placement), and the optional red top tube (see Section 4.5.4 for label placement). See Appendix, Exhibit 9, for a graphical representation of a sheet of subject ID labels and the location where each label should be placed.

A set of Subject ID labels is provided for each person enrolled in the LAP study. The format for the Subject ID is "**AAA-BB-CCCCC–D**", where:

AAA = Blood Center
- 210 = Blood Center of Wisconsin (BCW)
- 220 = Blood Centers of the Pacific (BCP)
- 230 = ARC Southern Region (SARC)
- 240 = Hoxworth Blood Center (HBC)
- 250 = Institute for Transfusion Medicine (ITxM)
- 260 = ARC New England Region (NEARC)

BB = Protocol Indicator 01 = LAPS

CCCCC = Sequential Subject ID

D = ID Check Digit

Please note that the Subject ID labels have an additional two-letters added to the end of the Subject ID ("AAA-BB-CCCCC–D-**XX**") that is not read by the barcode scanner and is therefore not retained in the STS or SMS. The two-letter suffix, "**XX**", indicates where the Subject ID label should be placed:

XX = Location to adhere the label
- LF = Log form
- IC = Informed Consent
- IC = Informed Consent
- QX = Questionnaire
- PT = Purple top, EDTA vacuum tube (if a donor consented for the LAP study)
- ST = Red top, serum vacuum tube (if a donor consented for the repository)
- X1 = Extra label
- X2 = Extra label
- X3 = Purple top, EDTA vacuum tube (if a donor consented for the repository only)

Center's choosing to recruit transfused male donors using the short form review method (see Section 3.2) will use a "dummy" Subject ID as described in Section 4.5.1 until consent is obtained and a "real" Subject ID is assigned.

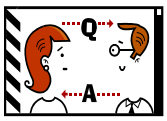
2.5 Eligible Donors

All donors making an allogeneic whole blood donation or an apheresis donation at the designated site should be considered eligible for the LAP study if they are 18 years or older. Donors under 18 years of age, donors making a directed or autologous donation, and donors deferred for whatever reason that day should ***not*** be asked to participate in the LAP study. Any donor who enrolls, but for whatever reason does not have a sample available, or who is later found to be reactive on routine infectious disease testing is not eligible to participate. In both of these cases, donors will be de-enrolled from the study. It should be noted that de-enrollment of donors in these instances does not require subject notification since the consent form informs the subject that this would be the case. Blood Centers are responsible, however, for performing the necessary steps for de-enrolling a subject (see Section 2.11 for de-enrollment procedures). In addition, donors who have already enrolled in the LAP study once are not eligible to enroll in the study again.

Box 2B
LAPS Eligibility

- Allogeneic whole blood donors or apheresis donors, 18 years or older, eligible to donate blood that day
- Directed or autologous donors are not eligible
- Deferred donors are not eligible
- Enrolled donors with no sample are not eligible and should be de-enrolled
- Enrolled donors who screen reactive on infectious disease testing are not eligible and should be de-enrolled
- Donors who have already enrolled in the LAP study once are not eligible to enroll again

2.6 Approaching a Donor



The LAPS information sheet (see Appendix, Exhibit 1) and informed consent document (see Appendix, Exhibit 2) should be included in the information package that all donors receive when they

come in to donate. This gives the donor an opportunity to read about the study prior to approaching them. After each donor has been screened by the health historian and found to be eligible to donate blood that day, approach them in sequential order and invite them to participate in the LAP Study. You can explain the study at this time and give each donor the opportunity to ask questions about the study. Make sure that the donor has not been previously enrolled in the LAP study as each donor is only eligible to participate once in the LAP study. Enrollment procedures are described in Box 2C. To minimize disruption to operational flow, Blood Center's can choose to approach and consent donors before the health history process. However, Subject ID's should be assigned only after the donor completes the health history process and is deemed eligible to donate blood that day.

2.7 Obtaining Informed Consent

Each Blood Center must have a signed IRB-approved informed consent on file for every donor participating in the LAP study. A template of an approved consent form can be found in the Appendix, Exhibit 2. Ensure that each donor willing to participate in the study signs the consent form, prints his/her name on the form and dates the form correctly. Arrange for a witness to sign the informed consent document.

Note that donors can consent to participate in the current LAP study and the repository, or for either the current study or the repository, alone. Because of this, the consent form is designed to obtain separate consent for each of the two main goals of the study. The donor must indicate on the form by marking the appropriate check boxes whether they are consenting for both or only one part of the study. Consenting for the repository alone will likely be rare, therefore make sure that such consent is not in error and try to stress to the donor the merits of participating in both the current study and the repository, since the purpose for both are the same – transfusion safety research.

At this time, as described in Box 2C, assign the next available Subject ID to the enrolled donor. There are two (2) Subject ID labels with the suffix IC. Place one on the signed copy of the informed consent form, on the first page, upper right-hand corner box. Place the other on the donor's copy of the informed consent form and give it to the donor to retain for his/her records.

Box 2C
Enrolling a donor in the LAP study

- Invite each sequential eligible donor to participate in the study following the interview with the donor historian.
- Explain the study at this time and answer questions.
- Ensure that the donor has not previously enrolled in the LAP study.
- Ensure that each donor willing to participate correctly checks the appropriate boxes on the last page and signs the consent form; prints his/her name on the form; and dates it with the correct date.
- Arrange for a witness to sign the informed consent form.
- Assign the next available Subject ID to the donor.
- Place one Subject ID label with the **suffix IC** on the signed informed consent form on the first page, in the upper right-hand corner box.
- Place the second Subject ID label with the **suffix IC** on the donor's copy of the informed consent form and give the form to the donor to retain for his/her records.

2.8 Labeling Specimen Tubes

All centers will need to collect 6-7ml of whole blood in a purple-top tube and if possible, an extra 6-7ml in a red-top tube containing no additives or separators. Each of these tubes needs to be labeled with the Subject ID label (for a description of Subject ID label see Section 2.4) and the Blood Unit Identifier (BUI), preferably barcode labels. You will have to check the consent form to see if the donor has consented to participate in the current LAP study and the repository or if he/she has consented to only one or the other. Accordingly, label the tubes as described below in Box 2D. Essentially, the label with the suffix PT (plasma tube) will always be placed on the purple-top tube, unless the donor only consents for the repository. If this is the case, the purple-top tube will be labeled with the X3 label, indicating for the laboratory technicians that this is a plasma tube that is only to be processed and aliquoted for storage in the repository and will not be tested for the current study. Labels with the ST suffix are for serum tubes.

Box 2D
Labeling specimen tubes

- **Study and Repository or Study only**: If the donor has consented to the current LAP study and the repository, or for the current LAP study alone, place the label with the **suffix PT** on the purple-top tube and the label with the **suffix ST** on the red-top tube. Now, label both tubes with the **BUI labels.**

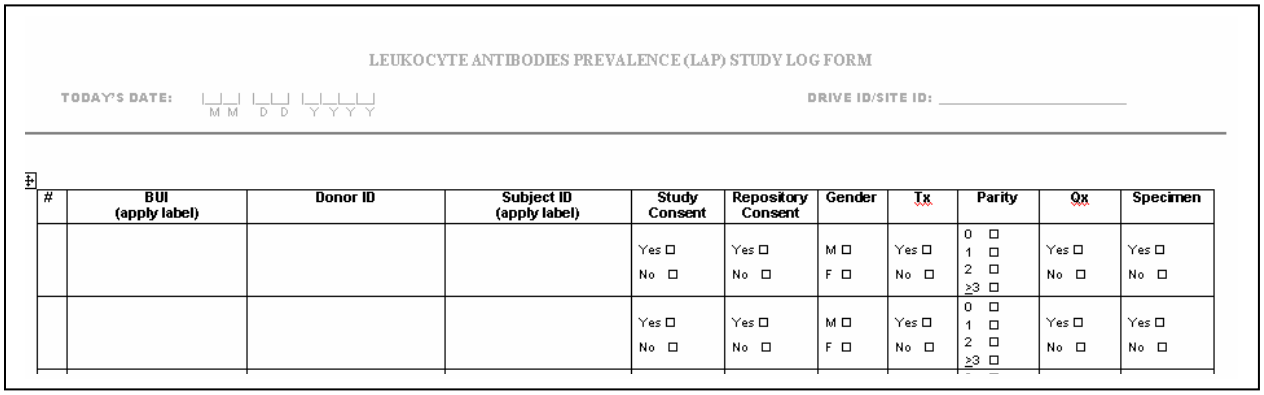
- **Repository Only:** In rare cases when the donor consents to the repository only, place the label with the **suffix X3** on the purple- top tube and the label with **suffix ST** on the red-top tube. Now, label both tubes with the **BUI labels.**

Detailed descriptions of label placement are given in Section 4.5.4. Determine the best time to label the specimen tubes based on your center's operational procedures. The Study Coordinator could apply the Subject ID and BUI labels on the tubes while enrolling the donor and have the tubes accompany the donor to the donation table, or alternatively, the labeling could take place at the donation table itself if the BUI labels are assigned only at that point. Once the sample is collected the tubes are sent to the processing lab.

Some centers are expecting a lag time before serum is available to the processing lab following routine donor testing. This delay may be 5 days or possibly even longer for the red-top tube or a frozen aliquot, to be returned from the Blood Center testing facility. These centers, therefore, must have a system in place where the laboratory processing staff will have access to the Subject ID labels. We suggest that at the time of subject recruitment, the Study Coordinator prepare a Subject ID folder. Each folder should be labeled with the BUI of the donor and corresponding left over Subject ID labels, already assigned should be placed in here. This folder should accompany the purple-top plasma tube to the processing lab. The lab should place the remaining Sample ID labels for this subject along with the Subject ID labels in the folder and file in BUI numeric order in a storage location convenient to laboratory staff. This way, when the red-top tubes arrive in the lab and are identified as those that need to be designated for the LAP study, the processing staff can retrieve the appropriate set of Subject ID labels by matching on the BUI and subsequently affixing the ST suffix label to the red-top tube or serum aliquot before processing and entering in the STS. The appropriate Sample ID labels will be applied to the serum aliquots prepared.

2.9 Documenting Enrolled Donor Information on the Log Form

Each donor enrolled in the study should be documented on the daily Log Form. An example of the Log Form can be found in the Appendix, Exhibit 3.



LEUKOCYTE ANTIBODIES PREVALENCE (LAP) STUDY LOG FORM

TODAY'S DATE: |_|_| |_|_| |_|_|_|_| (M M D D Y Y Y Y) DRIVE ID/SITE ID: _____

#	BUI (apply label)	Donor ID	Subject ID (apply label)	Study Consent	Repository Consent	Gender	Tx	Parity	Qx	Specimen
				Yes ☐ No ☐	Yes ☐ No ☐	M ☐ F ☐	Yes ☐ No ☐	0 ☐ 1 ☐ 2 ☐ ≥3 ☐	Yes ☐ No ☐	Yes ☐ No ☐
				Yes ☐ No ☐	Yes ☐ No ☐	M ☐ F ☐	Yes ☐ No ☐	0 ☐ 1 ☐ 2 ☐ ≥3 ☐	Yes ☐ No ☐	Yes ☐ No ☐

Figure 2-1. Log form

At the start of each recruitment day, the Study Coordinator should start a new Log Form (note more than one may be needed on a given day). As seen in Figure 201, in the top left-hand corner, the coordinator must document "Today's Date". In the upper right-hand corner, the Study Coordinator must document the Drive ID or Site ID unique for that particular mobile or fixed site. Make sure that you enter the Drive ID or Site ID in exactly the same format as in the REDS-II donation database. Documentation of these two pieces of information is critical as it will provide the CC with needed capability of linking this information to the REDS-II donation data to examine enrollment rates by site and whether those donors who agree to be in the study are demographically any different than those who do not.

For each enrolled donor, document the information listed below on the Log Form. The short form information that is already collected routinely as a part of REDS-II should be referenced for the completion of items 3 through 5.

1. Place the BUI label, and the Subject ID label with the **suffix LF** in the appropriate columns. Write in the Donor ID.

2. Document the level of consent by checking the appropriate boxes (yes/no) for "Study Consent" and "Repository Consent".

3. Indicate the gender of the subject (M/F) by checking the appropriate box;

4. Indicate whether the donor has ever had a transfusion by appropriately checking the corresponding yes/no box.

5. For females, check the appropriate box indicating the number of pregnancies under the column, "Parity".

6. Check the questionnaire "yes" box once the completed questionnaire is received.

7. Finally, check the specimen "yes" box once the specimen is collected.

The log form is meant to be a useful tool to determine at-a-glace the number and types of donors you enroll during the day.

2.10 Entering Enrolled Donor Information into the Study Management System (SMS)

At the end of each day, enter all the enrolled donor information from the Log Form into the Study Management System (SMS). The SMS is a web-based system that can be accessed by the unique username and password assigned to each person at each center. See SMS Users Guide for detailed instructions on how to enter data into the SMS.

2.11 De-enrolling Donors from SMS

Subjects who screen positive for routine infectious disease tests and those who for whatever reason do not have a sample, should be de-enrolled from the study. The Study Coordinator will pull up the subject's record in SMS using the Subject ID and update the "Subject Status" field to "De-enrolled". On a weekly basis run the De- enrollment Report on SMS (see SMS Users Guide for instructions) and send it to the processing lab. The lab will have to remove these specimens from the specimen box before shipping. The CC will also run the same report and delete the specimen record from STS.

2.12 Questionnaire

Place the Subject ID label with the **suffix QX** on a questionnaire and hand it to the enrolled donor to complete. The LAP study questionnaire is a self-administered form. A sample of the LAPS

questionnaire is provided in the Appendix, Exhibit 4. The donor may complete the questionnaire while waiting to donate blood or afterwards in the canteen. Donors should be strongly encouraged to complete the form before leaving the Blood Center. Make sure to collect the completed questionnaire from the donor and quickly scan to ensure that all appropriate questions have been completed.

2.13 Entering Questionnaire Data into the Questionnaire Data Entry (QDE) Website

At the end of each day enter the questionnaire data into the web based Questionnaire Data Entry (QDE) website. This form can be accessed by the unique username and password provided to each user. For detailed instructions on using the web form see the QDE Users Guide.

3. TARGETED RECRUITMENT FOR TRANSFUSED MALE DONORS

3.1 Overview

In addition to recruiting transfused males on-site, the centers will use a targeted recruitment plan to ensure that the target numbers for the enrollment of transfused male donors will be met. For the targeted recruitment, Blood Centers have 2 options to choose from. Each Blood Center should choose one option but may not use both strategies. A flow chart of operations is given in Figure 3-1.

3.2 Short Form Review Method

Review all REDS-II short forms at the end of each day and flag the transfused male donors from that day's donations. Retrieve specimens (retention tubes) from these flagged donors, and send them to the processing lab. Make sure that these tubes are labeled with the BUI. The lab should process, aliquot, and temporarily store these specimens following the instructions in Chapter 4 of this manual. When accessioned into the Specimen Tracking System (STS), the system will automatically generate a "dummy", or non-consented Subject ID for each specimen. For a description of the non-consented Subject ID see Section 4.5.1.

Study staff should then mail a recruitment letter to these donors along with two (2) consent forms, one (1) questionnaire and a postage paid business reply envelope for mailing the consent forms and questionnaire back to the center. A sample recruitment letter is provided in Exhibit 5. After 3-4 days, the donors should be contacted by phone to provide them with an opportunity to ask the study staff questions about the study or consent form.

Upon Blood Center receipt of the signed consent forms and questionnaire, the Study Coordinator will assign the donor a "real", or consenting donor Subject ID. Each of the consent forms and the questionnaire should be labeled with the subject IDs as described in Sections 2.7 and 2.12. Mail one copy of the consent form to the donor for his records and enter the donor's information into the SMS. For detailed instructions on entering a subject in the SMS see SMS Users Guide.

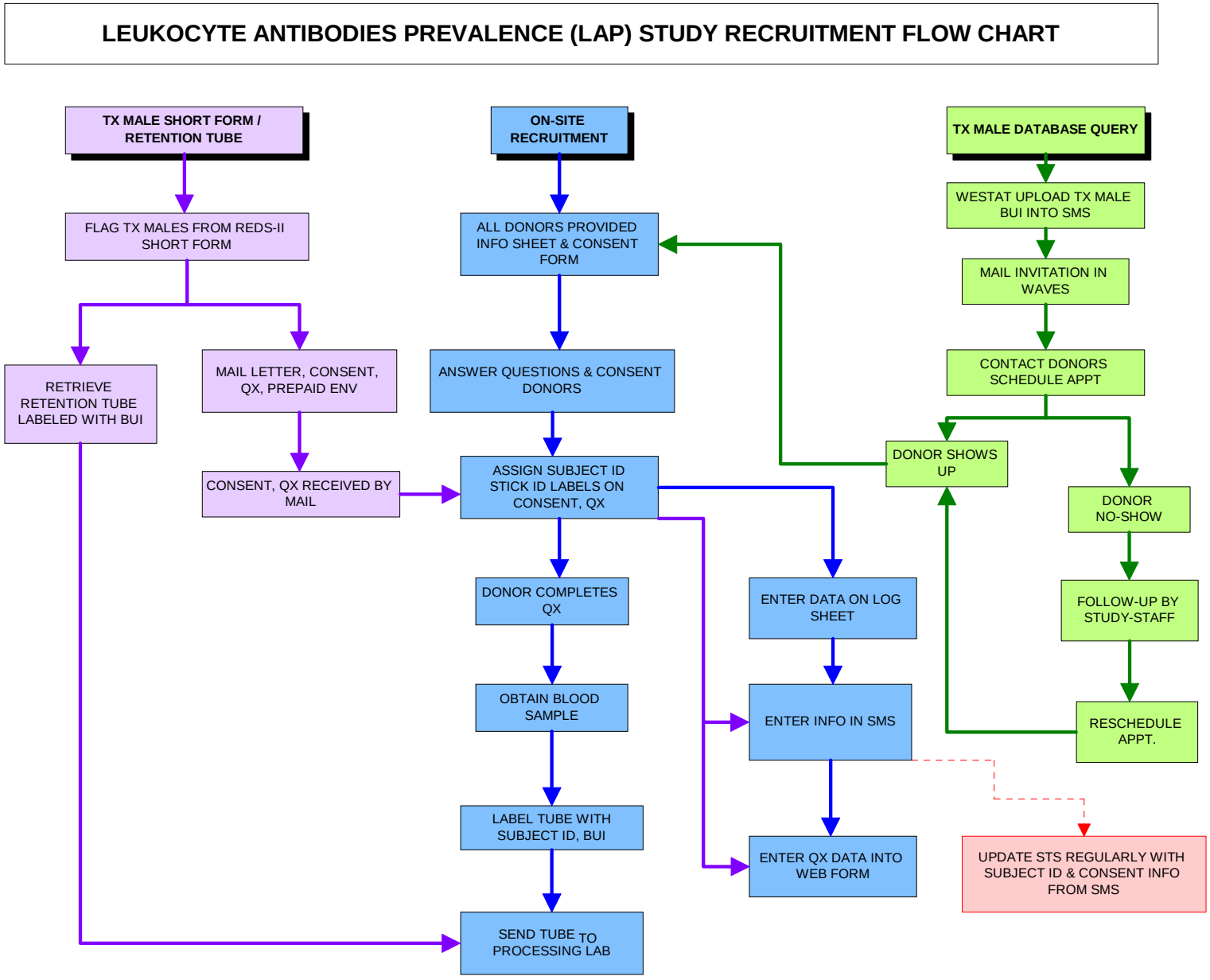


Figure 3-1. Recruitment flow chart

The CC will routinely update the STS with data documented in the SMS. Specifically, searching on BUI, the record in the STS will be updated with the subject ID assigned to the donor along with level of consent information. Before shipping, specimens should be reconciled against consent to avoid shipping non-consented specimens (see Section 4.8). At the end of the study recruitment period all non-consented specimens will be discarded.

Box 3A
Procedures for Short Form Flagging Method

- On a daily basis, review all REDS-II short forms for transfusion status and flag transfused males
- Pull retention tubes labeled with BUIs and send to processing lab
- Lab will process, aliquot and store specimen using "dummy", or non-consent subject ID
- Mail transfused male donors packet containing invitation letter, 2 consent forms, a questionnaire and a postage paid envelope
- Call the donor 3-4 days later and answer questions about the study
- Upon Blood Center receipt of signed consent forms and the questionnaire, assign the next available subject ID
- Place the labels with **suffix IC** on the 2 signed informed consents and mail one back to the donor for his records
- Place the label with **suffix QX** on the questionnaire
- Enter the donor in SMS
- CC will run regular updates from SMS to STS.

3.3 Donation Database Query Method

If your center has chosen to follow the Donation Database Query method of targeted recruitment for transfused male donors, then your SMS will be pre-loaded with the BUI numbers of all transfused male donors who gave blood in the previous three months at your Blood Center. In addition, a data file containing the BUI #s of these donors organized into three (3) waves will be provided to you. This information should be merged with your Blood Center database to retrieve the donors' name and

mailing addresses. Splitting the sample into three waves will assist in managing the workload for study staff. Sampling donors from the previous three months frame is ideal since these were donors who gave in the not so distant past and are eligible to be re-contacted by Blood Center tele-recruiters to come back to donate again and participate in the study.

For each wave, donors should be mailed a letter inviting them to participate in the study. A sample of the recruitment letter is provided in the Appendix, Exhibit 6. Following the mailing, optimally in 3-5 days, Blood Center tele-recruiters should call these donors and introduce the study using the script provided. For a sample telephone script see the Appendix, Exhibit 7. The tele-recruiters can schedule the donors for their next donation, or if the donor desires, schedule only a study visit, at a location and date that the Study Coordinator will be available. Centers choosing this option should have procedures in place for alerting the Study Coordinator of scheduled appointments, for example a flag in the Blood Center system indicating that it is a potential LAPS donor. The coordinator can routinely print a list of these scheduled appointments and then pull up the donor in the SMS using the donor's BUI from their last donation and enter the appointment information into the scheduler. This SMS scheduler can be used for managing the donor appointments, cancellations, no-shows etc. For detailed instructions on how to use the scheduler in SMS please see the SMS Users Guide. When the donor comes for his appointment, the Study Coordinator should follow the enrollment procedures for on-site recruitment detailed in Chapter 2. Study Coordinators will be responsible for re-contacting donors who miss scheduled appointments to reschedule them, or alternatively coordinate this effort with Blood Center tele-recruitment staff.

