HALT-C Trial Q x Q

Block Food Questionnaire

Preprinted Questionnaire: Version 98.2

Purpose of this Questionnaire: The Block Food Questionnaire is a self-administered form used to collect information about the patient's food intake. It is part of the Risk Factors Ancillary Study.

When to complete this Questionnaire: All HALT-C patients should complete The Block Food Questionnaire. The Questionnaire should be completed at the following study visits:

- **Screening Phase patients:** S00 visit.
  The Questionnaire should be handed to the patient at the second screening visit. The patient should be asked to complete the Questionnaire at home and bring to the Baseline visit (W00 or R00).

- **Randomized Phase patients**: Month 18 (M18) visit.
  The Questionnaire can either be:
  1. Handed to the patient at the Month 15 visit (M15) to be completed and returned at the M18 visit.
  2. Mailed to the patient before the M18 visit to be completed and returned at the M18 visit.
  3. Completed at the clinical site during the M18 visit.

  NOTE: If the patient fails to complete the Questionnaire for the M18 visit, he/she may complete this Questionnaire up through the end of enrollment in the HALT-C trial.

If a patient will never complete a Block Food Questionnaire, please notify the DCC with a reason for the incomplete Questionnaire. Some acceptable reasons for missing Blocks are "patient withdrew", "patient doesn't speak/read English", or "patient refused".

PATIENT IDENTIFICATION

The Block Food Questionnaire, version 98.2, is a copyrighted form. Therefore, the Questionnaire does not have the same format as the other HALT-C forms. It is an 8-page form printed in black and shaded in blue.

Inserted in the form is a separate black and white sheet, with "Serving Size Choices" pictures to help in filling out the Questionnaire. Please check to make sure that the picture is enclosed.

It is important that before you give the patient this form to fill out, that you write in the Patient ID and Visit Number as described below.

- **Use only a No. 2 pencil to fill out this form.** The clinical site may order pencils from the DCC for this use.

  - Record the patient's 6 digit ID number and visit number on the form under 'Respondent ID Number' (see example below)

Respondent ID Number

1	2	3	4	5	6		0	0

- Start by recording the first number of the Patient's ID in the first column on the left side of the form, and record all 6 digits up to the sixth column from the left.
- The seventh column from the left can be left blank
- In the right-most two columns, record the visit number. Record either 0 0 for the Screening visit or 18 for the Month 18 visit.
- Under each number of the patient's ID and the visit number fill in the corresponding circle completely, and erase completely if you make any changes.

- In the box asking to print the patient's name, please write the six digit Patient ID code and underneath it the visit # as S00 or M18. Please write this in pencil and remind the patient that she is not to put her/his name on the Questionnaire.

Please print your name in this box.
Pt ID 123456 Visit # S00

PATIENT INSTRUCTIONS

Instructions for completing the Questionnaire are printed on the food Questionnaire. Review the eight pages of the Food Questionnaire with the patient. The patient should understand the following:

- Use only a No. 2 pencil to fill out the form.
- No other marks should appear on the Questionnaire. Comments or notes should not be written on the Questionnaire.
- Fill in the answer bubbles (circles) completely. Do not simply make a checkmark or an 'X' over the bubble.
- Never mark two bubbles for the same answer—this will result in a missing answer.
- Do not staple anything to the Questionnaire or use staples on the Questionnaire.
- Do not insert any extra pages or notes into the Questionnaire
- Do not fold the Questionnaire.
- Do not punch holes in the Questionnaire.

- Explain to the patient the importance of completing each question. Explain to the patient the one page portion-size pictures, "Serving Size Choices" to assist with the portion-size section of the form. Review the example on Page 2 of the Questionnaire with the patient.

- If the patient is unable to complete the Questionnaire, it may be administered by patient interview using standard interview technique.

RETURNING BLOCK FOOD QUESTIONNAIRE

When a patient returns a completed Questionnaire, please check to make sure that all the questions were answered. Erase any stray marks. Please return the Questionnaire via FedEx to NERI:

HALT-C Data Coordinating Center
New England Research Institutes
9 Galen Street
Watertown, MA 02472
Phone: (617) 923-7747

HALT-C Trial Q x Q

Serum TGF-B1 – Serum Fibrosis Markers AS

Form # 100 Version B: 12/03/2003

Purpose of Form #100: The Serum TGF-B1 Form #100 records the results of the serum fibrosis marker TGF-B1 assay as part of the Serum Fibrosis Marker Ancillary Study.

When to complete Form #100: Form #100 will be completed for patients participating in the Serum Fibrosis Marker Ancillary Study at Site 18 (University of Michigan). Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible.

Form #100 should be completed at the following study visits:
- Lead-in phase: Baseline (W00) and Week 24 (W24).
- Randomization phase: Month 12 (M12), Month 24 (M24), Month 36 (M36), and Month 48 (M48).
- Responder phase: Week 48 (W48) and Week 72 (W72).
- Breakthrough/Relapser patients: Randomization (R00) visit.

The serum TGF-B1 assay will be performed at Site 18. Form #100 will be data entered at Site 18.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to the visit number at time of serum collection.

A4. Record the date of the serum collection in MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: RESULTS OF SERUM FIBROSIS MARKER TGF-B1 TEST

B1. Record the date of testing in MM/DD/YYYY format.

B2. Plasma TGF-B1 is tested only at Site 18.

Record the results of Plasma TGF-B1 protein levels in ng/ml. The field allows three numbers before the decimal point. Two numbers **must** be entered after the decimal point.

The normal range is 1.00 to 100.00 ng/ml. If the result falls outside of this range, please verify the result against the source documentation. If the abnormal result is correct, select the override button. Specify that the data was verified and is correct.

HALT-C Trial Q x Q

TGF-B1 mRNA – Serum Fibrosis Markers AS

Form # 101 Version A: 06/15/2000

Purpose of Form #101: The TGF-B1 mRNA Form #101 records the results of hepatic TGF-B1 mRNA measured by quantitative RT-PCR as part of the Serum Fibrosis Marker Ancillary Study.

When to complete Form #101: Form #101 will be completed for patients participating in the Serum Fibrosis Marker Ancillary Study at Site 18 (University of Michigan). Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible.

Form #101 should be completed at the following study visits:
- Screening (S00).
- Randomization phase: Month 24 (M24) and Month 48 (M48).

The TGF-B1 mRNA measurement will be performed at Site 18. Form #101 will be data entered at Site 18.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to the visit number at time of tissue collection.

A4. Record the date the form was completed in the MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: RESULTS OF TGF-B1 mRNA

B1. Record the date of TGF-B1 mRNA measurement in the MM/DD/YYYY format.

B2. TGF-B1 mRNA is measured only at Site 18.

Record the results of TGF-B1 mRNA in copies/ ml housekeeper gene. The normal range is 100 to 100,000,000.

HALT-C Trial Q x Q

Serum Fibrosis Marker AS Aliquot Form

Form # 102 Version A: 06/15/2000 (Revised 05/11/2006)

Purpose of Form #102: The Serum Fibrosis AS Aliquot form is used to record the specimens collected for the Serum Fibrosis Marker Ancillary Study that will be sent to the Central Repository (BBI).

Data entry of this form for a patient visit is the first step of the shipping and tracking procedures for HALT-C. All of the specimens entered as being collected on this form will go into a database of specimens available for shipment to the Central Repository for your clinical center. Entry of this form also allows NERI to link the HALT-C Trial ID's and study visits with the Sample ID assigned by the Central Repository.

When to complete Form #102: Form #102 should be completed in addition to the aliquot form specific for the regular study visit. Form #102 will be completed and data entered for patients participating in the Serum Fibrosis Marker Ancillary Study at the following clinical sites. Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible for this Ancillary Study.

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 13 (Massachusetts General Hospital).
- Site 19 (Virginia Commonwealth University).

Form #102 should not be completed for specimens collected at Site 18 (University of Michigan) because specimens will not be shipped to the Repository.

Form #102 should not be completed for patients who had a liver transplant.

Form #102 should be completed at the following study visits:

- Lead-in phase: Baseline (W00) and Week 24 (W24).
- Responder phase: Week 48 (W48) and Week 72 (W72).
- Breakthrough/Relapsers: Randomization (R00) visit.
- Randomization phase: Month 12 (M12), Month 24 (M24), Month 36 (M36), and Month 48 (M48).

SECTION A: GENERAL INFORMATION

A1. Affix a patient ID label in the space provided at the top of each page. If a label is not available, record the ID number legibly in ink.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Record the visit number for this visit.

A4. Record the date the form was completed in the MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: SAMPLE ID

At each visit, select the next available label packet supplied by the DCC or BBI. There are label packets for Screen 1, Screen 2, and each of Lead-In Phase, Randomized and Week 20 responder study visits.

B1. Record the sample ID for this patient and this visit in the space provided. An extra aliquot label from the label packet used for this patient may be placed on the form. If the label is not available, record the sample ID number legibly.

BBI and the DCC rely on the Sample ID as a link between the patient ID, the study visit, and location of collected specimens. It is very important that Sample ID is recorded and data entered accurately.

B2. Record the collection date in the MM/DD/YYYY format for the specimens to be aliquotted for shipment to BBI.

SECTION C: SPECIMEN INFORMATION

C1. Indicate if there were any problems or delays in specimen processing in C1.