Box 3B
Donation Database Query Method

- SMS comes pre-loaded with BUI #s of transfused male donors
- CC will provide a file of these BUI #s organized in waves that can be merged with the donor information
- Mail invitation letter to donors in waves
- 3-4 days later tele-recruiter calls donor and introduces study using telephone script
- Recruiter makes next blood donation appointment or study appointment for donor
- Recruiter alerts the Study Coordinator of appointments using flag in the Blood Center system
- Study Coordinator enters the appointment information for the donor in SMS scheduler.
- When donor comes for the appointment he is enrolled in the study by using regular on-site recruitment protocol

4. SPECIMEN COLLECTION & PROCESSING

4.1 Overview

Each Blood Center is responsible for processing all donor samples according to the procedures outlined in this chapter. As indicated in Section 2.8 of this manual, a whole blood sample and an optional serum sample will be collected from each donor for this study. Samples will be processed into the component types of plasma (PL) and packed red blood cells (PRBC) from the EDTA preserved blood and also into serum (SE) from a plain red top blood collection tube. Each of these component types will be placed into aliquot tubes in volumes appropriate to the testing identified by the study protocol or volumes deemed adequate for future testing if held in the repository for long term storage.

Aliquoted cryovials will be stored in freezers using either two sets of boxes, or in the case of centers storing samples from individuals who did not yet consent to be in the study (short form review method), in three sets of boxes. The first set of boxes will hold cryovials to be shipped to BSRI, the REDS-II Central Laboratory. The second set will hold cryovials to be shipped to SeraCare for storage in the NHLBI REDS-II repository. Cryovials in these two sets of boxes will be shipped to either BSRI or SeraCare on a twice a month schedule as will be discussed in Chapter 5. The optional third set of boxes will be used to hold cryovials from donors that have not yet given their consent for the LAP study and neither the boxes nor the cryovials will be shipped from the Blood Center until the donor gives consent. When consent is given by a donor, specimens will be transferred from these temporary non-consenting boxes into boxes destined for either the Central Laboratory for testing or to the Central Repository for storage. All cryovials that remain in the third set of boxes at the completion of this study will be disposed of if the donor did not give consent to have their specimens either tested for the study or stored in the repository (see Section 4.10 and the STS Users Guide).

4.2 Laboratory Supplies

Blood Centers will be responsible for supplying the following items:

- Blood collection/Vacutainer™ tubes and all other supplies associated with the actual collection of the blood.

- Blood processing supplies such as centrifuge, test tube rack, personal protective items for staff, -70°C freezer; an ice block, wet ice and/or dry ice.
- A computer with:
  - Microsoft Windows XP or Windows 2000 operating system,
  - Adobe Acrobat Reader (version 5.0 or higher),
  - Internet access,
  - Internet Explorer (6 Service Pack 1 (SP1) web browser with 128 bit encryption);
  - An optical scanner capable of reading both linear and 2-dimensional barcodes (we suggest catalog number CR2-USB-Gun Kit from Anthony Lee Associates); and
  - A printer.

The Central Lab, BSRI, will be responsible for supplying the following items to each of the Blood Centers:

- Cryovials
- Cryovial racks
- Graduated transfer pipets
- Freezer boxes
- Box ID - 3 label sets for freezer boxes
- Shipping containers, labels and shipping costs for any specimens going to the Central Laboratory for testing

The Central Repository, SeraCare, will be responsible for supplying the following items to each of the Blood Centers:

- Sample ID labels for the blood tubes and cryovials
- Shipping containers, labels and shipping costs for all specimens going to the Central Repository for storage

The Coordinating Center, Westat, will be responsible for supplying the following items to each of the Blood Centers:

- Subject ID labels (for recruitment and enrollment purposes)
- Web-based systems for tracking and reconciling study subjects, specimens and consent information
- Support for systems and study activities

4.3 Specimen Collection

During the blood donation process a 6 or 7-mL EDTA blood tube will be collected from each donor enrolled in the study. If serum can be collected from either a dedicated source or residual volume from a testing retention tube, this should also be placed into the repository.

For transfused male donors identified during short form review (Option 1) and who may consent for the study in the future, plasma, packed red blood cells and serum (if available), should be processed and placed into the repository.

4.4 Sample Volume Requirements

The **minimum** amount of blood required from each donor for this study is:

- 6.0-mL (7.0-mL preferred) EDTA tube for plasma (PL) and packed red blood cells (PRBC) aliquots

Contribution to the serum repository is **optional** (this option is Blood Center dependent and must be determined prior to the implementation of the LAP study for proper system configuration):

- 5.0 – 7.0-mL red top blood collection tube (no separator or additives) or the residual serum from same, to prepare anywhere from two 0.5-mL up to four 1.0-mL aliquots for the serum repository

4.5 Labeling system

In addition to the BUI, three types of labels will be used in the LAP study:

1. **Subject ID** labels (provided by the CC)
2. **Sample ID** labels (provided by the Central Repository)
3. **Box ID** labels (provided by the Central Laboratory)

Using these labels in conjunction with the REDS-II Specimen Tracking System (STS), will facilitate the tracking of blood collection tubes and cryovials.

4.5.1 Subject ID Labels

Subject ID labels will be used to identify and link different study components to an enrolled donor. As explained in section 2.4, labels will be placed in the designated areas on the signed Informed Consents, the Log Form, the Questionnaire, the EDTA blood collection tube (see 4.5.4 for label placement), and the optional plain red top blood collection tube (see 4.5.4 for label placement). A detailed description of the Subject ID labels to be used for all consented donors is given in Section 2.4.

Centers choosing to recruit transfused male donors using the short form review method will need to process and store the sample from the transfused male donors before obtaining consent. The Blood Center will enter this sample into the STS (see the Appendix of the STS User's Guide) using a sequential "dummy" Subject ID which is assigned by the STS. There is no physical label for the "dummy" Subject ID instead you will scan the Barcode Aid provided in the Appendix, Exhibit 10. For detailed instructions refer to the STS Users Guide. The "dummy" Subject ID will appear in the STS as "NC AAA BB CCCC", where:

NC = Designation that the Subject ID is for a Non-consented individual
AAA = Blood Center ID
BB = Protocol Indicator 01 = LAPS
CCCC = Sequential Subject ID (automatically generated by the STS)

These donors will be assigned a "real" Subject ID when consent is obtained.

laboratory personnel will add the appropriate Sam ple ID label to the tubes (see Figure 4-2 f or where the labels should be placed on the tubes).

4.5.4.a Subject ID Labels – The appropriate Subject ID labels to be used are designated below:

The Subject ID labels to be used o n blood collection tubes from subjects that have **consented for the LAP study and the repository (or for the LAP study only)** have the following suffixes:

- For the EDTA purple top tube: **PT**
- For the residual serum or red top tube: **ST**

The Subject ID labels to be used on tubes fro m subjects that have **consented for the repository (but not the LAP study)** have the following suffixes:

- For the EDTA purple top tube: **X3**
- For the residual serum or red top tube: **ST**

For Blood Centers using short form review method (Option 1):

The Subject ID labels to be used on tubes from subjects that have **not yet consented (for anything)**:

- For the EDTA purple top tube: **No Subject ID label**
- For the residual serum or red top tube: **No Subject ID label**

A. Correct placement of the BUI or Subject ID label to the blood collection tube. The linear barcode should go the length of the tube and shou ld not be wrapped around the dia meter of the tube as the scanner may not see the entire symbol.

B. The BUI and Subject ID labels should be staggered on the blood collection tubes. By not aligning the barcodes the scanner will not inadvertently red the wrong barcode.

C. Incorrect placement of BUI and Subject ID labels

Figure 4-2. Applying BUI and Subject ID labels to a blood collection tube

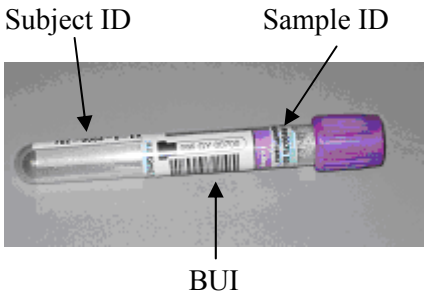
4.5.4.b Designation of Sample ID labels

A set of Sample ID labels (i.e. each label in the set has the same BSI root ID) will be used for each unique subject. The appropriate Sample ID label to be used for each tube type is determined by the sequence numbers which are designated below:

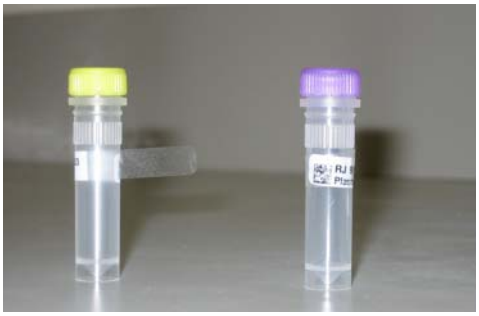
Sequence number	Sample description	Example sample ID for BCW
001	EDTA whole blood tube (7.0ml)	RI 000001 001
002	Plasma (0.5mL)	RI 000001 002
003	Plasma (0.5mL)	RI 000001 003
004	Plasma (1.0mL)	RI 000001 004
005	Plasma (0.5mL)	RI 000001 005
006	Plasma (0.5mL + residual)	RI 000001 006
007	PRBC/BC (0.5mL)	RI 000001 007
008	PRBC/BC (0.5mL)	RI 000001 008
009	Red Top, Serum tube (2.0ml)	RI 000001 009
010	Serum (0.5mL)	RI 000001 010
011	Serum (0.5mL)	RI 000001 011
012	Serum (0.5mL)	RI 000001 012
013	Serum (0.5mL + residual)	RI 000001 013

A. Correct placement of the Sample ID label on blood collection tubes. The Sample ID label should be placed at the top of the blood collection tube. The clear portion of the label should be wrapped around the tube to cover and laminate the barcode.

B. Incorrect placement of the Sample ID label on blood collection tubes.



C. Once all 3 labels are on the blood collection tube, it should look something like this.



D. Correct placement of the Sample ID labels on cryovials. The barcoded end of the label is first placed on the cry ovial, then the clear end of the label is wrapped around the vial (as shown on the yellow capped cryovial on the left). The clear end of the label should overlap the barcode (as shown on the purple capped cryovial).

E. Correct placement of the Sample ID labels on cryovials is shown on the left vial and incorrect placement of the Sample ID labels is shown on the right vial.

Figure 4-3. Applying sample ID labels to a blood collection tube and cryovials.

4.6 Labeling, Recording collection, Processing into aliquots, and Storing samples

This section describes the procedures for labeling, processing and storing specific collection and storage vials.

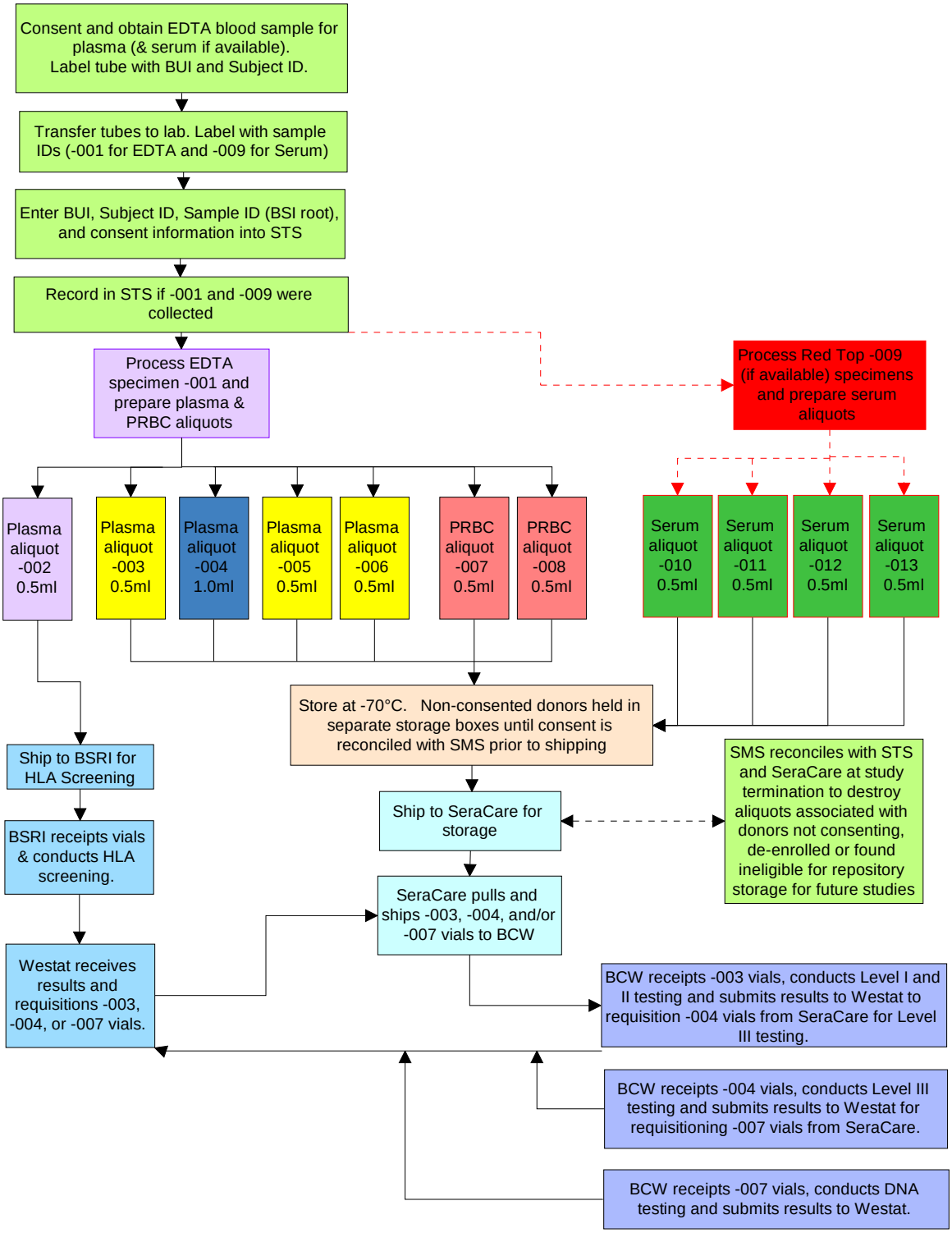


Figure 4-4. REDS-II LAP Study: Specimen collection, processing and testing flow diagram

4.6.1 Labeling

1. Collect an EDTA tube (and the optional serum tube, if appropriate) from a donor for the LAP study.

2. Label it with the BUI and appropriate Subject ID labels (see Figure 4-2). Remember: If the donor did not consent for either the study or repository, a Subject ID label should not be placed on the tube.

3. If possible place the tubes in refrigerated temperatures of 2 – 8°C as soon as feasible. The specimens may remain at room temp for up to 72 hours but this is not optimal and should be refrigerated within 4- 6 hours of collection. Specimens should be fully processed and frozen within 48-72 hours of collection for best specimen integrity.

4. Upon receipt in the REDS-II processing area, these tubes will be logged into the specimen tracking system for reconciliation through this system that the donor has consented.

5. Select a set of Sample ID labels and adhere the appropriate labels to the EDTA (and serum) tubes (sequence -001 is for the EDTA tube and -009 is for the serum, red top tube) (see Figure 4-3).

6. Retain the remaining Sample ID labels from the "set" for use on the aliquot cryovials.

7. Create a new entry for the subject in the STS by scanning in the Subject ID, BUI ID, and sample BSI ID (you can scan either the EDTA tube ID label (sequence -001) or the serum, red top tube ID label (sequence -009); only the BSI root ID "AABBBBBB" without spaces will be captured at this time in the STS) and entering the consent information. See the STS Users Guide (LAPS Appendix) for details on how to enter this information.

Remember:

a. If the EDTA tube has a Subject ID label with "**PT**" as the suffix, then the person consented to be in the study. They may or may not have consented for the repository; you can leave the "consent for repository" field in the STS blank for now.

b. If the EDTA tube has a Subject ID label with "**X3**" as the suffix, then the person consented only for the repository. In this case, you should not create and store aliquot -002.

c. **For centers using short form review method (Option 1)**: If the EDTA and serum tubes have no Subject ID label, the person has not yet consented for the study or the repository. Leave both consent fields in the STS as default, "No."

8. Record in the STS (see Users Guide, LAPS Appendix) that the EDTA tube (sequence -001) and serum, red top tube (optional; sequence -009) were collected.

9. Begin processing the samples.

4.6.2 Processing

Laboratory staff should follow Universal Precautions and OSHA Bloodborne Pathogen Rules throughout the following sample processing procedure.

1. Allow the red top tube (with sequence number -009) to clot for a minimum of 30 minutes.

2. Centrifuge the EDTA purple top (with sequence number -001) and red top tubes at 2500g for 10-15 minutes. A refrigerated centrifuge is not required. However, if the samples are not immediately aliquoted and frozen, the samples should be held at refrigerated temperature of approximately 4°C following centrifugation. Specimens should be separated into serum or plasma and cells, aliquoted into the appropriate cryovials and frozen at the Blood Center within 48 - 72 hours of collection.

3. While the tube(s) is (are) being centrifuged, label the appropriate aliquot cryovials with the Sample ID labels associated with the parent tubes (EDTA and serum tubes) and place the vials in a rack. The following color scheme (also see Figure 4-5) should be followed when placing the color caps on the cryovials:

Cryovial Color Scheme:

Purple top cryovial =	Plasma 0.5mL	Sequence -002
Blue top cryovial =	Plasma 1.0mL	Sequence -004
Yellow top cryovial =	Plasma 0.5mL	Sequence -003, -005, -006
Red top cryovial =	PRBC 0.5mL	Sequence -007, -008
Green top cryovial =	Serum 0.5mL	Sequence -010, -011, -012, -013

Figure 4-5. Color scheme for cryovials

Vials with sequence -002 have blue caps, -003 yellow, -004 blue (these have 1.0ml plasma), -005 yellow, -006 yellow, -007 red, -008 red, and -010 through -013 green

4. After labeling the cryovials and placing them in the rack, use the STS (see STS Users Guide, LAPS Appendix) to select an appropriate box to store the cryovials. Retrieve the box from the freezer and place the box in/on an ice block or on wet or dry ice so that the aliquots already frozen and in the boxes do not have an opportunity to begin thawing (or label a new box and place the box on the bench top).

5. After the centrifuge has come to a stop, remove and aliquot appropriate amounts of plasma from the EDTA tube into 5 cryovials using a graduated transfer pipet (see Section 4.8 for aliquoting priority in case of low volume):

   i. -002 0.5-mL Plasma (Purple top cryovial)

   ii. -003 0.5-mL Plasma (Yellow top cryovial)

   iii. -004 1.0-mL Plasma (Blue top cryovial)

   iv. -005 0.5-mL Plasma (Yellow top cryovial)

   v. -006 0.5-mL (plus remaining) Plasma (Yellow top cryovial)

6. Gently mix/resuspend the packed red blood cells (PRBC) that remain in the tube with the same transfer pipet as was used to fill the cryovials with plasma. Do not confuse pipets from different donors, always use one pipet per donor or if uncertain get a fresh pipet. Resuspension of the buffy coat (layer of white cells and platelets) into the packed red blood cells is accomplished by drawing the blood up into and expelling it from the pipet a minimum of 5-6 times.

7. Transfer the PRBC into two cryovials using the graduated transfer pipet (see section 4.8 for aliquoting priority in case of low volume):

   i. -007 0.5-mL PRBC (Red top cryovial)

   ii. -008 0.5-mL PRBC (Red top cryovial)

8. Remove and aliquot the serum from the red top tube into 4 cryovials using a graduated transfer pipet:

   i. -010 0.5-mL Serum (Green top cryovial)

   ii. -011 0.5-mL Serum (Green top cryovial)

   iii. -012 0.5-mL Serum (Green top cryovial)

   iv. -013 0.5-mL (+ residual) Serum (Green top cryovial)

9. Record that the EDTA and serum (optional) tubes were processed into aliquots by scanning in the -002 and -010 (optional) cryovial Sample ID labels in the STS (see STS Users Guide, LAPS Appendix)

10. If the volumes in the cryovials differ from what was expected, adjust the volume accordingly in the STS (see STS Users Guide, LAPS Appendix). You can use the "Barcode Aid" for Routine Entries (found in Appendix, Exhibit 10) to scan in a volume, if desired.

11. Inspect the plasma and serum aliquots for hemolysis. If the either is red-tinged or pink, the blood sample is hemolyzed. Document the problem in the STS (see STS Users Guide, LAPS Appendix) and if possible grade the hemolysis from 1+ to 4+. Do not discard the sample.

4.6.3 Specimen Storage

**Note: Sections 4.6.3.B and C have special instructions for storing specimens from subjects that consented for the repository only or did not consent for anything yet (relevant for Blood Centers following short form review method,Option 1).*

A. Specimens from subjects that <u>consented for the study and repository</u>:

1. Cryovials with sequence numbers -002 (i.e. cryovials with purple caps) are destined for BSRI and should be stored in a box with a white Box ID label with "BS" as the suffix (such as RJ-01-00001-**BS**). The STS should be used to select a freezer box that has already been created or to create a new box (see STS Users Guide).

2. Cryovials with sequence numbers -003, 004, 005, 006, 007, 008, 010, 011, 012, or 013 are destined for SeraCare and should be stored in a box with a white Box ID label with "SC" as the suffix (such as RJ-01-00001-**SC**). The STS should be used to select a freezer box that has already been created or to create a new box (see Users Guide).

3. Place the samples in the appropriate boxes in the spaces designated by the STS (see STS Users Guide). Example box layouts are shown in Figure 4-1 and Figure 4-6 to help guide you. Keep in mind that the Box ID labels are located at the bottom right corner of the box; Row A, Column 1 is located at the top left slot; and Row I, Column 9 is always left empty.

4. Verify that the contents of the box are consistent (sequence numbers of the vials are appropriately grouped) and have specimens from subjects that have consented for at least the study. Use the STS to help with this process.

5. All processed samples from subjects that consented for the study and repository should be stored at -70°C until they are shipped to BSRI (sequence -002) or SeraCare (all cryovials except -002).

6. Following the shipping schedule detailed in Chapter 5, prepare shipments to BSRI and/or SeraCare using the STS (see STS Users Guide, LAPS Appendix).

7. Place the appropriate boxes holding frozen specimens (in cryovials) in the appropriate shipping container provided by either BSRI or SeraCare with dry ice. Print the shipment manifest from the STS (see STS Users Guide, LAPS Appendix) and place the hard copy of the manifest in a plastic bag. Cover freezer boxes with additional dry ice. Put the lid of the shipper in place. Then, place the manisfest on top of the lid in the shipper container. Seal the shipper container and label the outside as appropriate.

8. Ship the package using an overnight courier with package tracking capabilities such as FedEx.

9. Once the package has been shipped, confirm in the STS (see STS Blood Center, LAPS Appendix) that the package is in transit.

10. You can use the STS to track the package and to ensure that SeraCare or BSRI received the package and its contents.

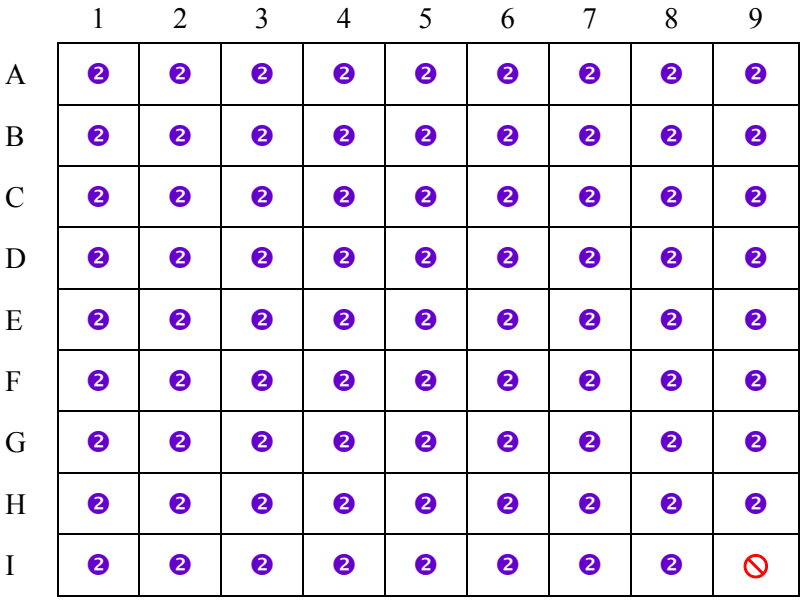


Figure 4-6. Example layout for Cryovial box with "consented" aliquots to BSRI

B. Specimens from subjects that <u>consented for the study only</u>:

Treat these the same way as above ("Specimens from subjects that consented for the study and repository"). At the end of the study, if samples are not needed for testing to complete the LAP Study protocol, the samples will be identified, pulled, and destroyed.

C. Specimens from subjects that <u>consented for the repository only</u>:

Specimens from subjects that consented for the repository alone should not be sent for testing to BSRI. Therefore cryovials with sequence numbers -002 should be stored in the neon labeled non-consenting freezer box until the end of the recruitment period. All other cryovials (sequence numbers -003, 004, 005, 006, 007, 008, 010, 011, 012, or 013) are destined for SeraCare and should be stored in a box with a white Box ID label with "SC" as the suffix (such as RJ-01-00001-**SC**).

D. Specimens from subjects that <u>did not yet consent (either for the study or repository)</u>:

All vials from a subject's donation, regardless of sequence number, will be put into one neon labeled box. This box will not be shipped.

1. All cryovials (sequence numbers -002, 003, 004, 005, 006, 007, 008, 010, 011, 012, 013) should be stored in a box with a neon Box ID label with "**NC**" as the suffix (such as RJ-01-00001-**NC**). The STS should be used to select a freezer box that has already been created or to create a new box (see STS Users Guide); leave the "ship to" destination field blank for these boxes in the STS.

2. Place the samples in the appropriate boxes in the spaces designated by the STS (see STS Users Guide).

3. All processed samples from subjects that have not yet given consent should be stored at -70°C.

4. Samples from donors that have not consented should NOT be shipped.

5. At the conclusion of the study, any samples from donors that have not consented will be destroyed (see section 4.9 and STS Users Guide). This will be done by first conducting a final update/comparison between the SMS and the STS (see STS Users Guide, LAPS Appendix).

6. Use the STS to identify samples (and the boxes that hold the samples) from donors who have not yet consented (see STS Users Guide, LAPS Appendix).

7. Work with Westat to arrange for the specimens in those boxes to be destroyed (see Section 4.9).

4.7 Aliquoting (including priority in case of insufficient sample quantity)

The total sample volume that is to be aliquoted into 11 cryovials is 6.0mL. This includes a total of five cryovials with plasma (four 0.5mL and one 1.0mL aliquots), two cryovials with packed red blood cells (PRBC) (two 0.5mL aliquots), and four cryovials with serum (four 0.5mL aliquots). In the event that there is not enough volume for all of the aliquots to be made, the priority is specified in the far left column in the table below. Also shown below are the optional serum cryovial aliquots.

Cryovial priority order	Vial sequence number	Material type	Volume
1	-002	Plasma (or serum)	0.5mL
2	-003	Plasma (or serum)	0.5mL
3	-004	Plasma (or serum)	1.0mL
4	-007	PRBC/BC	0.5mL
5	-005	Plasma (or serum)	0.5mL
6	-006	Plasma (or serum)	0.5mL + residual
7	-008	PRBC/BC	0.5mL
8	-010 (optional)	Serum	0.5mL
9	-011 (optional)	Serum	0.5mL
10	-012 (optional)	Serum	0.5mL
11	-013 (optional)	Serum	0.5mL + residual

4.8 Entering Information into STS

The STS is a tool designed to track and monitor specimen collection, processing, and shipping of REDS-II protocol samples. The Section 4.6 ("Labeling, processing, and storing samples") in this MOP indicates actions that should be carried out with the STS. The STS Users Guide, LAPS Appendix has been developed to provide users with step-by-step instructions for how to use the STS to carry out those actions.

Below is an overview of when the STS will be used for LAPS. For details on how to use the STS and overview flow charts for using the STS for LAPS, please refer to the STS Users Manual (LAPS Appendix).

a. Once the EDTA and serum blood collection tubes are collected from a donor, they are transferred to the laboratory for processing and labeled with Sample IDs.

b. The subject's information (Subject ID, BUI, Sample ID, consent information) is entered into the STS.

c. The STS expects that certain blood collection tubes will be or have been collected (EDTA tube -001 (and for some Blood Centers, serum tube -009)).

d. After confirming that the expected tube(s) has been collected, the STS expects that aliquots will be created from those tubes; if the expected EDTA (and serum, if applicable) were not collected, this is recorded in the STS and no aliquot vials will be expected.

e. Once the aliquots have been created, this is recorded in the STS.

f. The aliquot vials are then stored in aliquot boxes in spaces designated by the STS. The STS expects that vials with certain sequence numbers are destined for specific locations (i.e. -002 vials go to BSRI; all others go to SeraCare) and has validation tools to ensure that the vials are stored in appropriate boxes. Specimens from donors who did not consent for anything should not be shipped (at least until the end of the study); the STS associates consent statuses with specimens to help facilitate this process.

g. Once the aliquot boxes are ready to be shipped, the STS is used to create a virtual shipment and generate a list of all vials in boxes to be shipped. The list shows whether the vial is from a donor that consented for the study and/or repository.

h. The STS has a validation tool to verify that all of the contents of the shipment are destined for the same place.

i. The STS can be used to track the shipment and see whether the recipient confirmed receipt of the shipment, the individual boxes, and/or the individual vials.

j. From the recipient's perspective, the STS can be used to see what shipments are being prepared to be sent, track the shipments, and receipt the shipment.

Using the STS for tracking specimens from non-consented donors identified from the short form review:

a. Once the EDTA and serum tubes are collected from a donor, they are transferred to the laboratory for processing and labeled with Sample IDs.

b. The subject's information (BUI, Sample ID, consent information) and a "non-consented" Subject ID (scanned from the "Barcode Aid" sheet) are entered into the STS.

c. The STS expects that certain blood collection tubes will be or have been collected (EDTA tube -001 (and for some Blood Centers, serum tube -009)).

d. After confirming that the expected tube(s) has been collected, the STS expects that aliquots will be created from those tubes; if the expected EDTA (and serum, if applicable) were not collected, this is recorded in the STS and no aliquot vials will be expected.

e. Once the aliquots have been created, this is recorded in the STS.

f. All of the aliquot vials (regardless of sequence number) from non-consented donors are stored together in one box (with a neon label) in spaces designated by the STS. The "ship to" designation in the STS is left blank for boxes holding specimens from non-consented donors. These boxes will not be shipped.

g. The CC will update the consent information in the STS from the SMS.

h. Any specimens from donors that have now given consent, will need to be moved from the "non-consented" boxes, into a "real" box (with white Box ID labels). Use the STS to identify which specimens in the "non-consented" boxes are now from donors who consented, locate those specimens, and record in the STS where those specimens have been moved.

Steps "f" through "j" in the "consented" process should now be followed.

4.9 Removing Samples for Donors Who De-enroll or are Found Ineligible

On a weekly basis the Study Coordinator will run the De-enrollment Report on the SMS (see SMS User's Guide for instructions) for donors who either asked to withdraw from the study or whose routine viral marker testing was found to be reactive. This report is provided to the processing staff who will in turn use the STS to identify and generate a list of all samples locations. The samples should be removed from the freezer boxes and disposed of through current and appropriate guidelines for disposal of biological waste. The CC will also run the same report and delete the specimen record from the STS.

1. Access the STS (see STS Users Guide, LAPS Appendix) to identify and generate a box location list for all samples identified on the De-enrollment Report.

2. Pull those samples from the boxes in the freezers and discard through current and appropriate guidelines for disposal of biological waste.

3. Send Debbie Todd at Westat the list of Sample IDs that you pulled and destroyed. Westat will remove the records for those samples from the STS.

4.10 Destroying Samples at the End of the Study

At the conclusion of the study, samples from donors who did not consent for the repository or those who did not consent for both study and repository that were stored in the neon labeled box will be destroyed. This will be done by following the following procedures:

1. CC will run final update of STS with consent information from the SMS.

2. Use the STS to identify and generate a list of all samples located at your site that are from donors who did not consent for the repository (see STS Users Guide, LAPS Appendix). Note: Samples from donors who consented for the study but not repository will likely be at SeraCare since you should have shipped them following the procedures above. Sera Care will be responsible for destroying those samples (see below). Samples with sequence number -002 from donors who consented for the repository but not the study should be identified (see STS Users Guide, LAPS Appendix).

3. Pull those samples from the boxes in the freezers and discard through current and appropriate guidelines for disposal of biological waste.

4. Send Debbie Todd at Westat the list of Sample IDs that you pulled and destroyed. Westat will remove the records for those samples from the STS.

Special Instructions for SeraCare

1. Westat will update the STS with consent information from the SMS for donors at all sites.
2. Westat will then use the STS to identify and generate a list of all samples located at SeraCare that are from donors who did not consent for the repository (see STS Users Guide, LAPS Appendix).
3. Westat will send SeraCare that list of samples via a "Requisition" in the inventory system, BSI-II.
4. SeraCare will pull those samples from the boxes in the freezers and discard of the cryovials through current and appropriate guidelines for disposal of biological waste.
5. SeraCare will send Westat confirmation that those vials were destroyed.
6. Westat will record in the STS that those samples no longer exist.

5. SPECIMEN SHIPPING

5.1 Overview

Blood specimens collected for LAPS are processed into multiple aliquots, placed in freezer boxes and saved in the freezers at the Blood Centers for only a short time prior to being shipped to the REDS-II Central Laboratory for testing or to the NHLBI Central Repository for either short or long-term storage.

On an alternating twice a month schedule REDS-II Blood Centers will ship frozen LAPS specimens to the REDS-II Central Laboratory BSRI and to SeraCare BioServices. The CC will be periodically updating STS with the consent status on specimens from the SMS. Specimens, whose consent status had changed from non-consented to consented, will have to be moved to the appropriate consented freezer box for shipping. Any ineligible specimens due to infectious disease marker reactive assays, as well any samples that are associated with donors who are de-enrolled for any other reason, will need to be removed. Specimens not cleared for shipment will need to be removed from boxes that are destined for either the Central Lab or for the Central Repository.

The STS Users Guide details the process for preparing shipments and adding and removing any specimens, validating the contents of each freezer box and each shipment. Through the use of the STS shipping functions, the facility where the shipments are prepared as well as the facility where the shipments are received, will be able to monitor the status of each shipment in real-time. When the shipment reaches its destination and is "Receipted" in the STS the facility from which the shipment was sent will also be able to see the notation that the specimens were received in good order or if there were problems encountered.

5.2 Shipping Schedules

As a general rule of thumb, the first three Blood Centers will ship on the first and third Tuesday of each month.

- Blood Center of Wisconsin (BCW), Milwaukee, WI;

- Blood Centers of the Pacific (BCP), San Francisco, CA;
- Southern Region, American Red Cross (SARC), Atlanta, GA;

The second three Blood Centers will ship on the second and fourth Tuesday of each month. See the Appendix, Exhibit 8 for the current shipping schedule.

- Hoxworth Blood Center (HBC), Cincinnati, OH;
- Institute for Transfusion Medicine (ITxM), Pittsburgh, PA; and
- New England Region, American Red Cross (NEARC), Dedham, MA

Events that may cause an alteration to this scheduling are: Monday holidays where the shipments will be pushed back by one day and the shipments will occur on the Wednesday of that same week or if there are problems with weather or transportation events that are out of the control of study personnel, and in this case alternate scheduling may be devised on an ad hoc basis. All changes to scheduling should be first discussed with the Coordinating Center contact, Debbie Todd, to ensure that all parties are notified and are in agreement for the modified course of action.

An example of a monthly shipping schedule if the study begins at any time between September 1 and 25, 2006:

Group A Blood Centers BCW, **BCP** and **SARC** will perform the following activities on:

Friday, Oct. 13

Order dry ice for delivery Mon. or Tues. of the following week (i.e. Oct. 2 or 3)

Monday, Oct. 16

Prepare shipments in the STS as well as physical preparatory steps.

Tuesday, Oct. 17

Place freezer boxes and dry ice into shipping containers, arrange for FedEx pick-up, update STS with FedEx pick-up, send emails to BSRI and SeraCare (cc Westat) that a shipment is now in "transit".

Wednesday, Oct. 18

BSRI and SeraCare/Westat will update the STS that shipment(s) have been received and document condition and any special circumstances that may have occurred with

the shipment. BCW, BCP and SARC will monitor the STS/FedEx for information that the shipment has successfully navigated to it's destination. Any problems during transit will be handled by the recipient. Westat should be notified immediately if problems are encountered.

Oct. 20, 23, 24 & 25

Group B Blood Centers HBC, **ITxM** and **NEARC** will perform these same activities described above for Friday to Wednesday above.

Nov. 6, 7, 8 & 9

BCW, **BCP** and **SARC** will perform these same activities for the second time without the need to delay the Tuesday shipment to Wednesday due to the holiday.

Nov. 10, 13, 14 & 15

HBC, **ITxM** and **NEARC** will perform these same activities for the second time.

This process will be repeated throughout the course of LAPS until the final shipment when a procedure will be in place to also destroy the samples from the non-consenting and de-enrolled or additional ineligible donors.

5.3 Shipping Supplies

All supplies and costs related to shipping specimens for the LAPS Study, except for the dry ice, will be borne by the recipient of the shipment. Both the Central Lab and the Central Repository will supply each of the Blood Centers with shipping containers and the related supplies and labels prior to the first shipment of specimens to either facility. See Figure 5-1 for an example of a few of the items provided.

5.4 Instructions for Shipping to BSRI

Shipping of Frozen Samples to the REDS-II Central Laboratory

BSRI Contact Information

Blood Systems Research Institute
ATTN: Simon Ng
270 Masonic Ave.
San Francisco CA 94118
(415) 901-0751
Fax: (415) 775-3859
Email: ltobler@bloodsystems.org and sng@bloodsystems.org

Schedule: Shipments may be made Monday through Wednesday Only

Figure 5-1. Example of a few of the items provided with Saf-T-Pak STP 320 (Diagnostic Specimens).

The STP 320 will arrive at the REDS-II site with the following labels:

- Dry ice label (Class 9 label). There is space on this label for the amount of dry ice contained in the shipment, the shipper's name and address and the consignee's name and address
- A STP 111 Inner box
- Two STP 710 white secondary containers (envelope system)
- Two 250 mL absorbent strips

Rubber bands (at least ¼" thick)

Procedures Using the Saf-T-Pak STP 320

The Saf-T-Pak STP 320 shipping containers will be shipped to the REDS-II sites by FedEx ground and will be covered with brown paper. The empty shipping container will contain the labels listed above.

Preparing Shipment:

1. Remove polystyrene lid from polystyrene inner cooler.

3. Place White Absorbent Strip around Freezer box.

4. Place Rubber bands (at least ¼" thick) around Freezer Box.

5. Place Freezer box(es) in Clear Biohazard bag and seal according to instructions on the bag.

6. Place Clear Biohazard bag in White Envelope and seal envelope according to the instructions on the envelope.

7. Place White Envelope(s) in inner brown box (this inner box can hold 3-2" Freezer boxes or 2-3" Freezer Boxes) and tape the inner container shut.

8. Place inner box in reusable outer box containing polystyrene cooler.

9. Add dry ice to bring total amount to the same level as the top of the inner box. Note that the total amount of dry ice used will be ~16 lbs or 9 kg. The STP 320 shipping container will maintain a temperature of between 0^0 C and minus 44^0 C for 83 hours when using 7.8 kg of dry ice.

10. Place the Styrofoam lid onto the inner poly styrene container (do not tape the Styrofoam lid), and then seal the cardboard box.

11. Complete the FedEx Airbill with your shipping address and the amount of Dry Ice placed in box:

    a. Section 2 - The Internal Billing Reference Section must have the following information " REDS-II, Diagnostic Specimens UN 3373"

    b. Section 4a - Check the "FedEx Priority Overnight" box

    c. Section 5 - Check the "other" box

    d. Section 6 - Check the box that says, "Yes Shipper's Declaration not required". Check the "Dry Ice box" and write "1" in the first blank line and the "kg" of dry ice used on the second line; i.e., 1 x 9 kg

e. Section 7 - Check Recipient. The account number is pre-printed on the FedEx airbill provided by BSRI.

11. Fill in the Dry Ice Label on box with the amount of dry ice used, the sender's and consignee's name and address.

12. A paper copy of the Shipping Manifest must be included in the shipment, it can be downloaded from the STS. You may also attach this to the email or fax notifications.

13. Please fax a copy of the REDS-II LAP Study - Shipping Notification (Exhibit 11) **prior to the shipment** to Simon Ng at (415) 775-3859 at Blood Systems Research Institute. You may do this either by using a traditional hard copy fax or electronically through the STS (see the STS User's Guide – attachments such as the shipping manifest can also be included with this method).

14. Send an e-mail **prior to the shipment** to REDSIICC@westat.com. You may do this either electronically formatted through the STS (see the STS User's Guide) or by using your own email system.

15. Include the following information in your e-mail.

    a. Subject Line of E-mail should read: REDS-II (Blood Center Name), FedEx, "insert tracking number", "insert date of shipment":

    b. Shipper's Name:

    c. Shipper's Address:

    d. Shipper's Phone:

    e. Shipment Date:

    f. Courier:

    g. Tracking Number (no spaces):

If you should have any questions regarding these instructions please contact BSRI using the contact information above.

5.5 Instructions for Shipping to SeraCare

Shipping of Frozen Samples to the REDS-II Central Repository

Repository Contact Information

NHLBI Repository
ATTN: Christine Demasco
SeraCare BioServices
217 Perry Parkway
Gaithersburg, MD 20877
(301) 208-8100
Fax: (301) 208-8829
Email: nhlbi@bbii.com

Schedule: Shipments may be made Monday through Wednesday Only

Figure 5-2. Example of a few of the items provided with Saf-T-Pak STP 310 (Diagnostic Specimens).

Materials supplied by SeraCare when using the Saf-T-Pak STP 310:

Saf-T-Pak STP 310 or other appropriate shipping container supplied by recipient
~ 16 lbs (9 Kgs) Dry Ice to fill each shipper
Dry Ice Un 1845 Label with space to add weight
UN3373 Diamond Diagnostic Specimens Label
Inner brown box (the shipping contai ner can hold 3- 2" Freezer boxes or 2-3" Freezer Boxes)

To Label (Recipient)
From Label (From your site)
24 Hour Emergency Contact Label
Responsible Person Label
Class 9 Diamond Label
Tape
Shipping manifest printed from the STS
Freezer boxes for shipping
Rubber band (at least ¼" thick)
White Absorbent Strip
White Biohazard bag Clear Biohazard bag

Procedures:

1. Remove Empty Packaging Flap from front of box. A cardboard flap with the words "empty packaging" has been taped to the front of the box to cover the shipping labels when we ship the supplies to y ou. This flap can easily be cut fro m the box and removed. Once removed all shipping labels should be present.

    a. Once Empty Packaging Flap is rem oved the box should contain the following labels. If any of the labels are missing please contact us for replacements

        i. To Label (To Christine Demasco)

        ii. From Label (From your site)

        iii. 24 Hour Emergency Contact Label

        iv. Responsible Person Label

        v. Class 9 Diamond Label

        vi. UN3373 Diamond Diagnostic Specimens Label

        vii. Dry Ice Un 1845 Label with space to add weight

2. Place Dry Ice around the s mall inner brown box (between brown box and St yrofoam container).

3. Place Rubber band (at least ¼" thick) around Freezer Box.

4. Place White Absorbent Strip around box.

5. Place Box in Clear Biohazard bag and seal according to instructions on the bag.

6. Place bag in White Biohazard bag and seal according to the instructions on the bag.

7. Place bag in the inner brown box (the shipping container can hold 3-2" Freezer boxes or 2-3" Freezer Boxes) and tape the inner brown box shut.

8. Add additional dry ice to bring total amount to the same level as the top of the brown inner box. Note that the total amount of dry ice will be ~16lbs or 9 Kgs

9. Place the Styrofoam lid onto the container (do not tape the Styrofoam lid), place the "empty" packaging flap on top of the Styrofoam, and then seal the cardboard box.

10. Complete FedEx Airbill with your shipping address and the amount of Dry Ice placed in box:

    a. Section 2 - The Internal Billing Reference Section must have the following information "138, Diagnostic Specimens UN 3373"

    b. Section 4a - Check the "FedEx Priority Overnight" box

    c. Section 5 - Check the "other" box

    d. Section 6 - Check the box that says, "Yes Shipper's Declaration not required". Check the "Dry Ice box" and write "1" in the first blank line and the "kg" of dry ice used on the second line; i.e., 1 x 9 kg

    e. Section 7 - Check Recipient. The account number is pre-printed on the airbill provided by SeraCare.

11. Fill in the Dry Ice Label on box with the amount of dry ice used.

12. **Prior to the shipment, p**lease fax a copy of the airbill to SeraCare BioServices at (301) 208-8829 to the Attention of Christine Demasco. You may do this either by using a traditional hard copy fax or electronically through the STS (see the STS User's Guide – attachments such as the shipping manifest can also be included with this method).