Circle "No" for C1 if serum was separated within 2-4 hours of collection.
- Questions C2a and C2b must be completed for each aliquotted specimen.
- Questions C2c and C2d do not need to be completed.

Circle "Yes" for C1 if there was a problem with specimen processing.
- Questions C2a, C2b, C2c, and C2d must be completed for each aliquotted specimen.
- Question C2c should be completed with one of the codes for specimen processing listed in the code box at the end of the form (below).

Codes for specimen processing

1. okay
2. hemolysis
3. delay in processing-processed within 4-6 hours of collection
4. delay in processing-processed within 6-8 hours of collection
5. delay in processing-processed within 8-12 hours of collection
6. delay in processing-processed within 12-18 hours of collection
7. delay in processing-processed within 18-24 hours of collection
8. delay in processing-processed within 24-48 hours of collection
9. delay in processing-processed 48+ hours after collection
10. delay in shipping
11. collected in incorrect tube-plasma collected instead of serum
12. delay in snap freezing liver tissue
13. Vacutainer tube stored in refrigerator
99. Other-please specify

HALT-C Trial Q x Q

Serum YKL-40 – Serum Fibrosis Markers AS

Form # 103 Version A: 12/05/2003

Purpose of this form: The Serum YKL-40 Form #103 records the results of the serum fibrosis marker YKL-40 assay as part of the Serum Fibrosis Marker Ancillary Study.

When to complete this form: Form #103 will be completed for patients participating in the Serum Fibrosis Marker Ancillary Study at the following clinical sites. Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible.

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 13 (Massachusetts General Hospital).
- Site 18 (University of Michigan).
- Site 19 (Virginia Commonwealth University).

Form #103 should be completed at the following study visits:

- Lead-in phase: Baseline (W00) and Week 24 (W24).
- Randomization phase: Month 12 (M12), Month 24 (M24), Month 36 (M36), and Month 48 (M48).
- Responder phase: Week 48 (W48) and Week 72 (W72).
- Breakthrough/Relapser patients: Randomization (R00) visit.

The serum YKL-40 assay will be performed at Site 18. Form #103 will be data entered at Site 18.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to the visit number at time of serum collection.

A4. Record the date of the serum collection in MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: RESULTS OF SERUM FIBROSIS MARKER YKL-40 TEST

B1. Record the date of testing in MM/DD/YYYY format.

B2. Serum YKL-40 is tested only at Site 18.

Record the results of serum YKL-40 levels in ng/ml. The field allows four numbers before the decimal point. Two numbers **must** be entered after the decimal point.

The normal range is 1.00 to 1000.00 ng/ml. If the result falls outside of this range, please verify the result against the source documentation. If the abnormal result is correct, select the override button. Specify that the data was verified and is correct.

HALT-C Trial

HVPG Measurement—Portal Hypertension AS

Form # 111 Q x Q Version A: 06/15/2000 (Rev. 12/09/2005)

Purpose of the form: This forms documents the results of the HVPG measurement performed for the Portal Hypertension Ancillary Study.

When to complete this form: This form is completed for all patients participating in the Portal Hypertension Ancillary Study at Month 48. Patients eligible to participate in this ancillary study include all patients at VCU and UCHSC in the control arm not receiving peginterferon maintenance therapy and those patients in the maintenance therapy arm of HALT-C who have remained on peginterferon for the past 6 months. This form is an addable form under the Month 48 visit in the DMS.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed.
- When entering this date, use the MM/DD/YYYY format.
- Enter the 2 digit number for the month in the first 2 spaces provided (i.e., January = "01", February = "02", etc.) enter the 2 digit number for the day of the month in the second 2 spaces provided and the 4 digit number for the year in the final 4 spaces provided.

A5. Enter the initials of the person completing the form.
- Enter the first initial in the first space provided; middle initial in the second space provided and the last initial in the third space provided.
- If the patient does not have a middle name, enter the first initial in the first space provided, leave the second space blank, and enter the last initial in the third space provided.
- If the person has a hyphenated last name or 2 last names, enter the initial of the first last name in the last space.

SECTION B: GENERAL INFORMATION

For more information on the performance of the HVPG measurement, see section K-5, Appendix 1, of the Manual of Operations.

This form should be completed by the person performing the HVPG procedure. Circle the number corresponding to the appropriate answer.

B1. Record the date the test was done.
- When entering this date, use the MM/DD/YYYY format.
- Enter the 2 digit number for the month in the first 2 spaces provided (i.e., January = "01", February = "02", etc.) enter the 2 digit number for the day of the month in the second 2 spaces provided and the 4 digit number for the year in the final 4 spaces provided.

B2. Indicate which type of conscious sedation was used. If other, please specify. Fifty characters (including punctuation and spaces) are provided.

B3. Answer YES if a medication was used to prevent dye allergy and go to question B3a.
Answer NO if there was no medication used to prevent dye allergy and go on to Section C.

B3a. Indicate the type of medication used to prevent dye allergy. If other, please specify. Fifty characters (including punctuation and spaces are provided).

SECTION C: STANDARDIZATION

Answer YES or NO for each question.

C1-C3.
- Answer YES for each measure of standardization set.
- Answer NO if the standardization was not set.

SECTION D: MEASUREMENTS

Record 3 measurements in mm/hg for each location.

D1. Pressure measurement in the inferior vena cava will be made at the level of the hepatic orifice.

D2. Free Hepatic Venous Pressure (FHVP) are then made with the catheter tip free in the hepatic vein (the FHVP should not differ from the inferior vena cava pressure by more than 1-2 mm Hg).

D3. For each Wedged Hepatic Venous Pressure (WHVP) measurements taken, the tracing must be 45-60 seconds long.

SECTION E: OTHER ABNORMALITIES

E1.
- Answer YES if other abnormalities were noted, or any problems or adverse events occurred during the procedure. If yes, describe in the space provided. 500 characters (including spaces and punctuation) are provided.
- Answer NO if there were no other abnormalities, and no problems or adverse events occurred. Go on to Section F.

SECTION F: SOURCE DOCUMENTATION

A source document is a part of the patient's medical record which serves to validate data collected on the data entry forms. The appropriate source documents should be attached to this form with all identifying patient information, such as patient name and medical record number blacked out. The HALT-C Trial requires the following source documents for each HVPG measurement:

F1. A written report of the HVPG measurement findings.

F2. A recording of the HVPG measurement.

F2a. The recording should show the establishment of the zero point.

F2b. The recording should show the calibration of the transducer and recording equipment.

Answer YES or NO for each source document provided.

HALT-C Trial Q x Q

Glycosylated Hemoglobin - Steatosis AS

Form # 121 Version A: 06/15/2000

Purpose of Form #121: The Glycosylated Hemoglobin form is used to record the glycosylated hemoglobin (HBA1c) results from the local lab report. A copy of local lab report should be attached to Form #121.

When to complete Form #121: The Glycosylated Hemoglobin form will be expected when question B5 (Diabetes?) on Form #3: Screening Medical History Interview is answered "Yes".

Form #121 should be completed during Screening for any patient who has diabetes. Patients who do not have diabetes do not require this form. Form #121 will be data entered at each clinical site.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. The visit number, S00, is pre-printed on the form. S00 must be data entered.

A4. Record the date the form was completed in MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: GLYCOSYLATED HEMOGLOBIN (HbA1c)

B1. Enter the level of glycosylated hemoglobin, in %, as reported on the local lab report. The field allows two numbers before the decimal point. One number **must** be entered after the decimal point.

The normal range is 4.5% to 10.0%. If the result falls outside of this range, please verify the result against the source documentation. If the abnormal result is correct, select the override button. Specify that the data was verified and is correct.

If the test was not done or the result will never be available, set Form #121 to missing in the Data Management System.

HALT-C Trial Q x Q

Physical Activity – Risk Factors AS

Form # 140 Version B: 12/03/2001

Purpose of Form #140: The Physical Activity form records the patient's current recreational and non-recreational activity levels, at work or at home using a brief, self-administered questionnaire.

When to complete Form #140: This form should be completed for all patients at the following study visits:

- Lead-in patients: Baseline (W00).
- Express patients: Baseline (R00).
- Randomization phase: Month 12 (M12), Month 24 (M24), and Month 54 (M54).

Form #140 will be data entered at each clinical site.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date of the visit in MM/DD/YYYY format.

A5. Enter the initials of the person completing Section A of the form.

General Instructions for Sections B and C:

- The patient should complete sections B and C of Form #140 by following the directions written on the form.

- If the patient is not able to complete Form #140 by her/himself, the interviewer may read the questions and answers to the patient and record the answers given by the patient on the form. If the interviewer completes the form in this manner, please note so in the margins of the form by writing "form completed by interviewer" with the initials of the interviewer.

- It is important that the patient complete all of the items on Form #140.
  - Review the form for any missing items.
  - Make sure that each item has only a single answer selected.
  - Please ask the patient to complete any missing or doubly marked items.

SECTION B: NON-RECREATIONAL ACTIVITY (WORK-RELATED)

B1. The description for each activity is in parentheses on Form #140. The patient should circle the activity level that best describes his/her usual non-recreational activity. The patient should circle only one option.

B2. The patient should record the average amount of time per day in hours spent at this level of activity.

B3. The patient should record the average amount of time per day in hours spent sitting down.