13. Send an e-mail **prior to the shipment** to Chem-Tel (our 24-hour contact) at bbibiotech@chemtelinc.com. Please cc BBIBiotech at nhlbi@bbii.com and REDSIICC@westat.com. Include the following information in your e-mail. You may do this either electronically formatted through the STS (see the STS User's Guide) or by using your own email system.

    a. Subject Line of E-mail should read: Project # 138, FedEx, "insert tracking number", "insert date of shipment":

    b. Shipper's Name:

c. Shipper's Address:

d. Shipper's Phone:

e. Shipment Date:

f. Courier: FedEx

g. Tracking Number (no spaces):

h. Package Weight and Unit of Measure (i.e. 20 kg):

i. Total Volume: ____ (approximate volume is allowed)

j. Sample Identifier/Number of vials (Approximate number for Frozen vials is allowed).

k. Shipment Temperature: Dry Ice, UN1845, ___ kg (insert weight of Dry Ice)

l. Dangerous Goods Classification: Diagnostic Specimens UN3373, Dry Ice

m. A paper copy of the Shipping Manifest must be included in the shipment, it can be downloaded from the STS. You may also attach this to the email or fax notifications.

n. Recipient: Christine Demasco

o. Recipient Address: 217 Perry Parkway, Gaithersburg, MD, 20877

p. Recipient Phone: (301) 208-8100

Faxes may be sent to Chem-Tel only in an emergency situation when the e-mail system is not functioning at (813) 248-0582.

If you should have any questions regarding these instructions please contact SeraCare BioServices using the contact information above.

National Institutes of Health (NIH)
National Heart, Lung, and Blood Institute (NHLBI)
REDS-II Leukocyte Antibodies Prevalence (LAP) Study

Retrovirus Epidemiology Donor Study – II (REDS-II)

The Leukocyte Antibodies Prevalence (LAP) Study

QUESTIONNAIRE DATA ENTRY WEBSITE (QDE)

USER'S GUIDE

Westat, June 2006

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LIST OF FIGURES

INTRODUCTION

The **Leukocyte Antibodies Prevalence (LAP) Study** is a protocol developed under the **Retrovirus Epidemiology Donor Study- II** (**REDS-II**) umbrella. The LAP Study is a cross-sectional multi-center study to measure the prevalence of human leukocyte antigens (HLA) and neutrophil antibodies in blood donors with or without a history of transfusion or pregnancy, and the development of a repository of samples obtained from these donors. Specifically, 7900 adult blood donors across six blood centers will be enrolled in the study.

The LAP Study protocol requires enrolling donors in three different categories at each center: transfused male donors, untransfused male donors, and female donors.

A Study Management System (SMS), a Specimen Tracking System (STS), and a Questionnaire Data Entry (QDE) web-based system are three interacting components of a REDS-II group of systems that are currently developed to support the study data collection and tracking activities. The LAPS protocol requires enrolling donors in three different categories at each center: transfused male donors, non-transfused male donors, and female donors.

The enrolled donors will complete a self-administered study questionnaire. Blood center staff will then use the QDE to enter the paper questionnaire data into the QDE web system.

About This Guide

This guide provides a description of the hands-on utilization of the QDE.

Organization

The guide is task-driven.

Conventions Used in the Guide

Standard conventions are used throughout the guide.

Table 1: Common conventions used in the guide

Character Face	Meaning
Menu options	Menu options are presented in the format **Menu name > Option**. Menu titles also appear in a special typeface, oftentimes bolded.
Mouse commands	"Click" instructs you to click the left mouse button once. "Double click" means to click the left mouse button twice in rapid succession. "Right click" tells you to click the right mouse button once. (NOTE: These instructions are for users with a right-hand mouse setup. If the mouse is set up for left-handed use, please reverse the instructions for clicking left or right mouse buttons.)
Bolded text	References to window titles, buttons, dialog boxes, or tabs appear as **bolded typeface**.
Numbered paragraphs	Steps to complete a task appear as numbered paragraphs.

Logging In

You will be provided with the Uniform Resource Locator (URL) address – also called web address – of the QDE system, and you will also receive user name and password identification (ID). Once you have the address, click on it. The **Logon** dialog box will appear (Figure 1).

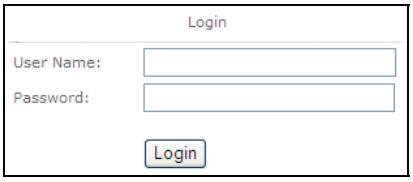


Figure 1: *The Log-in dialog box*

Type your user name and password and click **Login**. If the information provided is incomplete or incorrect, the system will display error messages. If messages appear, read them and try again, providing complete and correct information. If the system still rejects your credentials, contact Help Desk or call Westat for help. If the information provided is valid and accepted, the system will be launched (Figure 2).

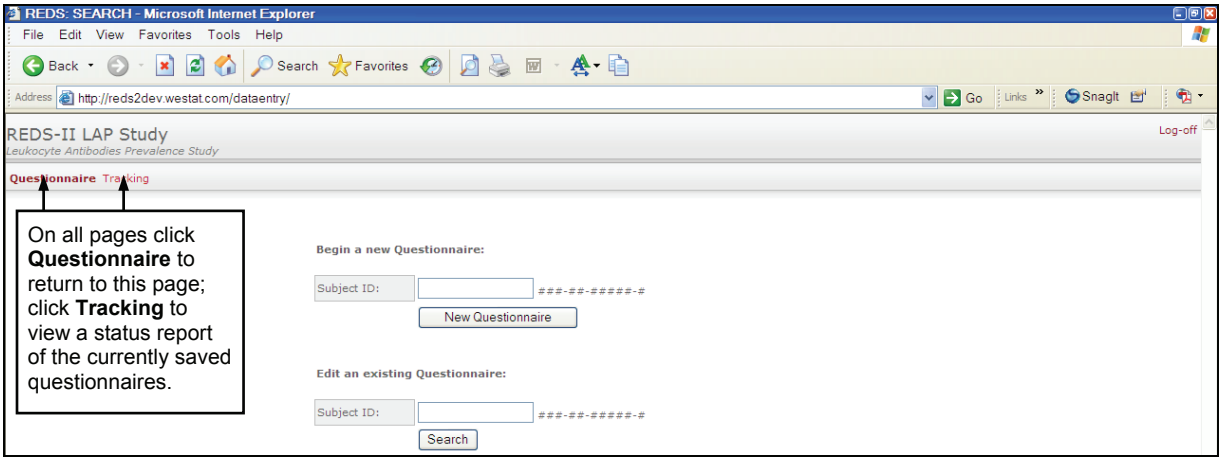


Figure 2*: The Questionnaire Data Entry (QED) web system*

Logging Out

There are several ways in which you can log out: (1) Select **File > Close** from the browser's menu, (2) click the **Close** button ( ) at the top right of the screen, or (3) click on the **Log-off** link at the top right of the system screen. If you log off by method 1 or 2, the browser will close and the system will also close without warning and will disappear from the screen. If you log out by method 3, the system will log you off, will return to the **Log-in** dialog box, and the browser will stay open.

BEGIN A NEW QUESTIONNAIRE

1. Log on.
2. Type the subject identification (ID) number in the **Subject ID** box.
3. Click **New Questionnaire**. The questionnaire form will appear (Figure 3).

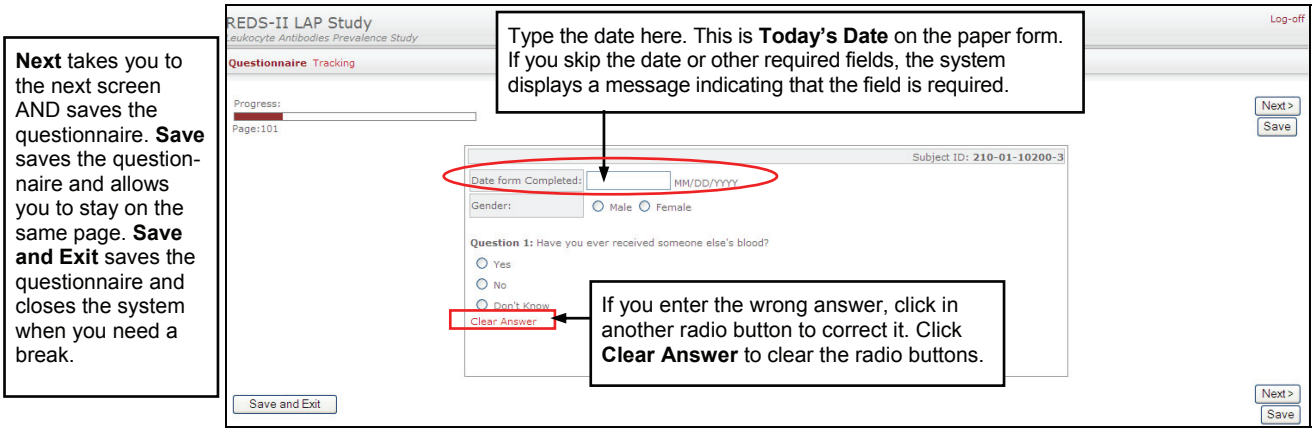


Figure 3: *The questionnaire form*

4. Type the correct date in the **Date form Completed** field. This date is **Today's Date** on the paper form. You do not have to type the slashes. The system will add them when you click elsewhere.
5. Select a gender, answer **Question 1** (Q1) and click **Next**. There is no **Gender** on the paper form, but if the donor has answered the female questions, assume **Gender** is **Female**.

Next takes you to the next screen and saves the questionnaire. **Save** saves the questionnaire and keeps you on the same page. Click **Save and Exit** to break the session.

Male Answers

Untransfused Male Subjects

If the gender is **Male** and the Q1 answer is **No** or **Don't Know**, on **Next** the questionnaire is completed, and the system will display a message to that effect (Figure 4).

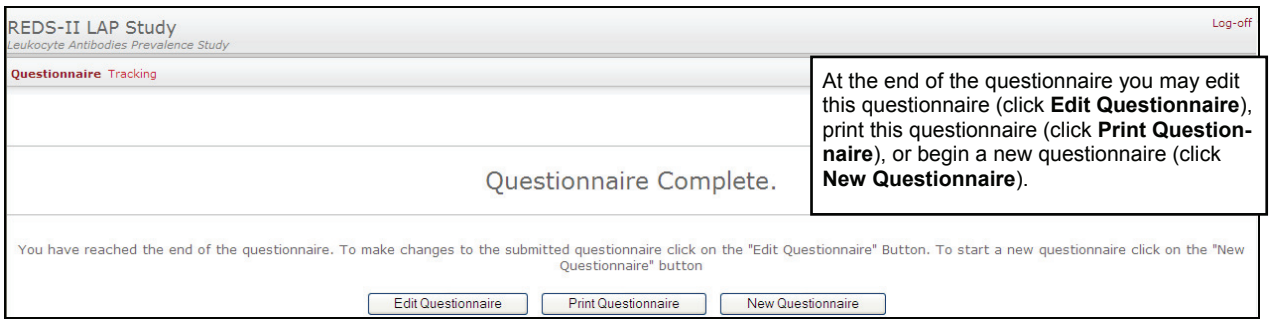


Figure 4: *End-of-questionnaire message and page*

Transfused Male Subjects

If the gender is **Male** and the Q1 answer is **Yes**, the progress bar will show the progress of the questionnaire, and the next page will appear (Figure 5), displaying places for the answers given in the **box** by **transfused male subjects**.

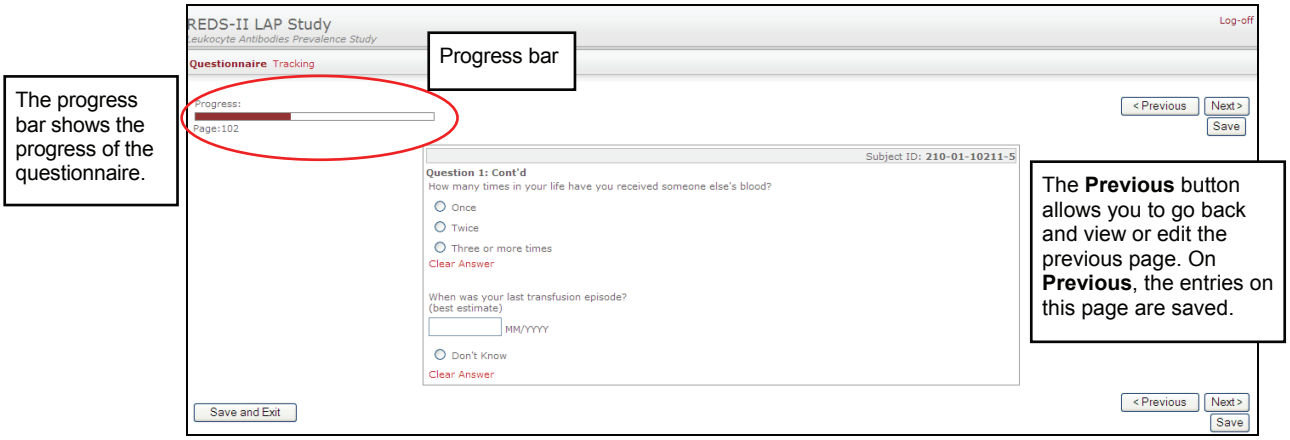


Figure 5: *The next page – the "box" answers from the paper form*

1. Enter the number of times the subject has received transfusion.
2. Type the month and year of the last transfusion. You do not have to type the slash. The system will add it when you click elsewhere. If the date (MM/YYYY) is not specified, click in the **Don't Know** button. Click **Clear Answer** to clear the fields and correct your entries.
3. When this page is correct, click **Next**. The system will display the end-of-questionnaire message and page (Figure 4).

Female Answers

Untransfused Female Subjects

If the gender is **Female** and the Q1 answer is **No** or **Don't Know**, on **Next** the questionnaire will continue with the pages for the answers provided by female subjects to questions 2–7 to the end.

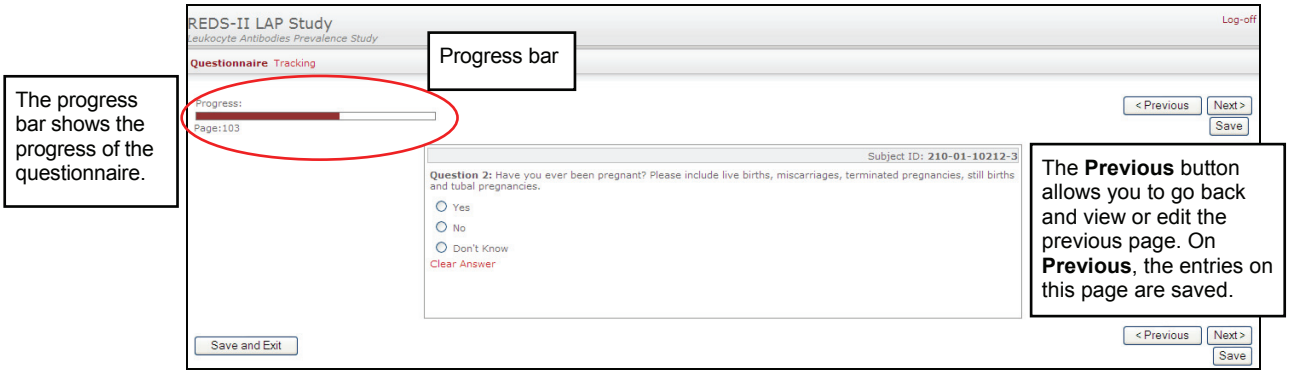


Figure 6: *Answers to Q2 – the first pregnancy question*

If the Q2 answer is **No** or **Don't Know**, on **Next** the questionnaire is completed, and the system will display a message to that effect (Figure 4).

If the Q2 answer is **Yes**, the other pregnancy questions will be displayed to the end of the questionnaire. Enter the answers as shown on the paper form and click **Next**.

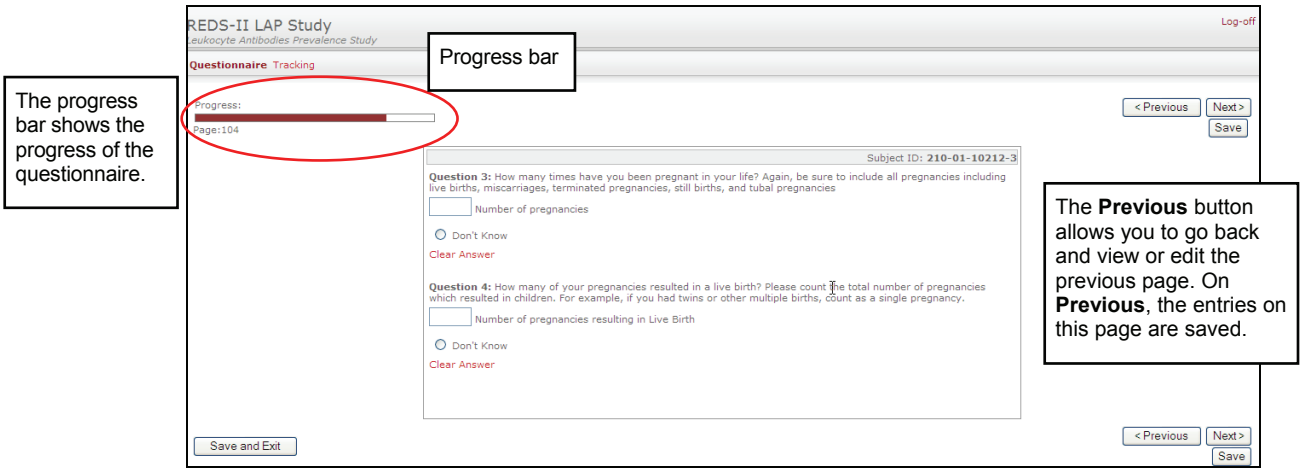


Figure 7: *Answers to Q3 and 4 – how many total and live pregnancies*

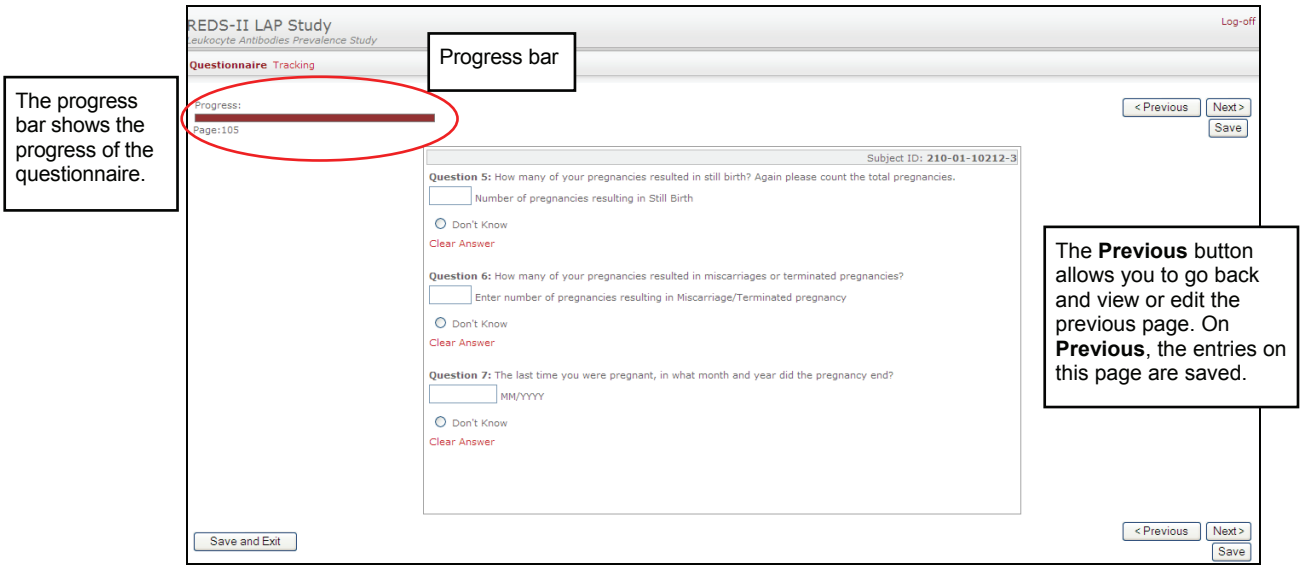


Figure 8: *Enter here the answers to Q5 through 7 and click Next*

On the last click on **Next** the questionnaire is completed, and the system will display a message to that effect (Figure 4).

NOTE: When the Q2 answer is **Yes**, the system will take you all the way to the end, displaying the pages shown in Figure 7 and Figure 8, even if the answer to some or all subsequent questions is **Don't Know**.

Transfused Female Subjects

If the gender is **Female** and the Q1 answer is **Yes**, on **Next** the questionnaire will continue with the **box** answers given by **transfused female subjects**.

After a **Yes** Q1 answer, the system will continue with the Q2 and then the Q3 through Q7 answers (the pregnancy answers) in exactly the same way and order as described above. See the section on Untransfused Female Subjects for details. In other words, if the Q1 answer is **Yes**, the "box" answers are simply inserted in between the date field and the pregnancy questions.

On the last click on **Next** the questionnaire is completed, and the system will display a message to that effect (Figure 4).

NOTE: When the Q2 answer is **Yes**, the system will take you all the way to the end, displaying the pages shown in Figure 7 and Figure 8, even if the answer to some or all subsequent questions is **Don't Know**.

Existing ID in Begin Questionnaire Box

If you specify an existing **Subject ID** in the **Begin a new Questionnaire Subject ID** box and click New Questionnaire, the system will display a message indicating that the specified ID already exists, but you can edit it (Figure 9).

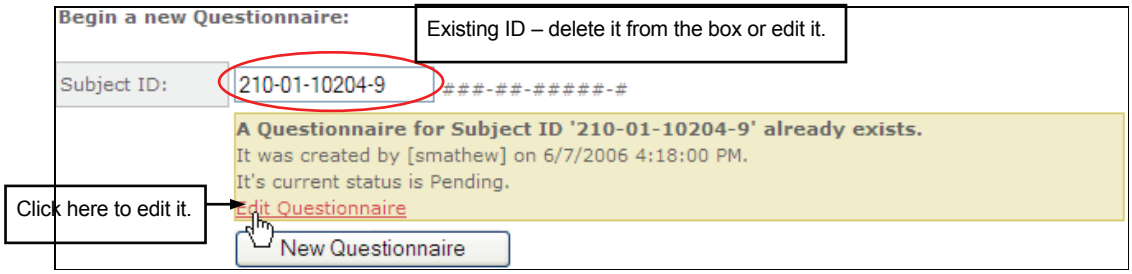


Figure 9: *Entering an existing ID in the New Questionnaire box*

If that happens, delete the existing ID number from the box, enter a genuinely new ID, and complete the questionnaire as described above. Alternatively, you may wish to edit the existing questionnaire. In that case, click on the **Edit Questionnaire** link and proceed as described in the section on Editing an Existing Questionnaire.