SECTION C: RECREATIONAL ACTIVITY

For each activity listed in Section C, the patient should consider whether s/he participates in the activity for at least 15 minutes a week. For each activity that s/he participates in for at least 15 minutes per week, the patient should circle that activity and write the number of hours or minutes that s/he does that activity per week in the spaces to the right. The patient does not need to make any marks for activities in which s/he does not participate. The patient may skip those activities.

Additional instructions for data entry:

Data entry personnel should note that there is an additional question in the electronic version of the form in the Data Management System that does not appear on the paper copy of the form. For each activity listed on the paper form, an additional question appears in the DMS asking the data enterer to record whether or not the patient replied that s/he participates in that activity. For each activity, the questions is “C#a” (where # is replaced by the number corresponding to the listed activity). The options for this question are YES (code of 1) and NO (code of 2).

- If the patient has recorded hours and/or minutes in the spaces provided, then answer YES (code of 1) in question C#a, to indicate that the patient participates in this activity.

- If the patient has circled or otherwise marked an activity to indicate that s/he participates in this activity, then answer YES (code of 1) in question C#a. If, in addition to marking that activity, the patient did not record hours and/or minutes that s/he participates in the activity, then record the hours (question C#b) and minutes (question C#c) as “Missing" (code of –9).

- If the patient has not recorded hours and/or minutes and has not otherwise marked an activity, then answer NO (code of 2) in question C#a, to indicate that the patient does not participate in this activity.

HALT-C Trial Q x Q

Analgesics Medications History – Risk Factors AS

Form # 141 Version B: 12/03/2001

Purpose of Form #141: The Analgesics Medications History Form #141records the patient's historic use of analgesic medications using a self-administered questionnaire.

When to complete Form #141: This form should be completed for all patients at the following study visits. Form #141 will be data entered at each clinical site.

- Lead-in patients: Baseline (W00).
- Express patients: Baseline (R00).

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date of the visit in MM/DD/YYYY format.

A5. Enter the initials of the person completing Section A of the form.

SECTION B: PRESCRIPTION ANALGESICS

- The patient should complete Section B by following the directions written on Form #141.

- If the patient is not able to complete Form #141 by her/himself, the interviewer may read the questions and answers to the patient and record the answers given by the patient on the form. If the interviewer completes the form in this manner, please note so in the margins of the form by writing "form completed by interviewer" with the initials of the interviewer.

- It is important that the patient complete all of the items on Form #141.
  - Review the form for any missing items.
  - Make sure that each item has only a single answer selected.
  - Please ask the patient to complete any missing or doubly marked items.

B1. The patient should circle one answer. If the patient answers NO (code of 2), then the form is complete, and the patient may stop here and return the form. If the patient answers YES (code of 1), then s/he should complete the rest of the form.

B2. For each prescription medicine medicine listed under B2, the patient should consider whether s/he has taken that medicine at least once a week over the last twelve months. For each medicine that s/he has taken at least once a week over the last twelve months, the patient should circle that medicine and circle the number to the right that best describes how often s/he has taken it. The patient does not need to make any marks for medicines that s/he has not taken at least once a week over the last twelve months (the patient may skip those medicines).

B3. For each non-prescription medicine listed under B3, the patient should consider whether s/he has taken that medicine at least once a week over the last twelve months. For each medicine that s/he has taken at least once a week over the last twelve months, the patient should circle that medicine and circle the number to the right that best describes how often s/he has taken it. The patient does not need to make any marks for medicines that s/he has not taken at least once a week over the last twelve months (the patient may skip those medicines).

Additional instructions for data entry:

Data entry personnel should note that there is an additional question in the electronic version of Form #141 in the Data Management System that does not appear on the paper copy of the form. For each medicine listed in Section B of the paper form, an additional question appears in the DMS asking the data enterer to record whether the patient replied that s/he has taken that medicine. For each medicine, the question is "B2x1" or "B3x1" (where x is replaced by the letter corresponding to the listed medicine). The options for this question are YES (code of 1) and NO (code of 2).

- If the patient has recorded how often they took the medicine, then answer YES (code of 1) in question B2x1 or B3x1, to indicate that the patient has taken this medicine.

- If the patient has circled or otherwise marked a medicine to indicate that s/he has taken it, then answer YES (code of 1) in question B2x1 or B3x1. If, in addition to marking that medicine, the patient did not record how often s/he took the medicine, then record the frequency (question B2x2 or B3x2) as "Missing" (code of –9).

- If the patient has not recorded a frequency and has not otherwise marked a medicine, then answer NO (code of 2) in question B2x1 or B3x1, to indicate that the patient did not take this medicine.

B4. For each medicine that the patient selected in Section B2 and B3, s/he should answer additional questions about in Section B4. The patient should fill in the name of the medicine in the space provided. Then s/he should select one of the four options listed. The answer should best describe how the amount the patient took of the medicine over the last twelve months compares to what s/he typically took over the last ten years.

    - The patient may report on up to four medicines.

    - For the first question that has **not** been answered (the patient has not written anything in the blank or circled one of the four answers), the data enterer should enter –1, for Not Applicable.

HALT-C Trial Q x Q

Cigarette Smoking History - Risk Factors AS

Form # 142 Version B: 12/03/2001

Purpose of Form #142: The purpose of the Cigarette Smoking History form is to determine how a patient's history of cigarette smoking influences the course of liver disease in persons with hepatitis C. This form records the patient's cigarette smoking history using a self-administered questionnaire.

When to complete Form #142: This form should be completed for all patients at the following study visits. Form #142 will be data entered at each clinical site.

- Lead-in patients: Week 8 (W08).
- Express patients: Month 9 (M09).

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date of the visit in MM/DD/YYYY format.

A5. Enter the initials of the person completing Section A of the form.

SECTION B: HISTORY OF CIGARETTE SMOKING

- The patient should complete section B by following the directions written on Form #142.

- All questions and answers refer only to cigarette smoking. Cigar and/or pipe smoking should not be considered when the patient is answering the questions. If the patient offers information on cigar and/or pipe smoking, this can be added as a form level comment.

- If the patient is not able to complete Form #142 by her/himself, the interviewer may read the questions and answers to the patient and record the answers given by the patient on the form. If the interviewer completes the form in this manner, please note so in the margins of the form by writing "form completed by interviewer" with the initials of the interviewer.

- It is important that the patient complete all of the items on Form #142.
  - Review the form for any missing items.
  - Make sure that each item has only a single answer selected.
  - Please ask the patient to complete any missing or doubly marked items.

B1. The patient should circle one answer. If the answer is NO, then the form is complete. The patient should stop and return the form. If the answer is YES, then s/he should continue to question B2.

B2. The patient should write in the age when s/he started smoking cigarettes in the space provided. If s/he has never smoked regularly or does not remember the age when smoking

cigarettes began, then s/he should circle the appropriate option. If the answer is I'VE NEVER SMOKED REGULARLY, then the form is complete. The patient should stop and return the form.

B3. The patient should circle one answer. If the answer is YES, then s/he should skip to question B6. If s/he answers NO, then s/he should continue to question B4.

B4. If the patient does not currently smoke cigarettes (answer to question B3 was NO), s/he should write in the age in the space provided when s/he quit smoking for the last time.

B5. If the patient does not currently smoke cigarettes (answer to question B3 was NO), s/he should circle one answer from the six choices provided. The form is complete. The patient should stop and return the form.

B6. If the patient currently smokes cigarettes (answer to question B3 was YES), s/he should circle one answer from the six choices provided. The form is complete. The patient should stop and return the form.

HALT-C Trial Q x Q

Current Cigarette Smoking - Risk Factors AS

Form # 143 Version A: 06/15/2000

Purpose of Form #143: The Current Cigarette Smoking form records the number of cigarettes the patient is currently smoking using a brief, self-administered questionnaire.

When to complete Form #143: This form should be completed at the Month 24 (M24) and Month 48 (M48) visit for all patients participating in the HALT-C Trial. Form #143 will be data entered at each clinical site.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date of the visit in MM/DD/YYYY format.

A5. Enter the initials of the person completing Section A of the form.

SECTION B: CURRENT CIGARETTE SMOKING

- The patient should complete section B by following the directions written on the form.

- All questions and answers refer only to cigarette smoking. Cigar and/or pipe smoking should not be considered when the patient is answering the questions. If the patient offers information on cigar and/or pipe smoking, this can be added as a form level comment.

- If the patient is not able to complete this form by her/himself, the interviewer may read the questions and answers to the patient and record the answers given by the patient on the form. If the interviewer completes the form in this manner, please note so in the margins of the form by writing "form completed by interviewer" with the initials of the interviewer.

- It is important that the patient complete all of the items on the form.
  - Review the form for any missing items.
  - Make sure that each item has only a single answer selected.
  - Please ask the patient to complete any missing or doubly marked items.

B1. The patient should circle one answer, YES or NO.

B2. The patient should circle one answer. If the answer is NO, then the form is complete. The patient should stop and return the form. If the patient answers YES, then s/he should continue to question B3.

B3. The patient should write down in the space provided the number of months s/he smoked cigarettes during the past twelve months.
- Note on data entry: If the patient reports months as fraction of a month, then round up.

B4. The patient should circle one answer from the six choices provided. The form is complete. The patient should stop and return the form.

HALT-C Trial Q x Q

Hormones and Women – Risk Factors AS

Form # 144 Version A: 06/15/2000 (Rev. 12/08/2003)

Purpose of Form #144: The Hormones and Women form uses patient interview format to record a female patient's history of pregnancy, history of contraception use, and history of hormone replacement medication. The purpose is to determine if female hormones and pregnancy affect the course of liver disease and hepatitis C.

When to complete Form #144: This form should be completed at Week 8 (W08) for all women in the Lead-in Phase, or at Month 9 (M09) for all women who entered the Trial as Express Patients. Form #144 is data entered at each clinical site.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date of the visit in MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

General Instructions for form: A calendar accompanies this form and may be used as a tool or worksheet to help the patient recall significant times in her life, and to help the patient remember her history of contraception use and hormone replacement therapy. This calendar is optional and should not be data entered.

Use the calendar as a memory probe to elicit the appropriate responses of hormone use, pregnancies, contraception use, and hormone replacement therapy. General probes for all questions would include tying the date to an event in the woman's life that may help her remember the year. For example, the woman does not remember when she started using birth control pills. Interviewer should probe "Do you remember what year in school you were?" The form asks you to pinpoint how old the woman was at the time.

The calendar starts with calculating the birth date of the woman, and then adding 8 years to the birth year and putting that year on the first line of the calendar. This was the year she turned from 7 to 8. Then write in every year until the current year. Record any event (i.e. such as bulleted items) as a reference date as appropriate or needed in order to obtain information on hormone use.
- Date of first menstrual period
- Date of first sexual intercourse
- End of pregnancies
- Date of marriages
- Date of divorces
- Date when stopped having monthly menstrual periods

If after appropriate probing, the patient cannot recall specific dates in her history of contraception use and hormone replacement therapy (i.e. she remembers the year but not the month of an event), **write, "don't know" or "DK" in the space provided** to enter a month.

SECTION B: HISTORY OF PREGNANCY

B1. If the answer is YES, circle 1 and continue to question B2. If the answer is NO, circle 2 and skip to question B3.

B2. Record how old the patient was at her first menstrual period using a two-digit number. Age under 10 should start with a 0.

B3. If the answer is YES, circle 1 and continue to question B4. If the answer is NO, circle 2 and skip to Section C.

B4. Record the number of times the patient was pregnant using a two-digit number. Any number under 10 should start with a 0. For example, 9 pregnancies would be recorded as 0 9.

B5a-c. For each time the patient was pregnant, ask questions B5a, B5b, and B5c. As you repeat the questions for each pregnancy, complete the table row by row for each pregnancy. For question B5a insert First Pregnancy, Second Pregnancy, etc. where you see [FIRST/NEXT].

If the answer to B5c is LIVE BIRTH, ask question B5d. If the answer to question B5c is Miscarriage, Abortion, or Still Birth, DO NOT ASK question B5d; skip to the next pregnancy. When all pregnancies have been completed, continue to Section C.

B5d. If the answer to question B5d is YES, circle 1 and continue to the next pregnancy. If the answer is NO, circle 2 and continue to the next pregnancy. When all pregnancies have been completed, continue to Section C.

SECTION C: HISTORY OF CONTRACEPTION USE

C1. If the answer is YES, circle 1 and continue to question C2a. If the answer is NO, circle 2 and skip to question C3.

C2a. For each time the patient used birth control pills, ask questions C2a and C2b. PROBE for each episode starting at age of first menstrual period and continue to PROBE for each episode. Record the date the patient began taking birth control pills in MM/YYYY format.

C2b. Answer if use of birth control pills is ongoing or has been discontinued. If use of birth control pills is ongoing, circle 1 and skip to question C3. If use of birth control pills has been discontinued, circle 2 and go on to question C2c.

C2c. Record the date the patient stopped using birth control pills in MM/YYYY format. When all episodes have been completed, continue to question C3.

C3. If the answer is YES, circle 1 and continue to question C4a. If the answer is NO, circle 2 and skip to question C5.

C4a. For each time the patient used birth control shots, ask questions C4a and C4b. PROBE for each episode starting at age of first menstrual period and continue to PROBE for each episode. Record the date the patient began using birth control shots in MM/YYYY format.

C4b. Answer if use of birth control shots is ongoing or has been discontinued. If use of birth control shots is ongoing, circle 1 and skip to question C5. If use of birth control shots has been discontinued, circle 2 and go on the question C4c.

C4c. Record the date the patient stopped using birth control shots in MM/YYYY format. When all episodes have been completed, continue to question C5.

C5. If the answer is YES, circle 1 and continue to question C6a. If answer is NO, circle 2 and skip to section D.

C6a. For each time the patient used birth control implants, ask questions C6a and C6b. PROBE for each episode starting at age of first menstrual period and continue to PROBE for each episode. Record the date the patient began using birth control implants in MM/YYYY format.

C6b. Answer if use of birth control pills is ongoing or has been discontinued. If use of birth control implants is ongoing, circle 1 and skip to Section D. If use of birth control implants has been discontinued, circle 2 and go on to question C6c.

C6c. Record the date the patient stopped using birth control implants in MM/YYYY format. When all episodes have been completed, continue to Section D.

SECTION D: HISTORY OF HORMONE REPLACEMENT

D1. If the answer is YES, circle 1 and skip to question D7. If the answer is NO, circle 2 and continue to question D2.

D2. Record the date of last menstrual period in MM/YYYY format.

D3. If the answer is THEY STOPPED NATURALLY, circle 1 and skip to question D7.

If the answer is THEY STOPPED AFTER A HYSTERECTOMY, circle 2 and continue to question D4.

If the answer is THEY STOPPED DUE TO ILLNESS OR MEDICATION, circle 3 and skip to question D7.

If the answer is BEGAN HORMONES BEFORE NATURAL PERIOD STOPPED, circle 4 and skip to question D7.

If the answer is HAVE NOT STARTED MENSTRUATING AFTER A RECENT PREGNANCY, circle 5 and skip to question D7.

If the answer is SOME OTHER REASON, circle 99. Specify the other reason. Skip to question D7.

D4. Record the date of hysterectomy using the MM/YYYY format.

D5. If the answer is YES, circle 1 and continue to question D6. If the answer is NO, circle 2 and skip to question D7. If the answer is DO NOT KNOW OVARIAN STATUS, circle -8 and skip to question D7.

D6. If ONE OVARY REMOVED, circle 1. If BOTH OVARIES REMOVED, circle 2. If unknown, circle –8.

D7. If the answer is NO, the form is complete. If the answer is YES, continue to question D8.

D8. For each time the patient used hormone replacement pills or patches, ask questions D8a, D8b, D8d, and D8f. PROBE for each episode starting at age of first menstrual period and continue to PROBE for each episode.

D8a. Record the date the patient began using hormone replacement pills or patches in MM/YYYY format.

D8b. If use of hormone replacement pills or patches is ONGOING, circle 1 and skip to question D8d. If use of hormone replacement pills or patches has been DISCONTINUED, circle 2 and continue to question D8c.

D8c. Record the date the patient stopped using hormone replacement pills or patches in MM/YYYY format.

D8d. Record the name of the hormone replacement pill or patch used.

D8e. Record Code from Hormone Code List after the interview is completed. This codebook is located in the HALT-C Trial Manual of Operations, Section K-7: Risk Factor Ancillary Study Appendix A.

D8f. Record the number of days the hormone replacement pills or patches were taken or worn during the episode. Continue to PROBE for each episode. When there are no more episodes, the form is complete.

HALT-C Trial Q x Q

Weight History - Risk Factors AS

Form # 146 Version B: 12/03/2001

Purpose of Form #146: The Weight History form collects information on the weight history of all patients enrolled in the HALT-C Trial using a brief, self-administered questionnaire.

When to complete Form #146: This form should be completed for all patients participating in the HALT-C Trial. For all Lead-in patients it should be completed at the Week 8 (W08) visit, and for all express patients at the Month 9 (M09) visit. Form #146 is data entered at each clinical site.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date of the visit in MM/DD/YYYY format.

A5. Enter the initials of the person completing Section A of the form.

SECTION B: WEIGHT HISTORY

- The patient should complete section B by following the directions written on the form.

- If the patient is not able to complete this form by her/himself, the interviewer may read the questions and answers to the patient and record the answers given by the patient on the form. If the interviewer completes the form in this manner, please note so in the margins of the form by writing "form completed by interviewer" with the initials of the interviewer.

- It is important that the patient complete all of the items on the form.
  - Review the form for any missing items.
  - Make sure that each item has only a single answer selected.
  - Please ask the patient to complete any missing or doubly marked items.

B1. The patient should write down in the space provided his/her weight in pounds at age 20.

If the patient is 20 years old, then the form is complete. The patient should stop and return the form.

If the patient is younger than 20 years, instruct the patient to enter his/her current weight. The form is complete. The patient should stop and return the form.

- Note on Data Entry: If the patient is younger than 20 years, enter a field level comment stating the patient's current age and weight.

B2. The patient should write down in the space provided his/her weight in pounds at age 40. If patient is younger than 40 years, s/he should skip this question and continue to question B3.

B3. The patient should record the weight in pounds of the most s/he weighed between age 20 and the present. For women, this weight does not include times when pregnant.

B3a. The patient should record the age in years when s/he first weighed the most in his/her lifetime. For women, this weight does not include times when pregnant.

B4. The patient should record the weight in pounds of the least the patient weighed between age 20 and the present. This weight should not include any time periods when the patient was ill.