EDITING AN EXISTING QUESTIONNAIRE

You can edit a questionnaire in one of several ways.

At all times you may click the **Previous** button, if visible, and go back to the previous page in case you notice errors that must be corrected on the previous page. If you click **Previous**, the entries on the current page will be saved – if any.

Also, on the end-of-questionnaire page (Figure 4) there is an **Edit Questionnaire** button. If errors are noticed right after submitting a questionnaire, click on the **Edit Questionnaire** button to edit the submitted questionnaire.

If errors are noticed later, or updates must be made, follow these steps to edit an existing questionnaire.

1. Log on.

2. If you know the subject identification (ID) number of the questionnaire that needs editing, type it the **Subject ID** box and click **Search**. A table will appear with the selected ID as the only record (first image in Figure 10). The **Subject ID** number is a link to the data entry forms.

   If you do not know exactly the ID number you are searching for, or wish to check whether it has been entered or not, click **Search** without specifying anything in the **Subject ID** box. The results table will display all the records that have been entered so far.

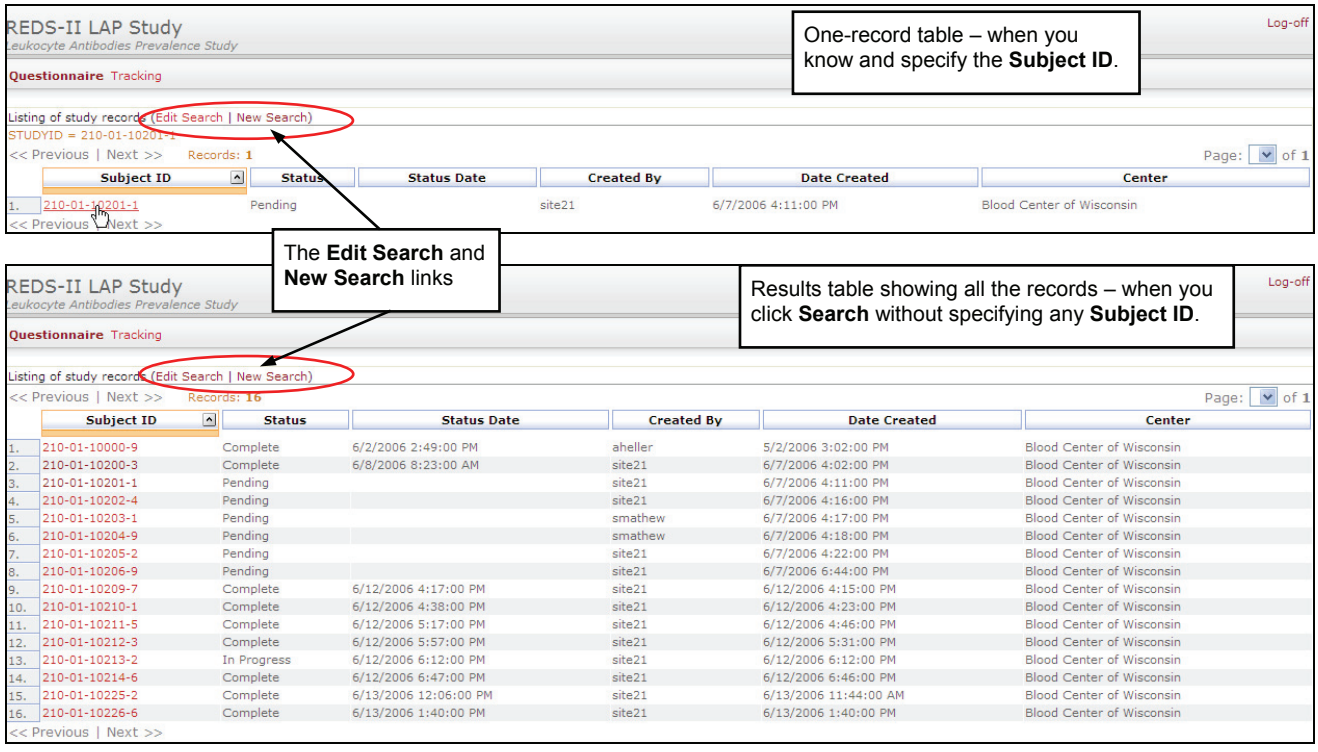
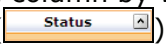


Figure 10: *The study records table*

The table can be resorted. The default sort order is ascending by **Subject ID**. The name of the column by which the table is sorted is surrounded by a colored rectangle (

). You can resort the table by any other column in ascending or descending order. Click once on a column heading. The table will be sorted by that column in ascending order, and an up arrow head () will indicate the sort order. Click again on the same column heading. The table will be sorted by that column in descending order, and a down arrow head () will indicate the sort order. Resorting the table will help you find records more easily. To restore the default order click the **Subject ID** heading to sort the table by **Subject ID** in ascending order.

In addition, when the table is long, you can use the **Previous**, **Next**, and **Page** links to navigate from page to page.

3. To continue with editing a questionnaire, click on the **Subject ID** number of the questionnaire in question. Its data entry pages will appear and you can enter or edit the data as described in the section on Begin a New Questionnaire.

Edit Search and New Search

Edit Search and **New Search** (Figure 10) are links to the first QED page (Figure 2). When you view the study records table shown in Figure 10, click **Edit Search** or **New Search** to return to the first QED page (Figure 2) either to begin a new questionnaire or to edit an existing one.

If you brought up the study records table (Figure 10) by clicking the **Search** button on the first page (Figure 2) while the **Subject ID** box was empty, there will be no difference between **Edit Search** and **New Search**. Either will display the first QED page with empty **Subject ID** boxes.

If you brought up the study records table by searching for a particular subject ID, **Edit Search** will prefill the **Subject ID** box with the ID number you first entered, whereas **New Search** will display an empty **Subject ID** box.

OTHER FEATURES

The Questionnaire Link

The word **Questionnaire** is a link to the first page (see Figure 2). It appears on all pages. Click on it to return to the first page (Figure 2).

Tracking

The word **Tracking** is a link to a **status report** (Figure 11). It also appears on all pages. Click on it to view the most recent status report (Figure 11).

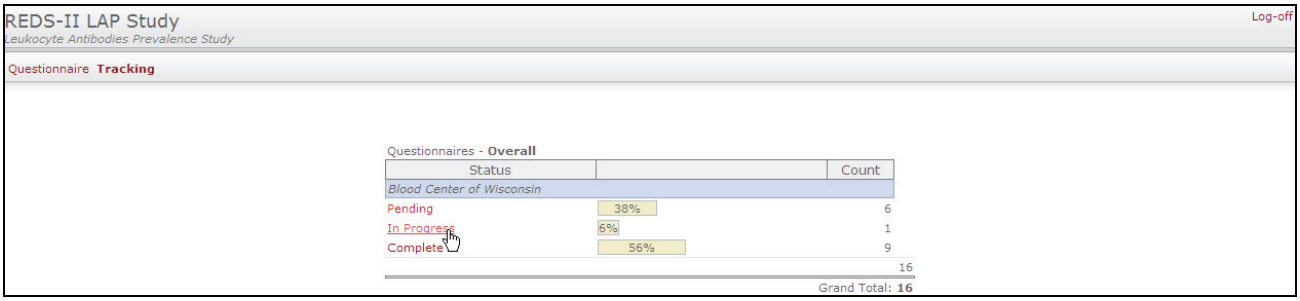


Figure 11: *The status report*

The status report entries – **Pending**, **In Progress**, and **Complete** – display the percentage and count of questionnaires that currently have the respective status. These entries are also links to a study records table view that displays only the records in the selected status category. For example, click on the **Complete** status. The resulting table will display only records with a **Status** of **Complete** (Figure 12). The **Subject ID** numbers are links to the edit pages. Click on any to edit it as described in the section on Editing an Existing Questionnaire.

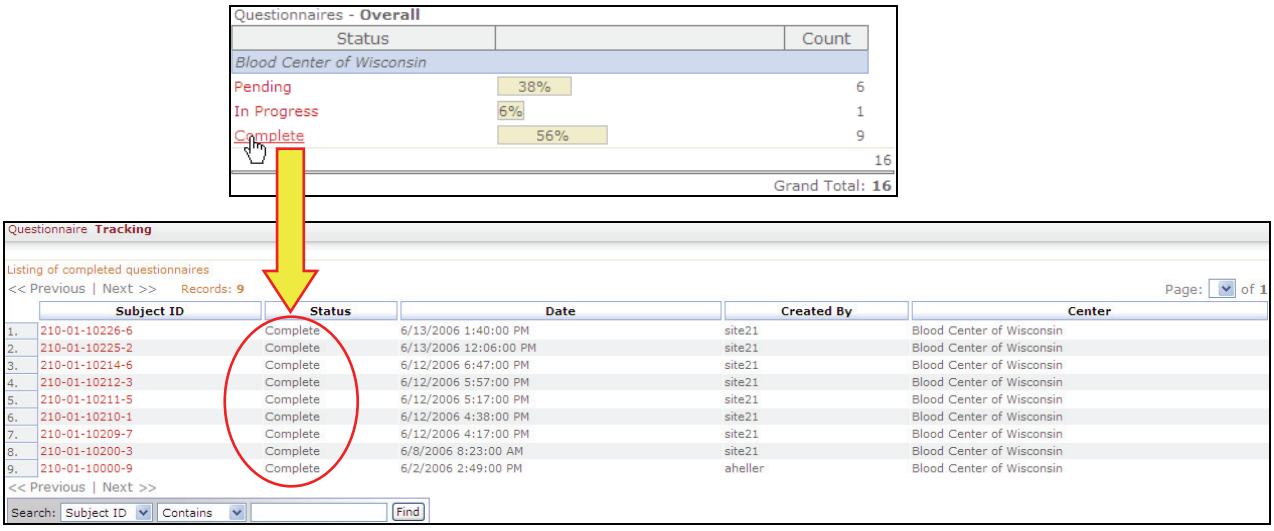


Figure 12: *Selecting only records from a status category*

The Search Engine

Under the **Tracking** tables there is a search engine. Use it to run queries and reduce the number of records to a manageable few. The search engine displays three boxes. In the first box select the **name of the column** in which you are searching for a value. In the second box specify the **search operator**. In the third box type the **value** or sequence of characters you want the system to look for. The following example is a mere illustration, but other queries can be written in the same way.

1. Select a column name in the first box.
2. Select an operator in the second box.
3. Type the desired value – or sequence of characters – in the third box.
4. Click **Find**.

Figure 13: *Specifying the elements of a query*

If, for example, you are looking for records that were entered by (**Created By**) a certain operator, when you finish specifying the search criteria, the **Search** fields should look like those in Figure 14.

Figure 14: *The criteria of a search*

On **Find** all the records that meet the specified criteria will be displayed in the table (Figure 15). If no records meet the search criteria, or the expression is incorrect, the system will display no records. Correct the expression and try again.

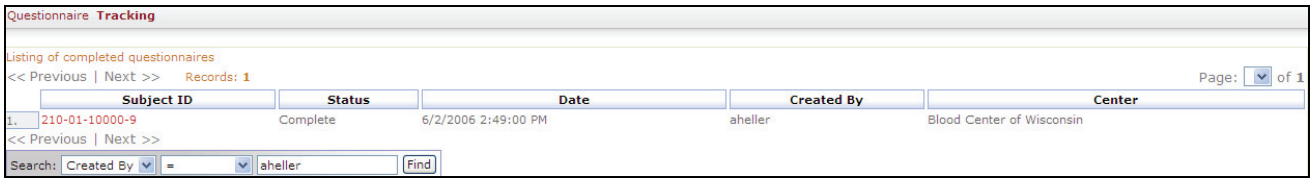


Figure 15: *Records that meet the specified criteria*

The following is another search example.

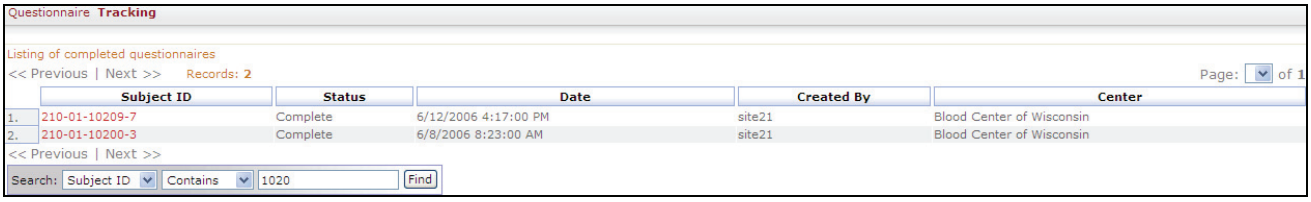


Figure 16: *Subject IDs that contain "1020" in the number*

Printing Questionnaires

There are two ways in which you can print a record: when you reach the end-of-questionnaire page, click on the **Print Questionnaire** button, or, alternatively, click on a **Subject ID** number in any of the **Tracking** tables – ID numbers in **Tracking** tables are links to the **Print Form** page. In either case the **Print Form** page of the selected ID will appear (Figure 17).

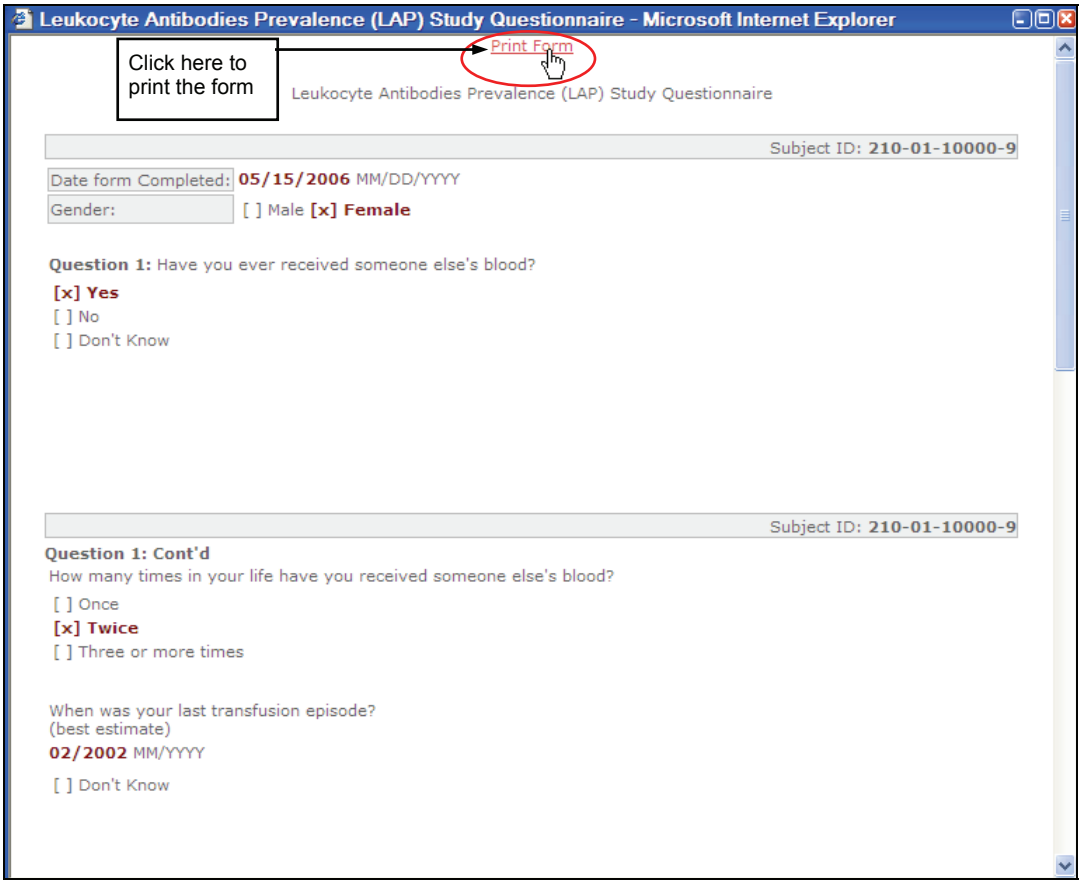


Figure 17: *The Print Form page of a selected ID*

Click **Print Form**. The Windows **Print** dialog box will appear. Set your print preferences and/or select a printer and click **Print**. The selected questionnaire form will be printed on the selected printer.

The URL for the STS is: https://sts.reds-ii.org

The link to the STS users guide ("STS User Guide for REDS") can be found on the "Home < About STS" page after logging into the system.

EXHIBIT 1
PRINTED ON BLOOD CENTER LETTERHEAD

Information sheet for the LAP study participants

The <*NAME OF BLOOD CENTER*> is participating in a research study, the Leukocyte Antibodies Prevalence (LAP) Study, sponsored by the National Heart, Lung, and Blood Institute.

Leukocyte antibody testing research:

One part of this research study involves the study of a disease process called "Transfusion-Related Acute Lung Injury (TRALI)". TRALI is a rare condition. However, it is the second leading cause of death resulting from blood transfusion in the United States. Blood recipients who develop TRALI feel sudden difficulty breathing, and they have serious injury to their lungs, after transfusion of certain blood products. Most of these people survive, but as many as 5-10% may die following the reaction.

It is possible that TRALI is caused by transfusion of unusual special antibodies produced in the bloodstream of blood donors, especially those donors who have been previously transfused or been pregnant. These antibodies are thought to be common and do not usually harm the person who has them, just by being there. In some cases, it is possible that these antibodies may cause harm (without knowing it) to certain people who receive that blood. This is why the investigators in this study are trying to find out how many blood donors have these special antibodies, and what kind of antibodies they have.

If you would like to join the study, you will be asked to answer a few questions about your medical history including whether or not you have been transfused with blood in the past, or for female donors, whether you have been pregnant in the past. You will also be asked to provide a blood sample that will be tested for White Blood Cell (WBC) antibodies. In the event that you have these antibodies then your blood sample will be used for typing your WBCs. A portion of your sample will also be frozen and kept in a repository. Whenever possible, this blood sample will be obtained from your routine blood donation. However, if an insufficient sample is available from your routine blood donation, you may be asked to donate one extra tube of blood when you donate your unit of blood today. Generally, this extra tube of blood can be taken from the arm used for the donation. The investigators have also made sure that not too much blood will be taken from your body if you choose to donate the tube of blood for this study. It will take 10-15 minutes of your time to participate in this study.

If you are interested in participating in the research described above, please read the "Informed Consent" form. This form will tell you more about the goals of this study. It will answer your questions about when you may be notified of certain test results and what this might mean for you as a blood donor. It will also explain to you about the potential risks and benefits associated with participation in this study.

Thank you for thinking about joining this study. For all those people who may receive blood transfusions in the future, it is very important to find out more about the presence of these antibodies. By participating in this study, you will be contributing to important medical knowledge for the future.

EXHIBIT 2

REDS-II Leukocyte Antibodies Prevalence (LAP) Study
Consent Form

INVITATION

Thank you for coming to donate blood at <*BLOOD CENTER*>. Today we are asking blood donors to participate in a research study called the Leukocyte Antibody Prevalence (LAP) Study.

WHO IS DOING THIS RESEARCH?

This research study is being conducted as part of a large blood safety and availability research program called REDS-II, and is funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health. As one of six participating REDS-II blood centers, <*BLOOD CENTER*> is enrolling eligible donors in this important research study.

WHY IS THIS RESEARCH PROJECT BEING DONE?

This research is designed to help improve the safety of the blood supply. White Blood Cells (WBC) help provide immunity and fight infections. Sometimes, people make antibodies to WBCs either when they receive a transfusion or in women, when they are exposed to their child's blood during pregnancy. These antibodies generally do not cause harm when transfused to patients, but in rare cases, they may contribute to a reaction called transfusion-related acute lung injury or TRALI. In this reaction, the patient can have severe difficulty breathing and become very sick. Our research aim is to find out how many blood donors have WBC antibodies (leukocyte antibodies) and to further characterize these antibodies in donors who have them. We need approximately 8,000 donors from 6 different blood centers across the country to take part in the LAP study.

WHAT IS INVOLVED IN PARTICIPATING IN THIS RESEARCH PROJECT?

- Participation requires about 10-15 minutes of your time.

- With your consent, a small sample of blood, an extra ½ tablespoon, will be collected from you in a separate tube. Your blood sample will be tested for white blood cell (WBC) antibodies, and be stored for later research.

- You will have to complete a short questionnaire about blood transfusion and/or pregnancy. You will be asked about whether you have ever received a blood transfusion in the past and for women, you will also be asked a few questions about previous pregnancies.

- If you screen reactive on any of the infectious disease screening tests routinely performed on your donation by the blood center then you will be de-enrolled from this study and your blood sample will be destroyed.

EXHIBIT 2

WHAT TYPES OF TESTS WILL BE DONE ON THE BLOOD SAMPLE?

Testing for White Blood Cell (WBC) Antibodies

The blood sample you provide for this research study will be tested for WBC antibodies. Since the presence of WBC antibodies is generally considered not to have any health consequence you will not receive the results of this testing. <*If you plan to notify and counsel donors of neutrophil abs of defined specificity then include that language here*>

Testing Your Blood to Characterize your White Blood Cells (WBCs)

If you have WBC antibodies, we may perform DNA testing of a portion of your blood sample to characterize your WBCs. WBC typing generally does not have any health consequence and therefore, you will not receive results of this test.

Storage and Future Testing of your Blood Sample

By consenting to participate in the second part of this study, you are agreeing to have a portion of your blood sample indefinitely stored in a repository maintained by the National Heart, Lung and Blood Institute. When you agree to have your blood sample stored, you are granting consent now for future uses of this sample. You may also be contacted in the future to provide additional information or an additional sample if necessary. All research on your stored or additional samples will be for the purpose of ensuring transfusion safety and understanding transfusion biology. This may include testing your blood for genetic (inherited) factors relating to WBC's and the body's immune response. The National Institutes of Health will give access to these samples only to its employees or approved researchers. Any future study must be reviewed and approved by an Institutional Review Board, the committee that protects your rights and welfare as a research participant.

ARE THERE BENEFITS TO TAKING PART IN THIS PROJECT?

If you agree to participate in this research study, there is no direct benefit to you other than the satisfaction of participating in this research for the benefit of making transfusions safer for future generations. Research performed on your blood sample will also contribute to the knowledge and understanding of transfusion and its consequences.

WHAT ARE THE RISKS?

The risks of taking part in this study are very small.

- In the unlikely event that we cannot obtain a sufficient sample from your routine blood donation, a separate needle insertion in your arm may be necessary. When blood is drawn you may feel a little discomfort as the needle goes through your skin. There may be local bruising or bleeding at the puncture site. Very rarely, the arm may become infected or you may feel faint. The risk is the same as that of having blood drawn at your doctor's office.