B4a. The patient should record the age in years when s/he first weighed the least in his/her lifetime. The form is complete. The patient should stop and return the form.

HALT-C Trial Q x Q

Cortisol as a Serum Marker of Mood Status – Cognitive Effects AS

Form # 150 Version C: 05/12/2004

Purpose of Form #150: To record the collection and results of research assays of plasma cortisol in patients participating in the Cognitive Effects Ancillary Study.

When to complete Form #150: This form should be completed only at Site 18 (University of Michigan) for subjects participating in the ancillary study "Cognitive Effects of Long-term Peginterferon alfa-2a. Express patients are not eligible for the Cognitive Effects Ancillary Study.

Form #150 should be completed at the following study visits:

- **Lead-In Phase patients:** Baseline (W00), Week 4 (W04), and Week 24 (W24).
- **W20 Responder Phase patients:** Week 48 (W48) and Week 72 (W72).
- **Breakthrough/Relapser patients:** Randomization visit (R00) if it is more than one month after the most recent Neuropsychiatric Testing (Form #152).
- **Randomized patients**: Month 12 (M12), Month 24 (M24), Month 36 (M36), Month 48 (M48), and Month 54 (M54).

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed using MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

Patient Preparation

In order to obtain valid data, it is imperative that patients be properly prepared for sample collection. Patient preparation includes:

1. Instruct patients receiving Pegasys™ to take their medication dose at least **2 days** prior to blood collection.
2. All patients should have blood drawn between 8:00 AM and 10:00 AM.
3. All patients should fast from 12:00 midnight on the evening before blood sample collection.

Sample processing- Plasma Cortisol

1. Draw 7 ml of blood into a green topped (heparinized) tube and keep on ice during processing.

2. Immediately centrifuge at 3000 rpm x 15 minutes.

3. Aliquot the 3 ml of plasma into 3 separate 1.0 ml screw topped storage tubes and freeze at –80° C within 1 hour of sample collection.

SECTION B: SAMPLE COLLECTION AND FASTING INFORMATION

B1. Record the date when the blood sample was collected using MM/DD/YYYY format.

B2. Record the time of day when the blood sample was collected. Circle 1 for AM or 2 for PM.

B3. Record the date when the when the patient reported he or she last ate or drank (other than water) using MM/DD/YYYY format.

B4. Record the time of day when the patient reported he or she last ate or drank (other than water). Circle 1 for AM or 2 for PM.

B5. Record the date at which the last dose of Peginterferon alfa-2a was administered in MM/DD/YYYY format.

SECTION C: ASSAY RESULTS

Plasma cortisol levels will be assayed in batches at the University of Michigan and data entered when results become available.

C1. Record the results of plasma cortisol levels in ug/dL. The field allows three numbers before the decimal point. One number **must** be entered after the decimal point.

The normal range of plasma cortisol levels is 001.0 to 999.0 ug/dL. If the result falls outside of this range, please verify the result against the source documentation. If the abnormal result is correct, select the override button. Specify that the data was verified and is correct.

HALT-C Trial Q x Q

Shipley Institute of Living – Cognitive Effects AS

Form # 151 Version A: 06/15/2000

Purpose of Form #151: To record the results of the Shipley Institute of Living Scale assessing cognitive function in patients participating in the Cognitive Effects Ancillary Study.

When to complete Form #151 This form should be completed only at Site 17 (University of Southern California) and Site 18 (University of Michigan) as part of the Cognitive Effects of Long-term Peginterferon alfa-2a Ancillary Study. Express patients are not eligible for the Cognitive Effects Ancillary Study.

The Shipley Institute of Living Scale will be administered once to Lead-In patients at Baseline (W00) who have consented to participate in this Ancillary Study.

A neuropsychology technician (NPT) will administer the Shipley Institute of Living Scale at the W00 visit in conjunction with the battery of neuropsychiatric tests. The NPT will score the Shipley Scale. Dr. Carla Back-Madruga (Site 17) and Dr. Linas Bieulauskas at (Site 18) will review the scoring.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. The visit number, W00, is pre-printed on the form and does not require data entry.

A4. Record the date the test was administered using MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

A6. Enter the initials of the Neuropsychologist reviewing the form.

SECTION B: SHIPLEY TEST RESULTS

B1. Enter the date the Shipley Institute of Living Scale test was administered in MM/DD/YYYY format.

B2. Conceptual Quotient: Enter the patient's score within the acceptable range of 44 to 178.

B3. Abstraction Quotient: Enter the patient's score within the acceptable range of 26 to 174.

B4. Intelligence Quotient: Enter the patient's score within the acceptable range of 34 to 139.

HALT-C Trial Q x Q

Neuropsychiatric Test Results – Cognitive Effects AS

Form # 152 Version B: 07/16/2001

Purpose of Form #152: To record the results of the battery of neuropsychiatric tests assessing cognitive function in patients participating in the Cognitive Effects Ancillary Study.

When to complete Form #152: This form should be completed only at Site 17 (University of Southern California) and Site 18 (University of Michigan) as part of the Cognitive Effects of Long-term Peginterferon alfa-2a Ancillary Study. Express patients are not eligible for the Cognitive Effects Ancillary Study.

Form #152 should be completed at the following study visits:

- **Lead-In Phase patients:** Baseline (W00) and Week 24 (W24).
- **W20 Responder Phase patients:** Week 48 (W48) and Week 72 (W72).
- **Breakthrough/Relapser patients:** Randomization visit (R00) if it is more than one month after the most recent Neuropsychiatric Testing (Form #152).
- **Randomized patients**: Month 12 (M12), Month 24 (M24), Month 36 (M36), Month 48 (M48), and Month 54 (M54).

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed using MM/DD/YYYY format.

A5. Enter the initials of the Neuropsychologist who scored and reviewed the form.

Neuropsychiatric Test Administration

1. A battery of neuropsychiatric tests will be administered to all study participants at Site 18 (University of Michigan) and Site 17 (University of Southern California) to assess serial changes in cognitive function over time.

2. The full battery of neuropsychiatric tests should take approximately 60 minutes to complete.

3. A neuropsychiatry technician (NPT) will administer the battery of neuropsychiatric tests. The NPT will score the neuropsychiatric tests. Dr. Carla Back-Madruga (Site 17) and Dr. Linas Bieulauskas at (Site 18) will review the scoring.

4. Neuropsychiatric tests will be administered in the order listed on the scoring sheet using standardized written instructions per the test manuals.

5. Patients will be asked to refrain from taking medications known to adversely influence cognitive function for 48 hours before testing (e.g. sleeping pills, anti-histamines, etc).

Neuropsychiatric Test Scores

All test scores are recorded as integers except for the Selective Reminding Test and the Continuous Visual Memory Test d-Prime scores, which have two digits after the decimal point. Note that each test has a defined range of possible values pre-printed on Form #152.

Calculation of Standard Scores

- Calculate Standard Scores (SS) for each representative variable according to raw scores and means and standard deviations using the given calculations. The tables used for Standard Score calculations follow the information for each test.
- Standard scores for reaction times will not be obtained at this time.
- X = raw scores on specified items from Form #152.

SECTION B: NEUROPSYCHIATRIC TEST SCORES

B1. Enter the date the neuropsychiatric tests were administered in MM/DD/YYYY format.

B2. **Selective Reminding Test**

- Record the score for questions B2a through B2j.
- Note that the d-Prime test has a range that includes negative numbers. You must record either + or – when completing question B2g.
- Question B2k: calculate and record the Standard Score using the formula below.

Recall = Item B2a

$$SS = \frac{(x^* - \text{mean for age})\ (10)}{\text{SD for age}} + 50$$

*x+5 for males

Table B2 - Selective Reminding Test Normative Data

	Age Groups						
Variables	18-29	30-39	40-49	50-59	60-69	70-79	80-91
Recall							
Mean	128.18	124.59	125.03	121.62	114.82	105.27	97.96
SD	9.16	13.40	12.00	10.46	15.77	16.67	17.49
LTR							
Mean	122.16	118.14	118.55	112.71	101.52	89.95	77.22
SD	13.12	20.64	17.95	16.10	24.68	29.23	26.26
STR							
Mean	6.14	6.72	6.48	8.96	13.52	17.47	20.74
SD	4.82	7.59	6.72	6.40	9.52	10.47	9.62
LTS							
Mean	124.00	121.62	122.45	116.67	107.00	95.54	87.48
SD	10.47	18.36	15.64	14.52	21.79	24.86	25.26
CLTR							
Mean	115.12	107.93	107.10	101.50	88.92	69.68	54.96
SD	19.67	27.62	26.62	22.39	35.85	38.96	29.04

B3. **Continuous Visual Memory Test**

- Record the score for questions B3a through B3f.
- Note that the d-Prime test has a range that includes negative numbers. You must record either + or – when completing question B3c.
- Question B3g: calculate and record the Standard Score using the formula below.

Total score = Item B3d

$$SS = \frac{(x^* - \text{mean for age})\ (10)}{\text{SD for age}} + 50$$

Table B3- Continuous Visual Memory Test Normative Data

Age	Mean Total Score	SD
18-29	82.07	4.05
30-49	79.03	4.78
50-69	75.00	5.50
70+	74.50	5.32

B4. **Digit Span**

- Record the score for questions B4a through B4d.
- Questions B4e and B4f: calculate and record the Standard Scores using the formulas below.