- There may be situations where testing will be done on the stored sample and the link between your name and the test results will be maintained. In these cases, the results will be shared with you if they are of medical significance. Notification of results from future

testing may be unexpected or upsetting to you. At the time of notification, you will be provided with more specific information about your test results and what they mean. It is your decision whether to share your test results with others.

- <Optional depending on BC deferral/notification plans> In the unlikely event that your blood is found to contain a rare, strong antibody to WBC that might be harmful to a blood recipient, the blood center may prevent you from giving blood in the future. <Optional depending on BC notification plans> In extremely rare cases, pregnant women with strong WBC antibodies may deliver a baby with a low neutrophil count. So you will be notified and counseled about their meaning.

WILL THE INFORMATION BE KEPT PRIVATE?

Information concerning your participation in the study will be kept confidential and used only for scientific purposes, in accordance with applicable state and federal laws. Every effort will be made to maintain the confidentiality of your study records. The specimens and questionnaire data will be labeled with a study number assigned to you instead of your name. Only the research staff at your blood center will have the ability to link the study number on your samples or questionnaire to your name and other identifying information.

While we will make every effort to keep information about the study confidential, confidentiality cannot be guaranteed. To provide additional protection of your privacy, the blood center has obtained a Certificate of Confidentiality in accordance with Section 301(d) of the Public Health Service Act. This certificate prevents study staff from being forced to disclose information that may identify you by court order or other legal action. This protection lasts forever (even after death) for all study participants. Any results of the study, such as scientific publications, will be reported as summaries that will not reveal your identity.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

The researchers will not voluntarily disclose without your consent, information that would identify you as a participant in the research project.

WHAT ABOUT COMPENSATION?

There is no cost to you for participating in the study and you will not be paid to participate. All research tests will be free. You will not receive financial compensation for any new scientific or medical testing procedures developed and marketed using the results of the research done on your sample.

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THIS PROJECT?

Your participation in this research is entirely voluntary. If you decide not to participate in this study, your decision will not adversely affect your ability to donate blood. If you decide to participate, you are free to withdraw your consent and to discontinue participation at any time. If

you later decide that you do not want your sample and information to be used for future research, contact <*Principal Investigator*> at < *Phone*> and submit a written request to < *Principal Investigator*> and we will destroy any remaining identifiable samples and information.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions, please feel free to ask now. If you have any questions about your rights as a research participant, now or in the future, you may call <*Principal Investigator*> at <*Phone*>.

STATEMENT OF CONSENT

I have read this form and understand the purpose of this study, procedures to be followed, and the potential risks and benefits. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I understand that I may withdraw at any time after signing this form. A signed copy of this consent form has been given to me.

I agree to participate in the research in the following ways (please check all that apply).

[ ] I consent to participate in white blood cell antibody testing and characterization research.

[ ] I consent to participate in storage of my blood sample and consent for future studies that may be performed with my blood sample that are designed to improve our understanding of transfusion biology and transfusion safety.

_____ _____

Signature of the participant Date

_____

Name of the Participant (PLEASE PRINT)

_____ _____

Witness Signature Date

EXHIBIT 3 LEUKOCYTE ANTIBODIES PREVALENCE (LAP) STUDY LOG FORM

TODAY'S DATE: |__|__| |__|__| |__|__|__|__|
M M D D Y Y Y Y

DRIVE ID/SITE ID: ________________________

#	BUI (apply label)	Donor ID	Subject ID (apply label)	Study Consent	Repository Consent	Gender	Tx	Parity	Specimen	Qx
				Yes ☐ No ☐	Yes ☐ No ☐	M ☐ F ☐	Yes ☐ No ☐	0 ☐ 1 ☐ 2 ☐ ≥3 ☐	Yes ☐ No ☐	Yes ☐ No ☐
				Yes ☐ No ☐	Yes ☐ No ☐	M ☐ F ☐	Yes ☐ No ☐	0 ☐ 1 ☐ 2 ☐ ≥3 ☐	Yes ☐ No ☐	Yes ☐ No ☐
				Yes ☐ No ☐	Yes ☐ No ☐	M ☐ F ☐	Yes ☐ No ☐	0 ☐ 1 ☐ 2 ☐ ≥3 ☐	Yes ☐ No ☐	Yes ☐ No ☐
				Yes ☐ No ☐	Yes ☐ No ☐	M ☐ F ☐	Yes ☐ No ☐	0 ☐ 1 ☐ 2 ☐ ≥3 ☐	Yes ☐ No ☐	Yes ☐ No ☐
				Yes ☐ No ☐	Yes ☐ No ☐	M ☐ F ☐	Yes ☐ No ☐	0 ☐ 1 ☐ 2 ☐ ≥3 ☐	Yes ☐ No ☐	Yes ☐ No ☐
				Yes ☐ No ☐	Yes ☐ No ☐	M ☐ F ☐	Yes ☐ No ☐	0 ☐ 1 ☐ 2 ☐ ≥3 ☐	Yes ☐ No ☐	Yes ☐ No ☐

OMB No. 0925-0566
Expiration Date: 05-31-2008

EXHIBIT 4
REDS-II LEUKOCYTE ANTIBODIES PREVALENCE (LAP) STUDY QUESTIONNAIRE

TODAY'S DATE: |__|__| |__|__| |__|__|__|__|
M M D D Y Y Y Y

SUBJECT ID #

Question 1: Have you ever received someone else's blood?

☐ Yes → **How many times in your life have you received someone else's blood?**
☐ No
☐ Don't Know

☐ Once
☐ Twice
☐ Three or more times

When was your last transfusion? |__|__| |__|__|__|__| ; ☐ Don't Know
(best estimate) M M Y Y Y Y

For Female Donors Only (Male Donors skip to end statement):

Question 2: Have you ever been pregnant? Please include live births, miscarriages, terminated pregnancies, still births, and tubal pregnancies.

☐Yes
☐No **SKIP TO END STATEMENT**
☐Don't Know

Question 3: How many times have you been pregnant in your life? Again, be sure to include all pregnancies including live births, miscarriages, terminated pregnancies, still births, and tubal pregnancies.

☐☐
Enter Number of Pregnancies

☐ Don't Know

Question 4: How many of your pregnancies resulted in a live birth? Please count the total number of pregnancies which resulted in children. For example, if you had twins or other multiple births, count as a single pregnancy.

☐☐
Enter Number of Pregnancies Resulting in Live Birth

☐ None
☐ Don't Know

Question 5: How many of your pregnancies resulted in still birth? Again, please count the total pregnancies.

☐☐
Enter Number of Pregnancies Resulting in Still Birth

☐ None
☐ Don't Know

Question 6: How many of your pregnancies resulted in miscarriages or terminated pregnancies?

☐☐
Enter Number of Pregnancies Resulting in Miscarriage/Terminated pregnancy

☐ None
☐ Don't Know

Question 7: The last time you were pregnant, in what month and year did the pregnancy end?

|__|__| |__|__|__|__|
M M Y Y Y Y

☐ Don't Know

END STATEMENT

Thank you for your participation in the Leukocyte Antibodies Prevalence (LAP) Study. We appreciate you taking the time to complete this questionnaire.

EXHIBIT 5
PRINTED ON BLOOD CENTER LETTERHEAD

OPTION 1
Short Form Review Method

Dear <*Mr. BLOOD DONOR*>,

Thank you for your recent blood donation to <*NAME OF BLOOD CENTER*>. Your contribution to our blood program is greatly appreciated. We are contacting you because the information you provided as part of your donation indicates that you have a history of blood transfusion. As a result, you have been selected to participate in a very important research project sponsored by the National Institutes of Health (NIH) called the **Leukocyte Antibodies Prevalence (LAP) Study**. This study will attempt to understand a rare complication of blood transfusion called "Transfusion Related Acute Lung Injury", or "TRALI", by measuring certain antibodies present in blood donated by individuals with a history of transfusion or pregnancy. These antibodies are thought to be common and do not harm the person who has them, but in rare cases may cause harm in people receiving their blood. We don't have sufficient information about the presence of these antibodies in people who have previously been transfused or pregnant. The goal of this research study is to find out how many blood donors have these special antibodies. By participating in this research study you will be contributing to important medical knowledge concerning TRALI that will make transfusions safer for everyone in the future.

Participation in this research study is voluntary and involves allowing us to use a small portion of your recently donated blood sample for research. Your blood will be tested for leukocyte antibodies and will be stored frozen for future research. Additionally, we have enclosed a questionnaire for you to complete that will help us understand your transfusion history.

We would really appreciate your help with this research study. Please sign the consent form and complete the questionnaire and mail both forms to us by using the postage-paid envelope provided. Be assured that the information you provide will be confidential. It will not be kept or reported in a way that could identify you to anyone else. If you have any questions about the study or the forms, please contact the research coordinator <*NAME*> at <*PHONE NUMBER*>.

Thank you in advance for participating in this important research study.

Sincerely,

<*PRINCIPAL INVESTIGATOR, MD*>
<*TITLE*>
<*BLOOD CENTER*>

EXHIBIT 6
PRINTED ON BLOOD CENTER LETTERHEAD

OPTION 2
Donation Database Query Method

Dear <*Mr. BLOOD DONOR*>,

Thank you for your recent blood donation to <*NAME OF BLOOD CENTER*>. Your contribution to our blood program is greatly appreciated. We are contacting you because the information you provided as part of your donation indicates that you have a history of blood transfusion. As a result, you have been selected to participate in a very important research project sponsored by the National Institutes of Health (NIH) called the **Leukocyte Antibodies Prevalence (LAP) Study**. This study will attempt to understand a rare complication of blood transfusion called "Transfusion Related Acute Lung Injury", or "TRALI", by measuring certain antibodies present in blood donated by individuals with a history of transfusion or pregnancy. These antibodies are thought to be common and do not harm the person who has them, but in rare cases may cause harm in people receiving their blood. We don't have sufficient information about the presence of these antibodies in people who have previously been transfused or pregnant. The goal of this research study is to find out how many blood donors have these special antibodies. By participating in this research study you will be contributing to important medical knowledge concerning TRALI that will make transfusions safer for everyone in the future.

Participation in this research study is voluntary and involves allowing us to use a small portion of the blood sample from your next donation for research. Your blood will be tested for leukocyte antibodies and will be stored frozen for future research. Additionally, you will have to complete a short questionnaire that will help us understand your transfusion history. Be assured that the information you provide will be confidential. It will not be kept or reported in a way that could identify you to anyone else.

We would really appreciate your help with this research study. One of our recruiters will be calling you soon to schedule an appointment for your next blood donation at a time that is convenient for you. Meanwhile, if you have any questions about the research study, please contact the study coordinator <*NAME*> at <*PHONE NUMBER*>.

Thank you in advance for participating in this important research study.

Sincerely,

<*PRINCIPAL INVESTIGATOR, MD*>
<*TITLE*>
<*BLOOD CENTER*>

EXHIBIT 7 TELEPHONE SCRIPT

Leukocyte Antibodies Prevalence Study (LAPS)
Tx Male Telephone Script
Donation Database Query Method

Hi, I'm calling on behalf of <BLOOD CENTER>. May I speak with <SUBJECT'S NAME>?

IF SPEAKING TO THE PERSON YOU ARE TRYING TO REACH:

Do you have a minute to talk?

If Yes: →

Thank you for your recent blood donation to our blood center. I'm calling to schedule your next blood donation appointment.
[Schedule next appointment using regular blood center script and procedures]
You may have received a letter from us about an important research study that our blood center is participating in. If you are interested, when you come in to make your next blood donation, our research coordinator will talk to you about it. Thank you so much. We really appreciate your help. Good Bye!

IF DONOR DOESN'T WANT TO GIVE BLOOD AGAIN:
You may have received a letter from us about an important research study that our blood center is participating in. If you are interested in participating in this study, I can make an appointment for you to come in just for that. When you come in our research coordinator will talk to you in detail about it.
[Make appointment for study visit]
Thank you so much. We really appreciate your help. Good Bye!

IF THE DONOR ASKS FOR MORE INFORMATION ABOUT THE STUDY GIVE THE PHONE NUMBER OF THE RESEARCH COORDINATOR <TELEPHONE NUMBER>

If No: →

When might be a good time for us to talk?
[Reschedule with donor]
Thank you so much. We really appreciate your help. Good Bye!

IF YOU ARE NOT SPEAKING TO THE PERSON YOU ARE TRYING TO CONTACT:

Do you know how we can reach <SUBJECT'S NAME>?
[Write down the subject contact information or time to call again]
Thank you so much. We really appreciate your help. Good Bye!

EXHIBIT 7 TELEPHONE SCRIPT

IF YOU REACH AN ANSWERING MACHINE THAT IDENTIFIES THE SUBJECT BY NAME:

Hi, I am calling on behalf of <BLOOD CENTER>. My name is <NAME>. Thank you for your last blood donation to our center. I'm calling to schedule your next blood donation appointment and to tell you about an important research study that our blood center is participating in. Please call me at <TELEPHONE NUMBER> at your convenience. Thank you and have a nice day!

IF YOU REACH AN ANSWERING MACHINE THAT DOES NOT IDENTIFY THE SUBJECT (EITHER DOESN'T GIVE A NAME OR GIVES A DIFFERENT NAME):

Hi, I'm calling on behalf of <BLOOD CENTER>. I'm trying to reach <SUBJECT'S NAME>. My name is <NAME>. If you know how I can reach <SUBJECT'S NAME>, please call me at <TELEPHONE NUMBER>. Thank you and have a nice day!

Exhibit 8

LAP STUDY
SHIPPING SCHEDULE

Shipment	Group A Blood Center of Wisconsin Blood Centers of the Pacific Southern Region ARC	Group B Hoxworth Blood Center Institute for Transfusion Medicine New England Region ARC
1	**Tuesday, Oct. 17, 2006**	**Tuesday, Oct. 24, 2006**
2	**Wednesday, Nov. 8, 2006**	**Tuesday, Nov. 14, 2006**
3	**Monday, Nov. 20, 2006**	**Tuesday, Nov 28, 2006**
4	**Tuesday, Dec. 5, 2006**	**Tuesday, Dec. 12, 2006**
No Shipments Dec. 14 - Jan. 2		
5	**Wednesday, Jan. 3, 2007**	**Tuesday, Jan. 9, 2007**
6	**Wednesday, Jan. 17, 2007**	**Tuesday, Jan. 23, 2007**
7	**Tuesday, Feb. 6, 2007**	**Tuesday, Feb. 13, 2007**
8	**Wednesday, Feb. 21, 2007**	**Tuesday, Feb. 27, 2007**
9	**Tuesday, Mar. 6, 2007**	**Tuesday, Mar. 13, 2007**
10	**Tuesday, Mar. 20, 2007**	**Tuesday, Mar. 27, 2007**
11	**Tuesday, April 3, 2007**	**Tuesday, April 10, 2007**
12	**Tuesday, April 17, 2007**	**Tuesday, April 24, 2007**
13	**Tuesday, May 1, 2007**	**Tuesday, May 8, 2007**
14	**Tuesday, May 15, 2007**	**Tuesday, May 22, 2007**

You must contact the Coordinating Center prior to any change to this schedule.

Exhibit 10. Barcode Aid Sheet

Non-consented Subject IDs				 [Non-consented Subject ID]
Box Names	 To SeraCare [Aliquots for SeraCare]	 To BSRI [Aliquots for BSRI]		 Non-consented [Non-consented aliquots from transfused males]
Volume Changes	 0.10-mL 0.01 to 0.10-mL	 0.25-mL 0.11 to 0.25-mL	 0.50-mL 0.26 to 0.50-mL	 0.75-mL 0.51 to 0.75 -mL
Volume Changes	 1.00-mL 0.76 to 1.00-mL	 1.25-mL 1.01 to 1.25-mL	 1.50-mL 1.26 to 1.50-mL	 1.75-mL 1.51 to 1.75-mL
Volume Changes	 3.00-mL 2.51 to 3.00-mL	 3.50-mL 3.01 to 3.50-mL	 4.0-mL 3.51 to 4.00-mL	 4.50-mL 4.01 to 4.50-mL
Volume Changes	 5.00-mL 4.51 to 5.00-mL	 5.50-mL 5.01 to 5.50-mL	 6.00-mL 5.51 to 6.00-mL	 6.50-mL 6.01 to 6.50-mL

Please fax this form to:
(No cover sheet required)

Simon Ng, BSRI
Fax #: 1 (415) 775-3859

Page: _____ of _____

Date of Shipment: _____

REDS-II LAP Study - Shipping Notification

1. Fax this form to Simon Ng (BSRI- 1.415.775.3859) the same day the specimens are sent to BSRI, this alerts our lab staff of sample's arrival the following day.
2. Include this form with shipment, fold and place inside box.

FedEx Tracking # 1: _____

FedEx Tracking # 2: _____

FedEx Tracking # 3: _____

Comments: _____ **shippers containing** _____ **boxes**

Scheduled Pick-Up Date:

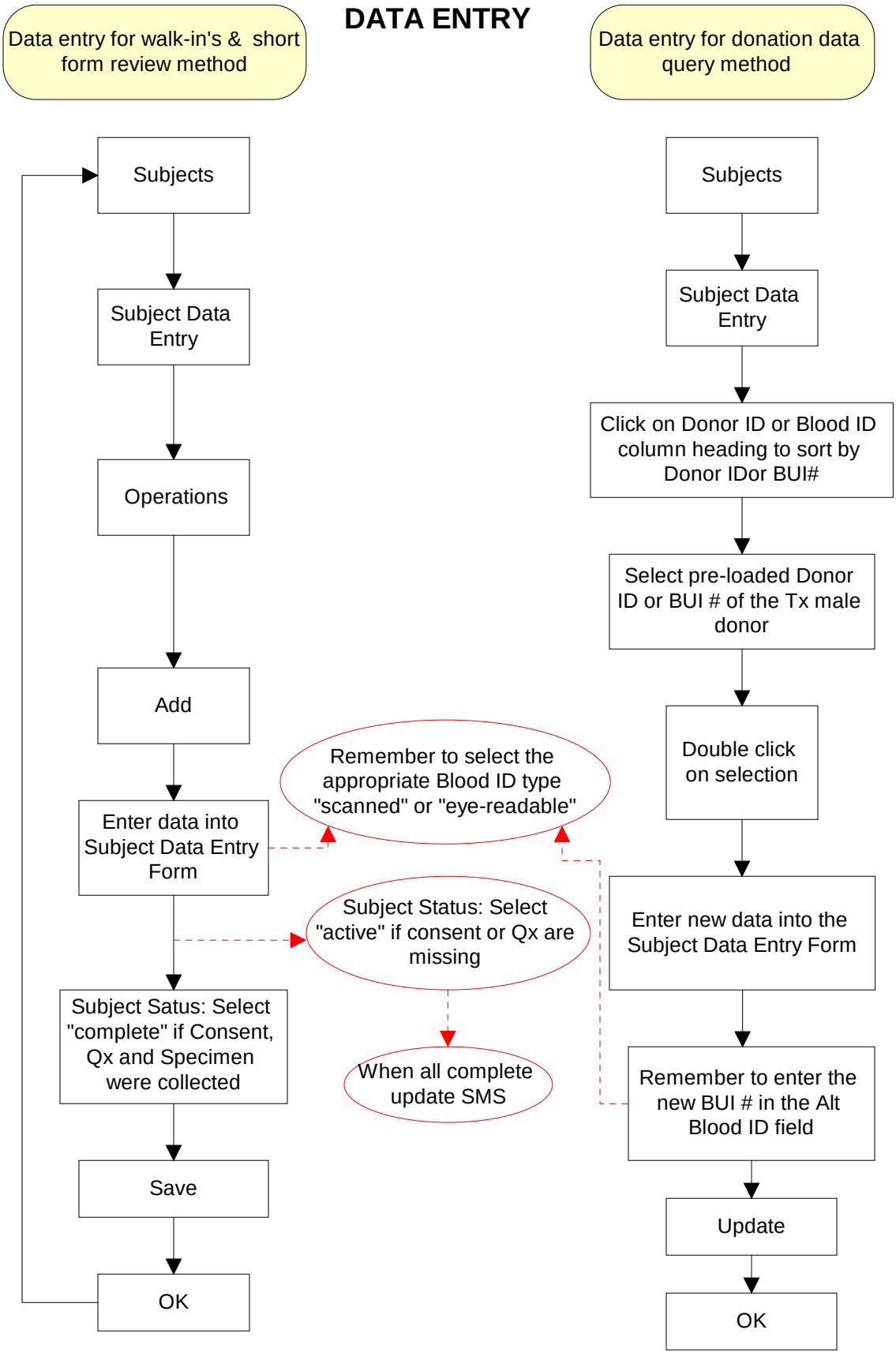
Scheduled Delivery Date:

Blood Center: _____ **Blood Center Contact:** _____

Contact Phone: _____ **E-mail:** _____

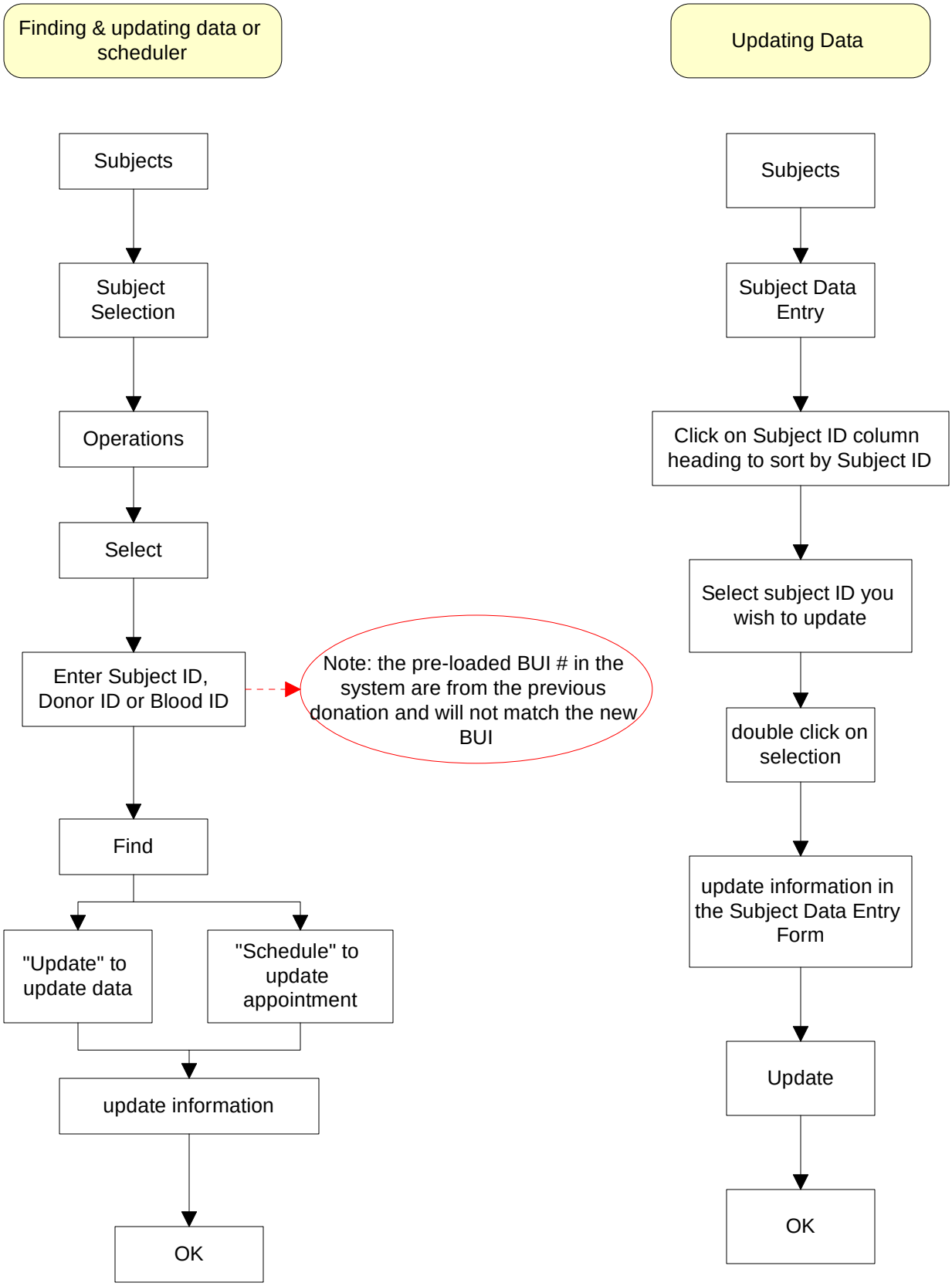
Exhibit 11
REDS-II LAPS STUDY
SHIPPING NOTIFICATION