Digits Forward = Item B4a

$$SS = \frac{(x - \text{mean for age})\ (10)}{\text{SD for age}} + 50$$

Digits Backward = Item B4b

$$SS = \frac{(x - \text{mean for age})\ (10)}{\text{SD for age}} + 50$$

Table B4 - Normative Data for Digits Forward and Digits Backward

Age	16-17		18-19		20-24		25-29		30-34	
	Forward	Back	Forward	Back	Forward	Back	Forward	Back	Forward	Back
Mean	6.72	4.88	6.66	5.04	6.80	5.10	6.68	5.04	6.61	4.87
SD	1.32	1.44	1.34	1.46	1.27	1.51	1.35	1.63	1.35	1.44

Age	35-44		45-54		55-64		65-69		70-74	
	Forward	Back	Forward	Back	Forward	Back	Forward	Back	Forward	Back
Mean	6.63	4.93	6.57	4.79	6.35	4.55	6.28	4.48	6.14	4.40
SD	1.31	1.49	1.38	1.42	1.45	1.56	1.42	1.44	1.39	1.16

Age	75-79		80-84		85-89		All Ages	
	Forward	Back	Forward	Back	Forward	Back	Forward	Back
Mean	6.06	4.31	5.89	4.25	5.69	4.10	6.43	4.70
SD	1.26	1.17	1.26	1.03	1.01	1.05	1.36	1.43

Note: For further information pertaining to the sample size for these tests, refer to the WAIS-III manual.

B5. **Digit Symbol**

- Record the score for questions B5a and B5b.
- Question B5c: calculate and record the Standard Score using the formula below.

Digit symbol= Item B5a

$$SS = \frac{(x - \text{mean for age})\ (10)}{\text{SD for age}} + 50$$

Table B5 - Normative Data for Digit Symbol

Age	Mean	SD
18-19	81	16
20-24	80	16.25
25-29	78	15.5
30-34	77	16
35-44	75	16.5
45-54	70	15.25
55-64	61	15
65-69	54	15
70-74	51	14.75
75-79	47	14.5

B6. **Serial Digit Learning**

- Record the score for question B6a.
- Question B6b: calculate and record the Standard Score using the formula below.

Serial digit learning

$$SS = \frac{(x\text{-mean for age/education})\ (10)}{\text{SD for age/education}} + 50$$

Table B6 - Normative Data for Serial Digit Learning

Education = 6-11		Education = 12-16	
age: 16-64	age: 65-74	age: 16-64	age: 65-74
Mean = 18	Mean = 14	Mean = 20	Mean = 20
SD = 4	SD = 5.5	SD = 4	SD = 7

B7. **Simple reaction Time**

- Record the time in milliseconds.

B8. **Choice Reaction Time**

- Record the time in milliseconds.

B9. **Trail Making Test A**

- Record the number of seconds required to complete the test for question B9a.
- Record the number of errors for question B9b.

- Question B9c: calculate and record the Standard Score using the formula below.

  Trails A= Item B9a

  $$SS = \frac{(\text{mean for age-x})\ (10)}{\text{SD for age}} + 50$$

Table B9 - Normative Data for Trail Making Test A

Age	n	Mean	SD	Range
15-17	32	23.4	5.9	15.2-39
18-23	78	36.7	9.4	12-60.1
24-32	57	24.3	7.6	11.8-46
33-40	18	27.5	8.3	16-52.7
41-64	10	29.7	8.4	16.5-42

Note: If the individual is over 64 years of age, then use the means from the 41-64 age group.

B10. **Trail Making Test B**

- Record the number of seconds required to complete the test for question B10a.
- Record the number of errors for question B10b.
- Question B10c: calculate and record the Standard Score using the formula below.

  Trails B = Item B10a

  $$SS = \frac{(\text{mean for age-x})\ (10)}{\text{SD for age}} + 50$$

Table B9 - Normative Data for Trail Making Test B

Age	n	Mean	SD	Range
15-17	32	47.7	10.4	25.4-81
18-23	78	51.3	14.6	23.3-101
24-32	57	53.2	15.6	29.1-98
33-40	18	62.1	17.5	39-111
41-64	10	73.6	19.4	41.9-102

Note: If the individual is over 64 years of age, then use the means from the 41-64 age group.

B11. **Finger tapping test**

- Record the number of taps for the dominant hand for question B11a.
- Record the number of taps for the non-dominant hand for question B11b.
- Questions B11c and B11d: calculate and record the Standard Scores using the formulas below.

  Dominant = Item B11a

  $$SS = \frac{(x - \text{mean for age/gender})\ \ (10)}{\text{SD for age/gender}} + 50$$

  Non-dominant = Item B11b

  $$SS = \frac{(x - \text{mean for age/gender})\ \ (10)}{\text{SD for age/gender}} + 50$$

Table B11 - Normative Data for Finger Tapping test

Males		Preferred Hand			Non-preferred Hand		
Age	n	Mean	SD	Range	Mean	SD	Range
15-17	17	47.6	5.8	38-55.6	43.6	4.9	33.4-51.8
18-23	44	49.5	6.9	26.6-64.6	45.4	6.9	26.8-58.6
24-32	31	50.6	6.6	38.2-66.2	46	6.1	28.8-55
33-40	12	53.4	5.9	39-61	49.8	4.7	41-57.8
41-64	4	44.4	5.8	35.8-48.2	41.4	3.5	36.6-44.4

Females		Preferred Hand			Non-preferred Hand		
Age	n	Mean	SD	Range	Mean	SD	Range
15-17	15	42.7	7.9	30.2-54	41.1	6.2	31.6-51
18-23	30	43.6	7.5	30.6-65.6	41.2	6.5	32.8-61.8
24-32	25	45.2	6.7	31-60	40.9	5.7	28.6-53.6
33-40	6	45.8	5.5	40.6-55.6	44.3	4.6	40.6-53.2
41-64	6	40.4	4.8	34.2-48.4	38.6	4.8	32-46.6

Note: For both of the proceeding tables, if the individual is over 64 years of age, then use the means from the 41-64 age group.

B12. **Wisconsin Card Sorting Test**

- Record the score for questions B12a through B12e.
- Question B12f: calculate and record the Standard Score using the formula below.

(WCST) = Item B12a

$$SS = \frac{(\text{mean for age} - x)\ \ (10)}{\text{SD for age}} + 50$$

Table B12 – Normative Data for Wisconsin Card Sorting Test Variables

	< 40 years (n=100)	40-49 years (n=19)	50-59 years (n=16)	> 59 years (n=15)
Full Scale IQ	113.9 (11.7)	112.4 (13.4)	120.3 (9.4)	109.7 (9.9)
Categories Achieved	5.6 (1.0)	4.8 (1.8)	5.6 (1.1)	4.2 (2.0)
Total Errors	21.6 (16.7)	31 (27)	20.9 (12.8)	44.1 (18.9)
Perseverative Errors	10.4 (8)	16 (13.9)	11.3 (6.9)	24.2 (12.8)
% Perseverative Errors	10.2 (5.6)	14.2 (9.6)	11.2 (4.6)	19.6 (9.2)
Nonperseverative Errors	11.2 (11.1)	15.1 (15)	9.6 (6.2)	19.9 (9.1)
Perseverative Responses	13 (9.1)	19.5 (14.9)	14.8 (9.0)	28.9 (13.7)
Trials to 1st Category	12.4 (4.7)	18 (26.7)	12.9 (5.2)	14.3 (7.0
% Conceptual Level Responses	72.8 (14.4)	64.4 (24)	70.7 (13.2)	50 (17)
"Learning to Learn"	-2.4 (4.9)	-5.9 (8.5)	-0.9 (2.0)	-5.7 (8.8)
Failures to Maintain Set	0.8 (1.3)	0.8 (1.5)	0.8 (1.1)	1.0 (1.3)

Note: Data presented as mean (SD)

B13. **Controlled Oral Word Association Test**

- Record the score for question B13a.
- Question B13b: calculate and record the Standard Score using the formula below.

(COWAT) = Item B13a

A. Adjust raw score for age and education
   1. If the raw score is greater than or equal to 10, add the appropriate value from Table 8 (x = raw score + value from Table 8).
   2. If the raw score is less than 10 no adjustment is needed to the raw score (x = raw score)

B. $SS = \frac{(x - 37.5)\quad (10)}{10.75} + 50$

Table B13 - Normative Data for Controlled Oral Word Association test

Education (years completed)	Age					
	25-54		55-59		60-64	
	Male	Fem	Male	Fem	Male	Fem
Less than 9	9	8	11	10	14	12
9-11	6	5	7	7	9	9
12-15	4	3	5	4	7	6
16 or more	-	-	1	1	3	3

Note: If the individual is over 64 years of age, then use the means from the 60-64 age group.

HALT-C Trial Q x Q

CIDI-12 – Cognitive Effects AS

Form # 153 Version A: 06/15/2000 (Rev. 05/28/2002)

Purpose of Form #153: To identify recent psychiatric diagnoses using the CIDI-12 Auto 2.1 modules of DEMOGRAPHICS (A), ANXIETY (D), and DEPRESSION (E), in patients participating in the Cognitive Effects Ancillary Study.

When to complete Form #153: This form should be completed only at Site 17 (University of Southern California) and Site 18 (University of Michigan) as part of the Cognitive Effects of Long-term Peginterferon alfa-2a Ancillary Study. Express patients are not eligible for the Cognitive Effects Ancillary Study.

Form #153 should be completed after the 12-month version of the CIDI-12 Auto 2.1 program has been administered to study participants. Form #153 should be completed at the following study visits:

- **Lead-In Phase patients:** Week 24 (W24).
- **W20 Responder Phase patients:** Week 48 (W48) and Week 72 (W72).
- **Breakthrough/Relapser patients:** Randomization visit (R00) if it is more than one month after the most recent Neuropsychiatric Testing (Form #152).
- **Randomized patients**: Month 12 (M12), Month 24 (M24), Month 36 (M36), Month 48 (M48), and Month 54 (M54).

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed using MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: CIDI-12

Administer the CIDI-12 Auto 2.1 12-month computerized interview per training manual and Manual of Operations instructions. Print out a hard copy of the patient's raw data from the file R[idnumber].ALL and store in patient notebook. Print out a hard copy of diagnostic data from the file R[idnumber].SCS and complete B1 through B7.

B1. Record the date the CIDI-12 test was administered in MM/DD/YYYY format.

B2. Record the seven-digit ID Code as follows:
- The first digit starting at the left is a visit number as follows:
  W24 = 1, M12 = 2, M24 = 3, M36 = 4, M48 = 5, M54 = 6, W48 = 7, W72 = 8, R00 = 9
- The last six digits are the patient ID number.

B3. If the CIDI-12 was self-administered by the RESPONDENT, circle 1. If the INTERVIEWER administered the CIDI –12, circle 2.

B4. If the CIDI-12 English version was administered, circle 1. If the CIDI-12 was administered in Spanish, circle 2.

B5. If a subject has any DSM-IV diagnoses printed on the hard copy of file R[idnumber].SCS then circle 1 for YES and continue to B6. If there are no DSM-IV diagnoses listed, then circle 2 for NO. The form is complete.

B6. Enter the number of DSM-IV diagnoses listed on the hard copy of file R[idnumber].SCS.

B7. CIDI-12 DSM-IV Diagnoses

This section provides important detailed information regarding the DSM-IV diagnoses generated from the CIDI-12 interview. All of the required information can be obtained from the file R[idnumber].SCS. Please note that the hard copy will have DSM-IV and ICD10 diagnostic scores printed. The DSM-IV will be only digits (e.g. 393.54) The ICD10 diagnostic score will start with a letter followed by digits (e.g. F41.0). Record **ONLY** the DSM-IV diagnostic score. Complete one row for each DSM-IV diagnosis present in the scoring file.

B7a. DSM-IV 5-digit diagnostic code: Enter the five-digit DSM-IV code in this field.
- If a listed code only has four digits, add a zero to the right side of the decimal point. (e.g. 300.4 = Dysthymia would be entered as 300.40)

B7b. Diagnostic criteria met: Enter one of the following one-digit codes for diagnostic criteria.
0 = Indeterminate diagnosis
1 = Criteria for diagnosis not met
3 = The positive criteria for diagnosis are met but exclusion criteria not met
5 = All diagnostic criteria are fulfilled

B7c. Onset code: Enter one of the following one-digit codes identifying the diagnosis onset.
1 = within last 2 weeks
2 = 2 weeks to less than 1 month ago
3 = 1 month to less than 6 months ago
4 = 6 months to less than 1 year ago
5 = in the last 12 months, don't know when
6 = more than 1 year ago

B7d. Age of onset: If B7c onset is coded other than 0, enter the two-digit age of onset.

B7e. Recency code: Enter one of the following one-digit codes identifying recency of the diagnosis.
1 = within last 2 weeks
2 = 2 weeks to less than 1 month ago
3 = 1 month to less than 6 months ago
4 = 6 months to less than 1 year ago
5 = in the last 12 months, don't know when
6 = more than 1 year ago

B7f. Age of recency: If B7e is coded other than 0, enter the two-digit age of diagnosis recency.

B7g. DSM-IV diagnosis text: Type the DSM-IV diagnosis verbatim in this field.

HALT-C Trial Q x Q

Brief Symptom Inventory (BSI) – Cognitive Effects AS

Form # 154 Version B: 07/16/2001

Purpose of Form #154: To record Brief Symptom Inventory (BSI) symptom and summary scale scores in patients participating in the Cognitive Effects Ancillary Study.

When to complete Form #154: This form should be completed only at Site 17 (University of Southern California) and Site 18 (University of Michigan) as part of the Cognitive Effects of Long-term Peginterferon alfa-2a Ancillary Study. Express patients are not eligible for the Cognitive Effects Ancillary Study.

Form #154 should be completed at the following study visits:

- **Lead-In Phase patients:** Baseline (W00), Week 4 (W04), and Week 24 (W24).
- **W20 Responder Phase patients:** Week 48 (W48) and Week 72 (W72).
- **Breakthrough/Relapser patients:** Randomization visit (R00) if it is more than one month after the most recent Neuropsychiatric Testing (Form #152).
- **Randomized patients**: Month 12 (M12), Month 18 (M18), Month 24 (M24), Month 30 (M30), Month 36 (M36), Month 42 (M42), Month 48 (M48), and Month 54 (M54).

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed using MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

Brief Symptom Inventory Administration

The BSI is a brief (approximately 5 - 10 minutes) 53-item self-administered questionnaire with established reliability and validity, designed to assess emotional distress in medical and psychiatric patients. Patients should complete each item using the five-point rating scale of 0 to 4 (0= Not at all, 4 = Extremely).

Brief Symptom Inventory Scoring

- The raw data from the respondent's answer sheet will be entered into the BSI scoring software (MICROTEST Q Assessment System Software) per manufacturer's instructions.

- The BSI software generates nine symptom scales (e.g. Depression, Anxiety, Somatization) and three summary scales (Global Severity Index (GSI), Positive Symptom Distress Index (PSDI), and Positive Symptom Total (PST)).

- For study purposes, T-scores will be used which have a mean value of 50 with a standard deviation of 10, and a range of 0-100.

- A Profile Report containing a graphic profile of the raw and normalized T-scores for all nine symptom scales and three summary scales will be generated.

- If a patient provides the same response to all 53 items of the BSI, the computer software will not generate a Clinical Profile Report. Under those circumstances, change the response to item #1 by lowering it one value (i.e. 2 to 1) and then a Clinical Profile Report can be generated. In addition, enter a field level comment indicating that data has been changed in order to generate a report.

- A hard copy of each Profile Report will be kept in the patient's notebook.

SECTION B: BRIEF SYMPTOM INVENTORY – PROFILE REPORTS

B1. Enter the date the BSI was administered using MM/DD/YYYY format.

B2. Enter the T-score for each symptom and summary scale from the Profile Report under in rows B2a through B2l using the non-patient norms.

- Three-digit entry is provided for each scale. Record a single zero to the left of a two-digit T score (e.g. 50= 050). Record two zeros to the left of a one-digit T-score when entering the data (e.g. 3 = 003).

HALT-C Trial Q x Q

Cognitive Effects AS Withdrawal Form

Form #155 Version A: 06/15/2000 (Rev. 07/03/2002)

Purpose of Form #155: The Cognitive Effects Withdrawal form documents that patients have withdrawn from the Cognitive Effects Ancillary Study and the reason(s) for patient withdrawal. Data entry of this form removes the expectancy of study forms from future visits in the Data Management System (DMS).

When to complete Form #155: This form should be completed upon withdrawal of a patient from the Cognitive Effects Ancillary Study. Form #155 can be added to any study visit by clicking on the "Additional Forms" button on the study visit screen. This form should be completed when a patient withdraws consent, is no longer at Site 17 (University of Southern California) or Site 18(University of Michigan), or if other problems are encountered during data or sample collection.

If all of the required samples for the study are collected at the first few visits (S00 and W00), the patient is eligible for the Cognitive Effects Ancillary Study. Patients may decide at a later date to withdraw from this Ancillary Study. However, if samples are missed at initial visits, they are ineligible and require a Form #155.

Express patients were not eligible for the Cognitive Effects Ancillary Study and do not require Form #155.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit or the most recent study visit.

A4. Record the date the form was completed in MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: WITHDRAWAL INFORMATION

B1. Record the date that the patient withdrew from the Cognitive Effects Ancillary Study in MM/DD/YYYY format. If you do not know the exact date that the patient withdrew from the study, then record the date the patient was last seen or the date you last had telephone contact with the patient.

B2. Circle the one primary reason why the patient withdrew from the Cognitive Effects Ancillary Study. If the reason is not listed, circle "Other" and specify a reason is (sixty characters including spaces and punctuation are available).

B3. Please enter any additional information regarding the patient's withdrawal from this study (four hundred characters including spaces and punctuation are available).

Data entry note: If there is no additional information recorded in B3, data enter -1. The form is complete.

HALT-C Trial Q x Q

Serotonin as a Serum Marker of Mood Status – Cognitive Effects AS

Form # 156 Version B: 05/12/2004 (Rev. 09/23/2004)

Purpose of Form #156: To record the collection and results of research assays of plasma cortisol and whole blood serotonin in randomized patients, W20 responders, and Breakthrough/Relapsers.

When to complete Form #156: This form should be completed only at Site 18 (University of Michigan) as part of the Cognitive Effects of Long-term Peginterferon alfa-2a Ancillary Study.