Cheat Sheet 1: SMS Flow Charts



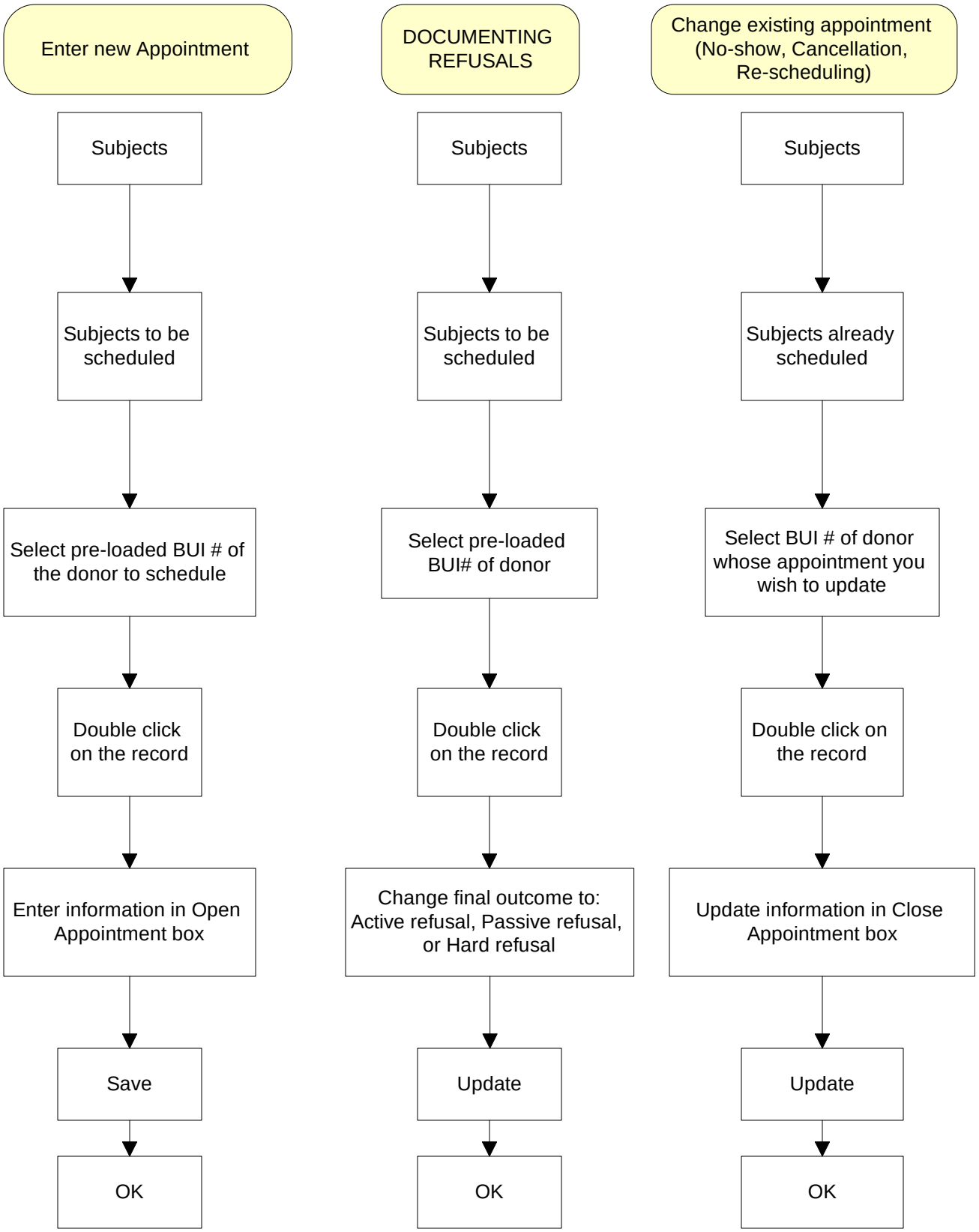
Cheat Sheet 2: SMS Flow Charts

FINDING & UPDATING A RECORD



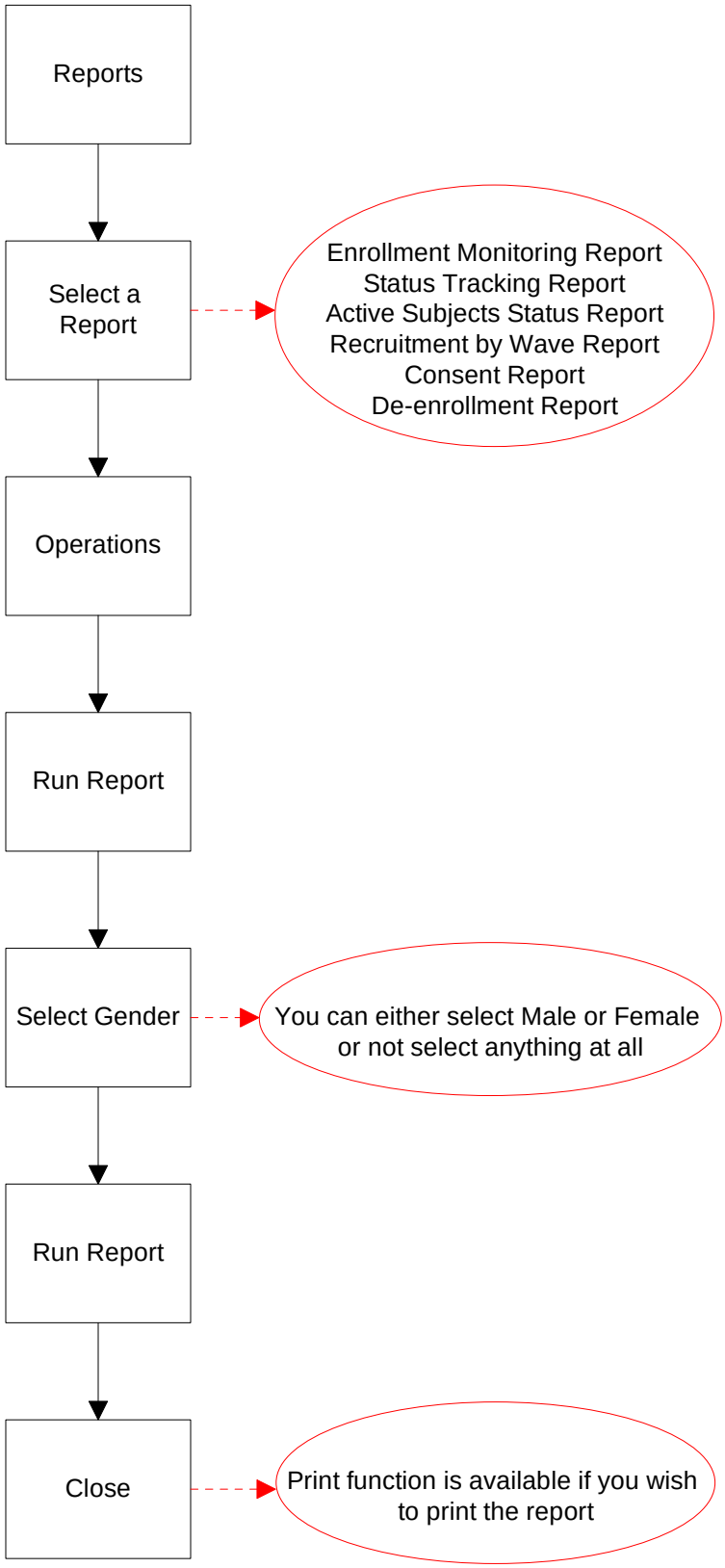
Cheat Sheet 3: SMS Flow Charts

SUBJECT SCHEDULING - DONATION DATABASE QUERY



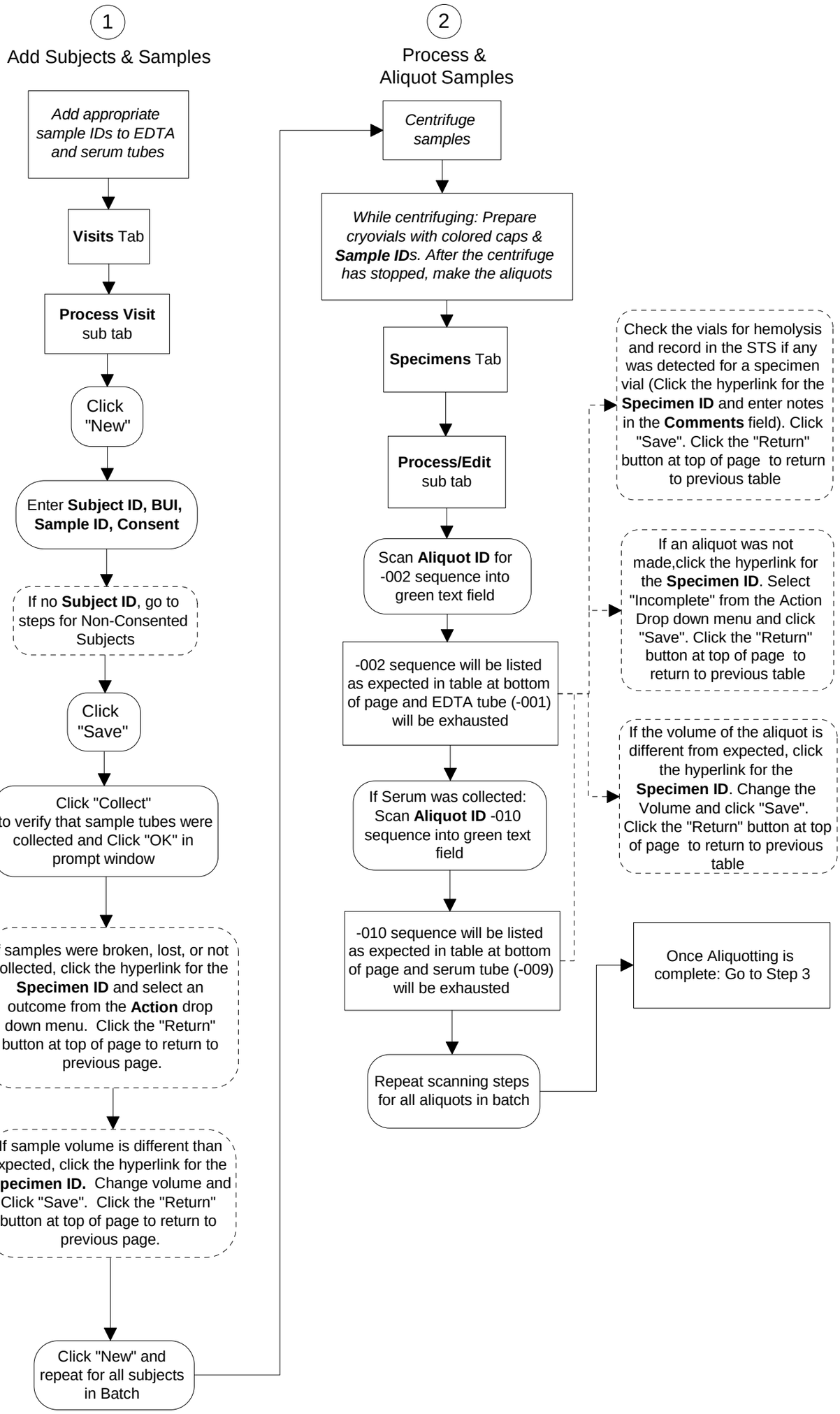
Cheat Sheet 4: SMS Flow Charts

SMS REPORTS



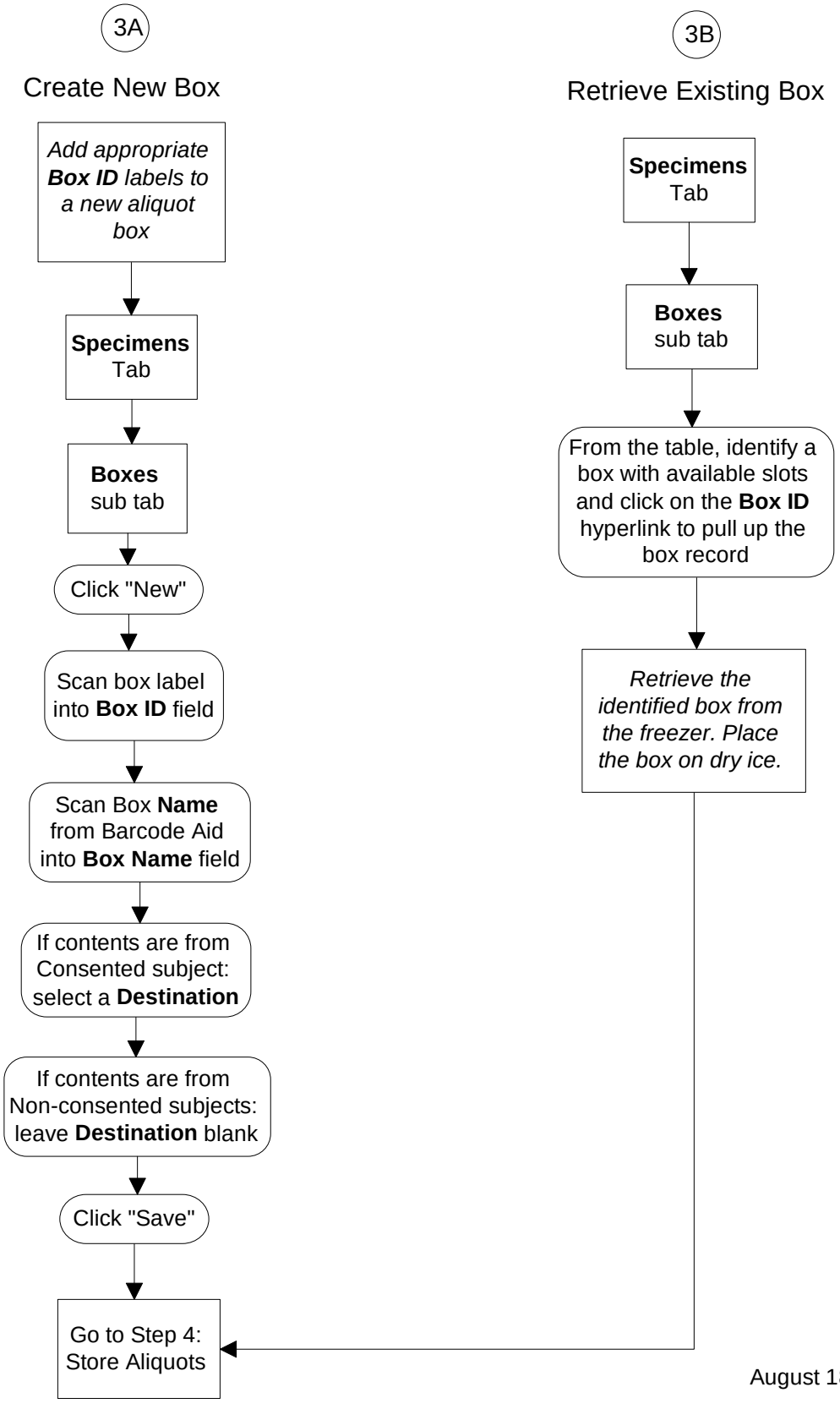
Cheat Sheet 5: STS Flow Charts

Consented Individuals



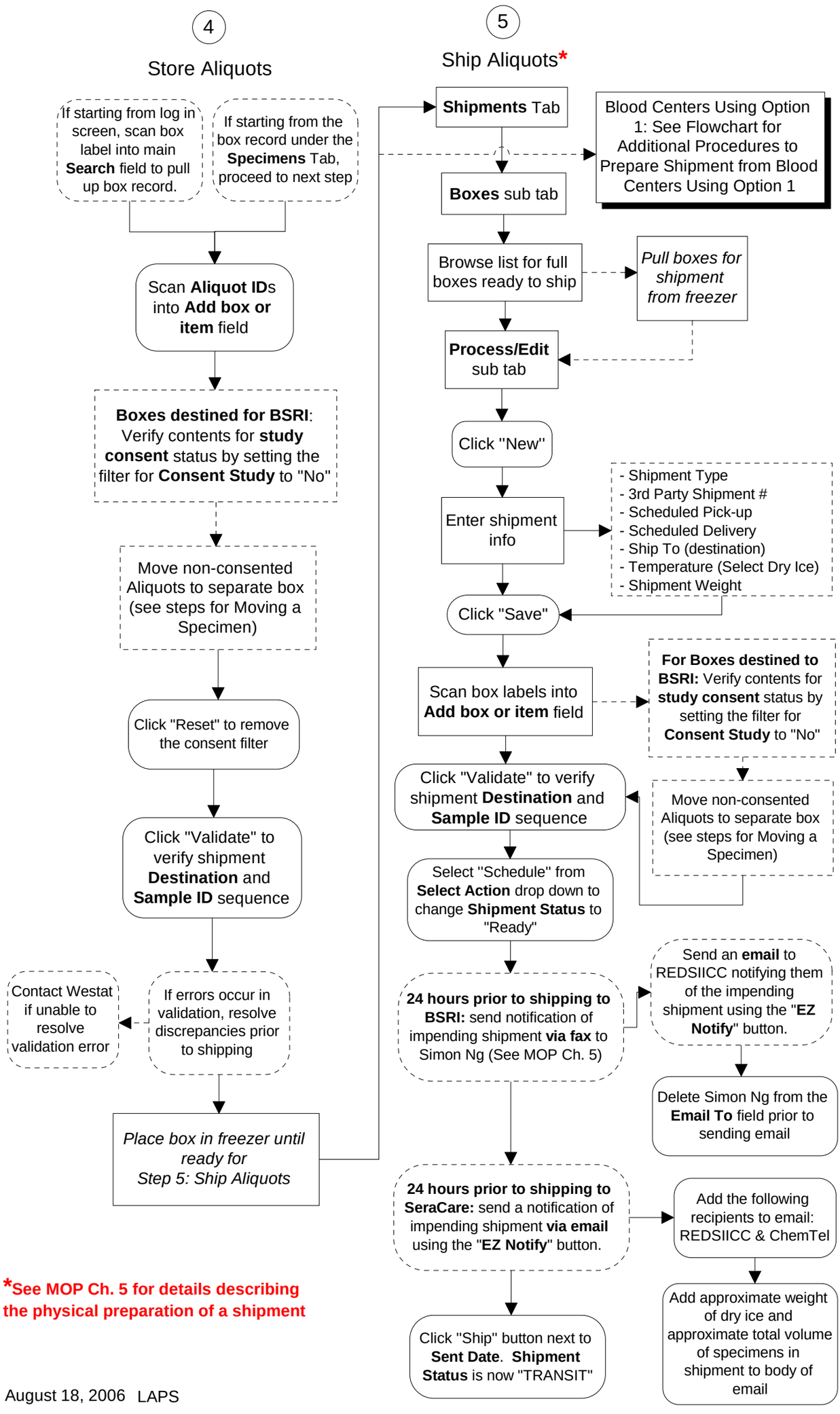
Cheat Sheet 6: STS Flow Charts

Consented Individuals



Cheat Sheet 7: STS Flow Charts

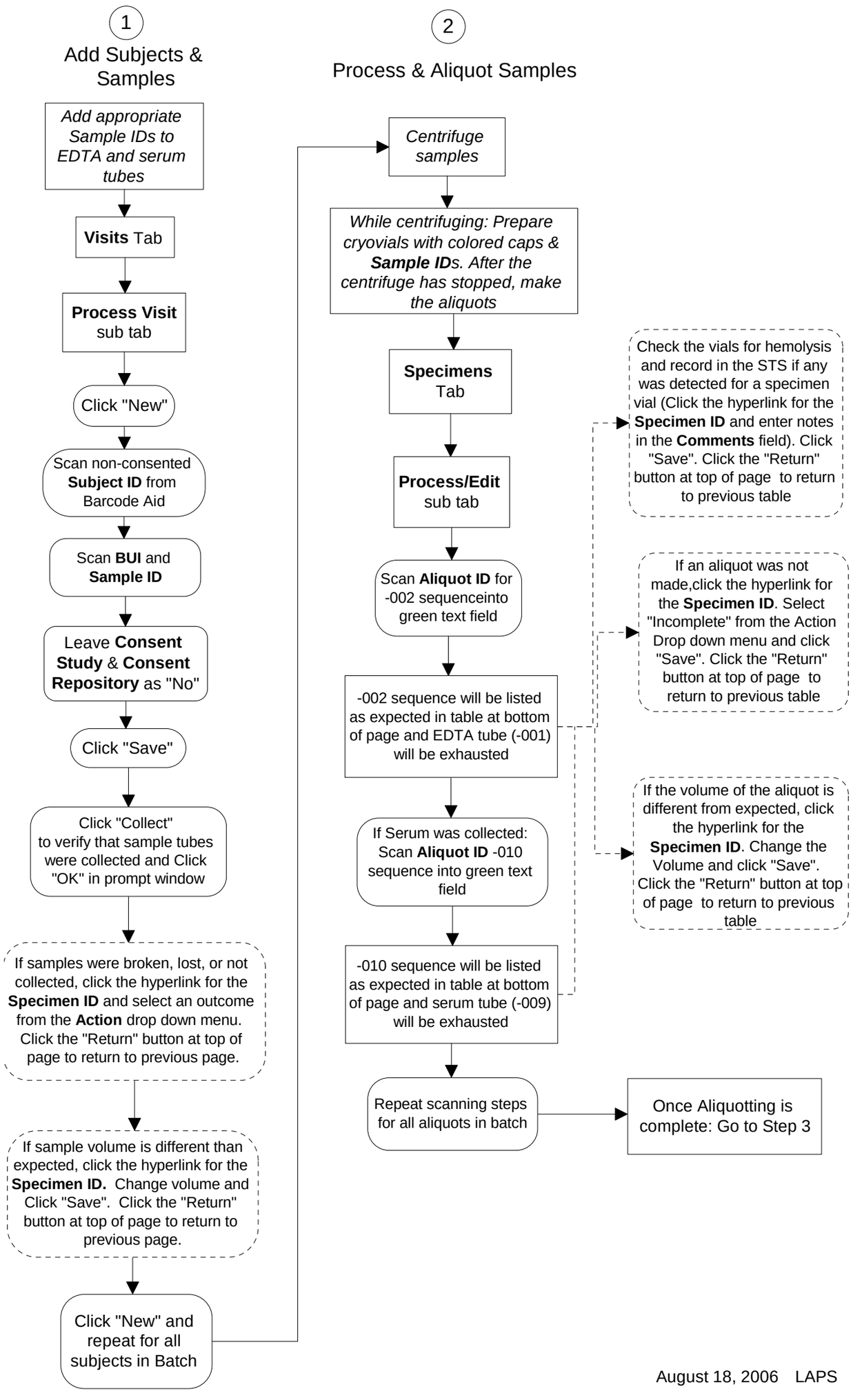
Consented Individuals



***See MOP Ch. 5 for details describing the physical preparation of a shipment**

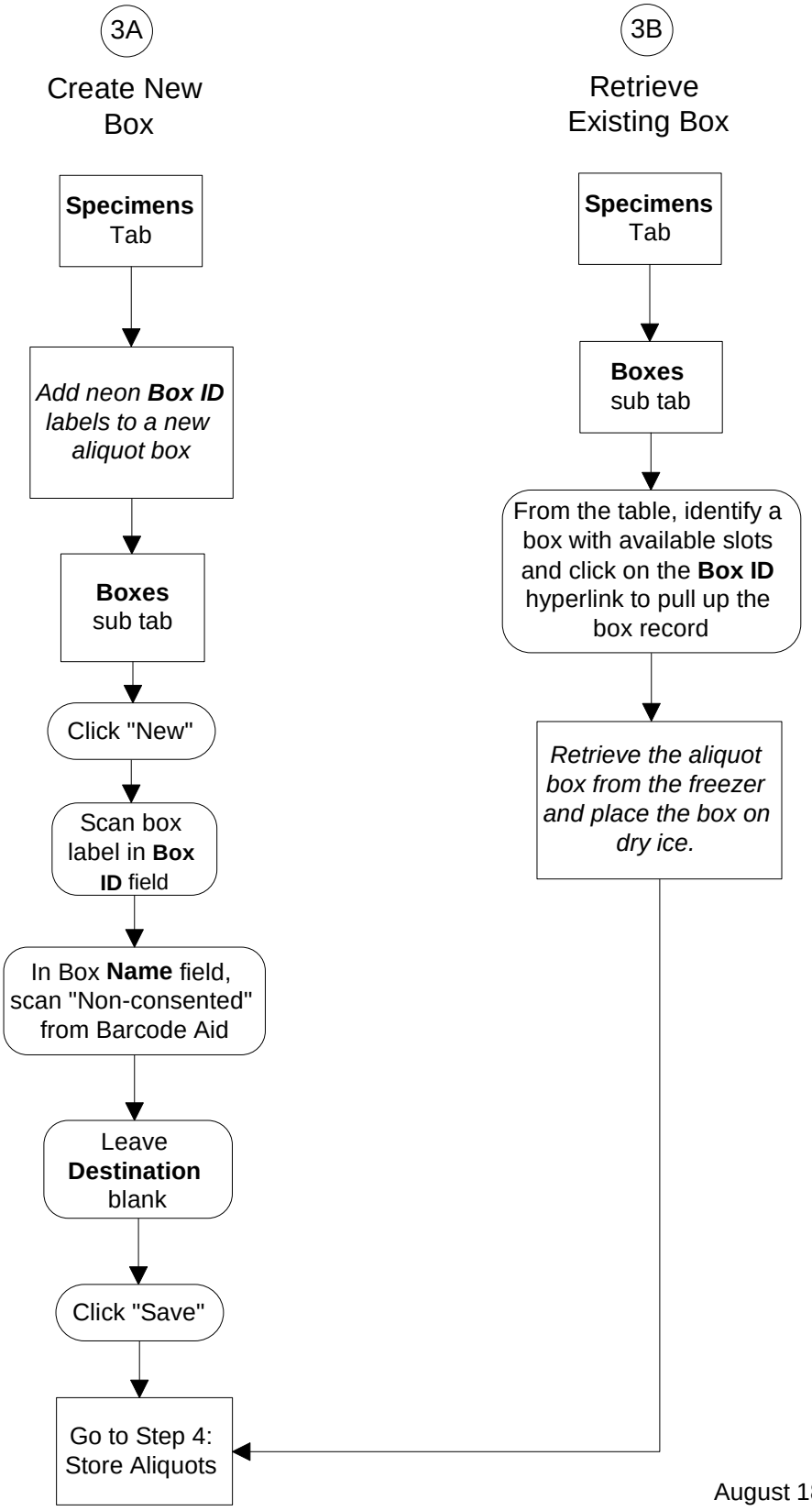
Cheat Sheet 8: STS Flow Charts

Non-Consented Individuals



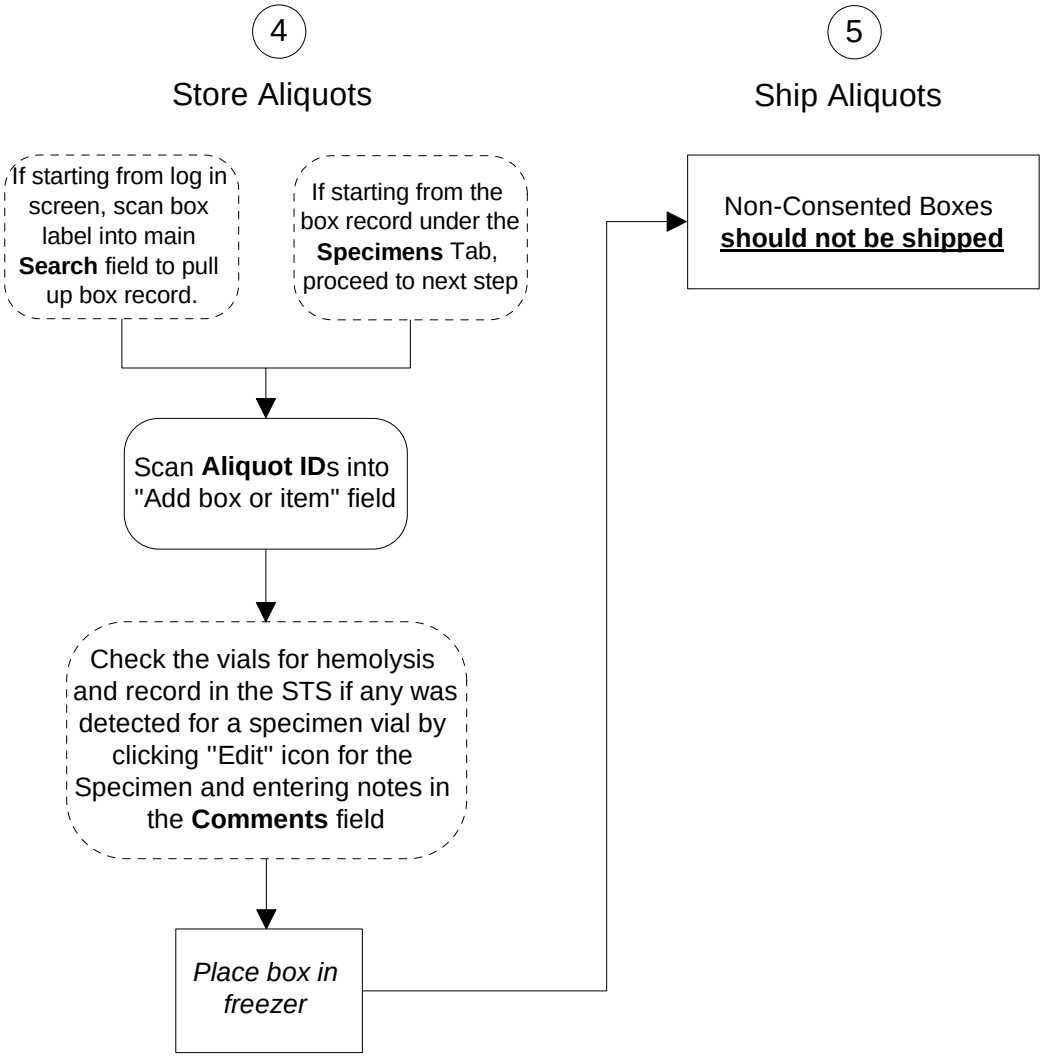
Cheat Sheet 9: STS Flow Charts

Non-Consented Individuals



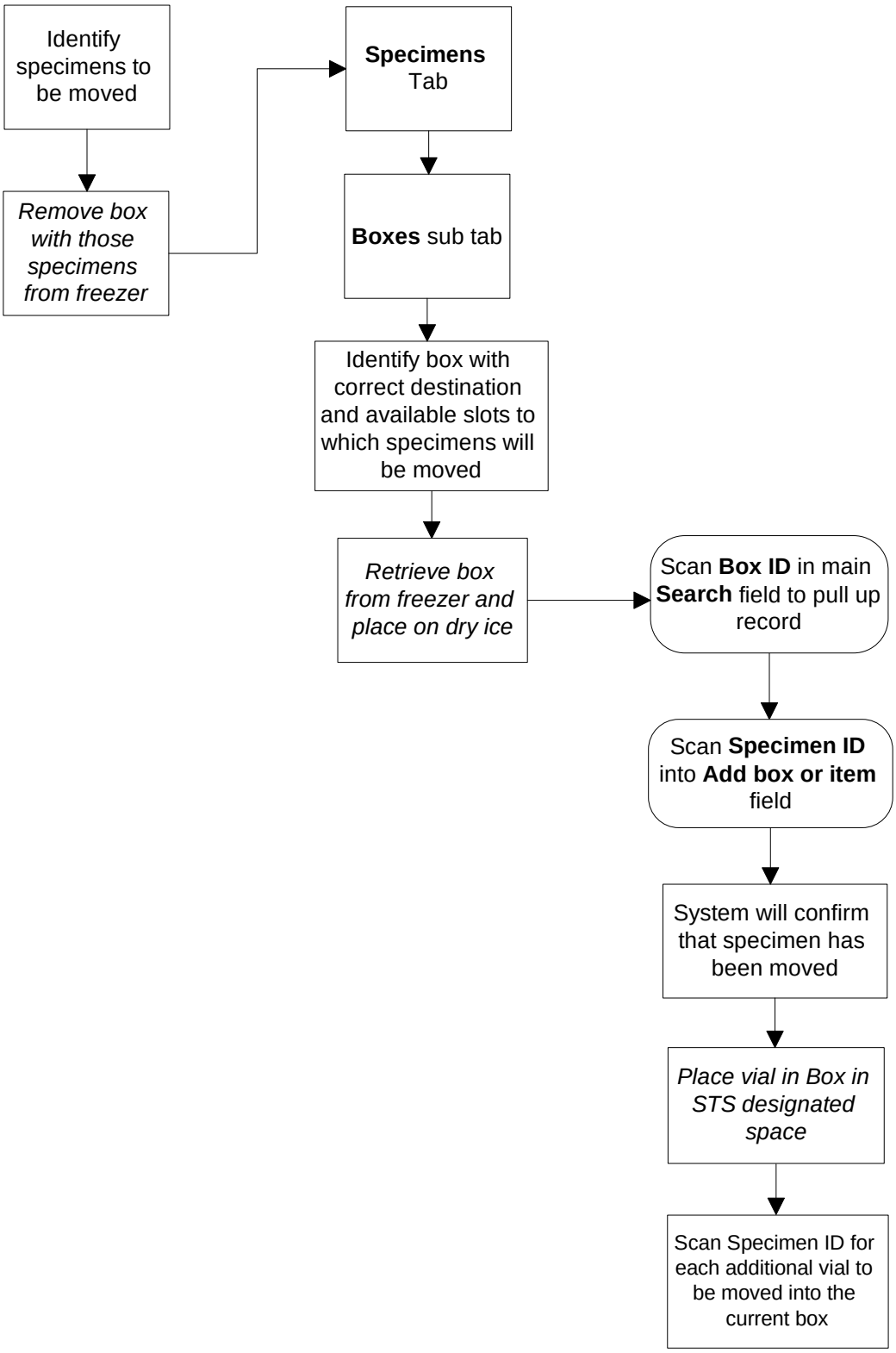
Cheat Sheet 10: STS Flow Charts

Non-Consented Individuals



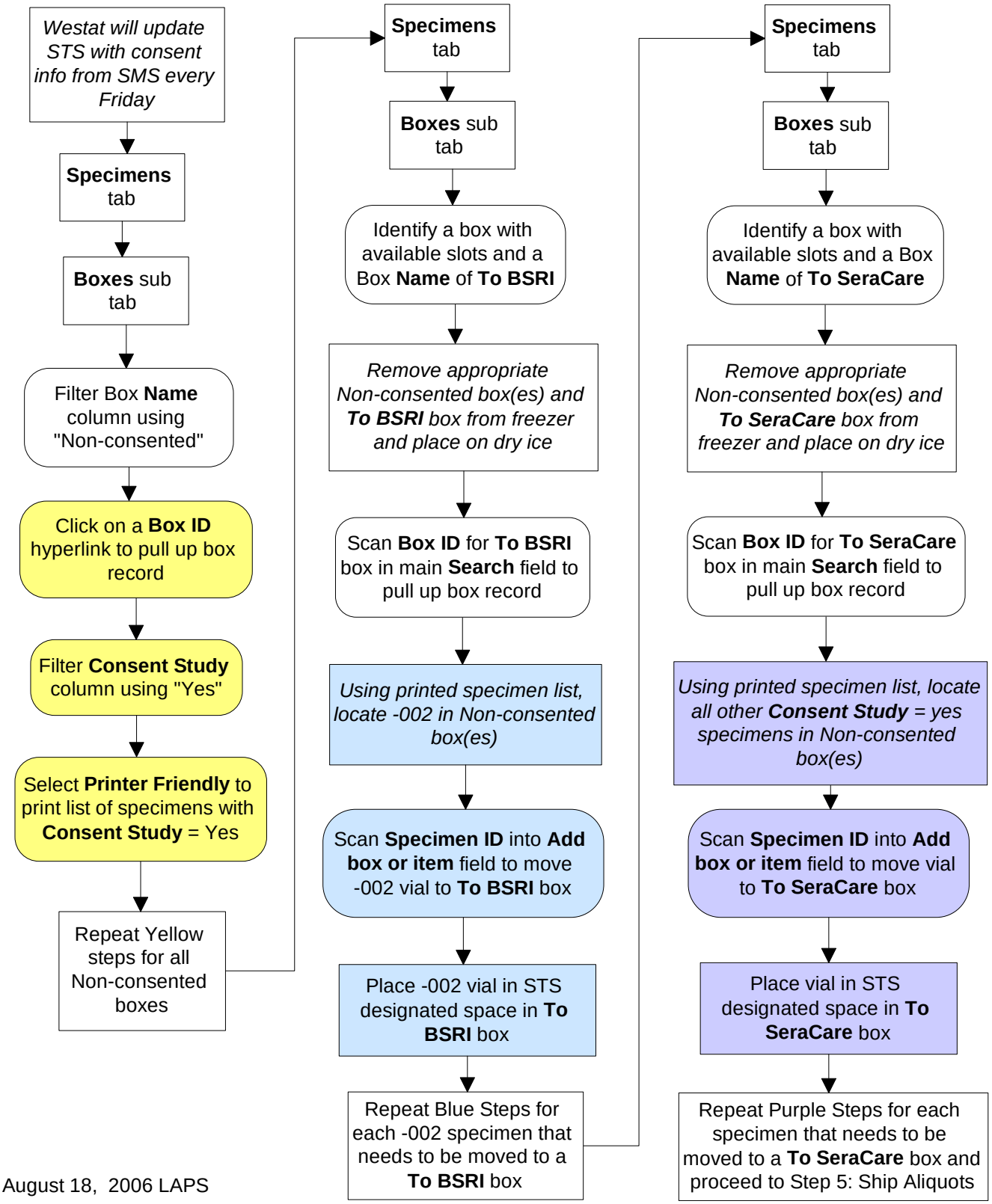
Cheat Sheet 11: STS Flow Charts

Moving a Specimen to a Different Box



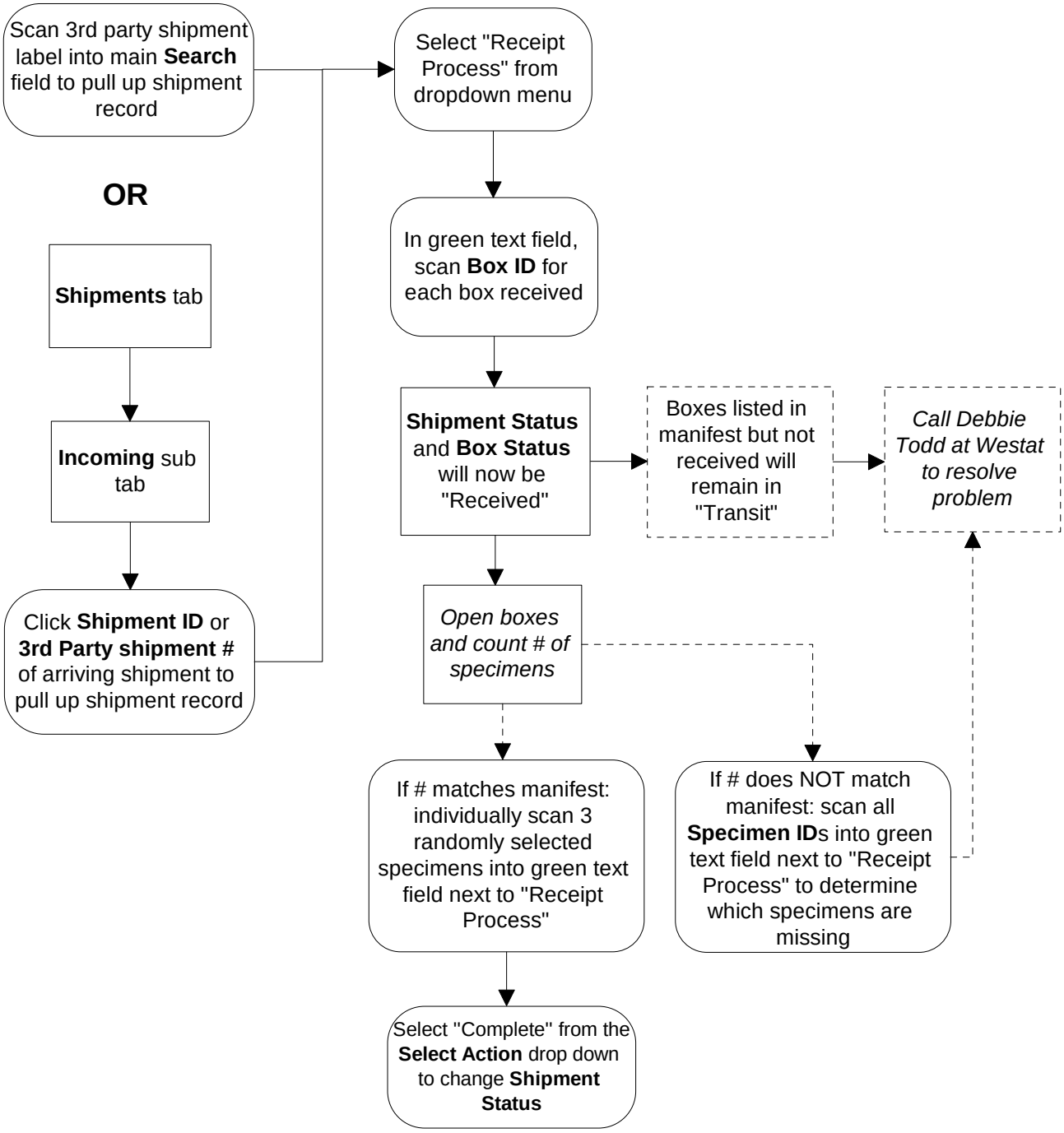
Cheat Sheet 12: STS Flow Charts

Additional Procedure to Prepare Shipment From Blood Centers Using Recruitment Option 1



Cheat Sheet 13: STS Flow Charts

Receipting a Shipment



Westat Contact List for the Leukocyte Antibody Prevalence Study

	Contacts	Phone	Email
General Questions	Sunitha Mathew	301.294.4472	sunithamathew@westat.com
SMS	Sunitha Mathew	301.294.4472	sunithamathew@westat.com
	Tesa Kochie	240.314.2540	tesakochie@westat.com
QED	Sunitha Mathew	301.294.4472	sunithamathew@westat.com
	Tesa Kochie	240.314.2540	tesakochie@westat.com
STS	Danielle Carrick	240.314.5896	daniellecarrick@westat.com
	Tesa Kochie	240.314.2540	tesakochie@westat.com
Specimen Collection / Lab Supplies / Shipping	Deborah Todd	301.738.8315	deborahtodd@westat.com
Lab Studies	Deborah Todd	301.738.8315	deborahtodd@westat.com
	Danielle Carrick	240.314.5896	daniellecarrick@westat.com
Recruiting	Sunitha Mathew	301.294.4472	sunithamathew@westat.com

Last updated: December 5, 2006