Form #156 should be completed for the following study visits:

- **Lead-In Phase patients:** Baseline (W00), Week 4 (W04), and Week 24 (W24).
- **W20 Responder Phase patients:** Week 48 (W48) and Week 72 (W72).
- **Breakthrough/Relapser patients:** Randomization visit (R00) if it is more than one month after the most recent Neuropsychiatric Testing (Form #152).
- **Randomized patients**: Month 12 (M12), Month 24 (M24), Month 36 (M36), Month 48 (M48), and Month 54 (M54).

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed using the MM/DD/YYYY format

A5. Enter the initials of the person completing the form.

Patient Preparation

In order to obtain valid data, it is imperative that patients be properly prepared for sample collection. Patient preparation includes:

1. Instruct patients receiving Pegasys™ to take their medication dose at least **2 days** prior to blood collection.
2. All patients should have blood drawn between 08:00 AM and 10:00 AM.
3. All patients should fast from 12:00 midnight on the evening before blood sample collection.

Sample processing- Whole Blood Serotonin

1. Draw 10 ml of blood into a purple-topped tube and keep on ice during processing.

2. Mix well 5 times.

3. Aliquot 3 ml of the whole blood into 3 separate screw topped storage tubes and freeze at –80° C within 1 hour of sample collection.

SECTION B: SAMPLE COLLECTION AND FASTING INFORMATION

B1. Record the date when the blood sample was collected using MM/DD/YYYY format.

B2. Record the time of day when the blood sample was collected. Circle 1 for AM or 2 for PM.

B3. Record the date when the when the patient reported he or she last ate or drank (other than water) using MM/DD/YYYY format.

B4. Record the time of day when the patient reported he or she last ate or drank (other than water). Circle 1 for AM or 2 for PM.

B5. Record the date at which the last dose of Peginterferon alfa-2a was administered in MM/DD/YYYY format.

SECTION C: ASSAY RESULTS

Whole blood serotonin levels will be assayed in batches at the University of Michigan and data entered when results become available.

C1. Record the results of whole blood serotonin levels in nmol/L. The field allows three numbers.

The normal range of whole blood serotonin levels is 010 to 999 nmol/L. If the result falls outside of this range, please verify the result against the source documentation. If the abnormal result is correct, select the override button. Specify that the data was verified and is correct.

HALT-C Trial Q x Q

Years of Education – Cognitive Effects AS

Form #157 Version A: 06/15/2000

Purpose of Form #157: The purpose of the Years of Education form is to determine the highest degree or level of school education completed by patients participating in the Cognitive Effects Ancillary Study.

When to complete Form #157: This form should be completed only at Site 17 (University of Southern California) and Site 18 (University of Michigan) as part of the ancillary study "Cognitive effects of long-term Peginterferon alfa-2a." The form should be completed with information concurrent to the patient's Baseline (W00) study visit.

Since these forms will be completed after the Baseline visit has occurred, please data enter this form under the W00 visit. The date the form is completed will be at a later date than the actual baseline visit.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the W00 code for Baseline Visit.

A4. Record the date the form was completed using the MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: PATIENT INTERVIEW

Note: Information in Section B should be collected by patient interview

B1. The interviewer reads the whole question to the patient: "What is the highest degree or level of school you have completed?"
- The interviewer circles the number that most closely corresponds to the answer from the patient. Probing is allowed if the answer is unclear.
- The number circled should correspond to the previous grade or highest degree the patient has completed of formal education. The term formal education means years of schooling - or years of education in the classroom.
- If the patient has received a GED, circle only the highest grade of formal education the patient completed.
- If the patient has been home schooled, circle the highest grade achieved in the home schooling curriculum as defined by state law.

HALT-C Trial Q x Q

Occupational Status – Cognitive Effects AS

Form #158 Version A: 07/29/2003

Purpose of Form #158: The purpose of the Occupational Status form is to determine the occupational status at the time of the Baseline visit (W00) of patients participating in the Cognitive Effects Ancillary Study.

When to complete Form #158: This form should be completed for all patients who participated in the Cognitive Effects Ancillary Study at Site 17 (University of Southern California) and Site 18 UMICH).

Since these forms will be completed after the W00 visit has occurred, please data enter this form under the W00 visit. The date the form is completed will be later than the actual baseline visit.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. The W00 code for Baseline Visit is pre-printed on the form and is programmed into the DMS.

A4. Record the date the form was completed in MM/DD/YYYY format.

A5. Enter the initials of the person completing Sections A and B of the form.

A6. Enter the initials of the neuropsychologist completing Section C of the form.

SECTION B: PATIENT INTERVIEW

Note: Information in Section B should be collected by chart review (medical records, or neuropsychiatric test records) or by patient interview (in-person or telephone).

B1. Review the completed baseline Form #45: Life Events Status Interview information on the patient's baseline work situation. This information is available in the patient's HALT-C chart, on the HALT-C DMS, or from a data report prepared by the DCC.

- Circle the number that corresponds to the most appropriate answer at the time of the Baseline visit.
- If the patient was working part-time or full-time at baseline, circle #1, then continue on to B2.
- If the patient was full-time homemaker or kept house full-time at baseline, circle #1, then continue on to B2.
- If the patient was not working part-time or full-time at baseline, circle #2, then go to question B3.

B2. Review information on the patient's baseline work situation. This information may be available in the patient's HALT-C chart, on documents collected at the time of baseline neuropsychiatric testing, or from the computerized neuropsychiatric testing data.

- In the space provided, write the patient's occupation at the time of the Baseline visit. The maximum number of characters that can be used is 200.
- For example, occupation might be "registered nurse", "auto mechanic", "accountant" or "truck driver".

B3. Review the completed baseline Form #45: Life Events Status Interview information on the patient's baseline work situation. This information is available in the patient's HALT-C chart, on the HALT-C DMS, or from a data report prepared by the DCC.

- For patients who were not working part-time or full-time, circle the number that corresponds to the most appropriate answer at the time of the Baseline visit.
- If the patient was going to school full-time, circle #1, then continue on to question B4.
- If the patient was retired, circle #2, then continue on to question B4.
- If the patient was unemployed, circle #3, then continue on to question B4.
- If the patient was unable to work because of illness or disability, circle #4, then continue on to question B4.

B4. Review information available in the patient's HALT-C chart, on the HALT-C DMS, or from a data report prepared by the DCC. If this information is not available, the patient must be interviewed (in-person or by telephone).

- Circle the number that corresponds to the most appropriate answer at the time of the Baseline visit.
- If the patient had not been working part-time or full-time for less than ten years, circle #1, then continue on to B5.
- If the patient had not been not working part-time or full-time for ten or more years, circle #2, then go to question C1.
- The number circled should correspond to the patient’s employment status at the time of the Baseline visit (W00).

B5. This question should be read to the patient only if the answer to B4 was #1. This can be collected by in-person or telephone interview.

- In the space provided, write the kind of work the patient reports doing at the time of the Baseline visit. The maximum number of characters that can be used is 200.
- For example, the answer might be "registered nurse", "auto mechanic", "accountant" or "truck driver".

B6. This question should be read to the patient only if the answer to B4 was #1. This can be collected by in-person or telephone interview.

- In the space provided, write the most important activities or duties that the patient reports doing at the time of the Baseline visit. The maximum number of characters that can be used is 200.
- For example, the answer might be "patient care", "repairing automobiles", "reconciling financial records" or "delivering merchandise to Kmart".

C1. The neuropsychologist at the site must complete the information for this question.

If a neuropsychologist previously scored occupation category for the patient's baseline occupation and the source document with the score is in the patient's chart, use this information to complete question C1. If the occupation category has not been scored previously or a source document is not available, question C1 must be completed by a neuropsychologist.

- Circle the number that corresponds to the most appropriate answer at the time of the Baseline visit.
- The number circled should correspond to the patient's employment status at the time of the Baseline visit (W00).

HALT-C Trial Q x Q

Scoring Sheet for Baseline NPT Batteries

Clinician Impairment Ratings: Cognitive Effects AS

Form # 159 Version A: 07/29/2003

Purpose of Form #159: The purpose of this scoring form is to determine the clinician impairment ratings of the patients at baseline visit (W00). It is used as a Scoring Sheet for Baseline NPT Batteries. This form is filled out by the neuropsychologists at site 17 USC and site 18 UMICH.

When to complete Form #159: The form should be completed for all the patients participating in the Cognitive Effects Ancillary Study from Site 17 (University of Southern California) and Site 18 (University of Michigan). After completion, the original Form #159 should be sent to the DCC to be data entered. A photocopy of the form may be filed in the patient's notebook.

Although this form will be completed after the W00 visit has occurred, please data enter this form under the W00 visit. The date the form is completed will be later than the actual baseline visit.

SECTION A: GENERAL INFORMATION

A1. Record the dummy ID provided by the DCC.

A2. The W00 code for Baseline Visit is pre-printed on the form and is programmed into the DMS.

A3. Record the date the form was completed (the date the scoring was done).

A4. Enter the initials of the neuropsychologist completing the form.

SECTION B: CLINICIAN IMRAIRMENT RATINGS

Note: The neuropsychologist should complete Information in Section B.

To score the items from B1 to B8 use the following domain ratings:

01 Above Average Functioning
02 Average Functioning
03 Below Average Functioning
04 Borderline/Atypical Functioning
05 Definite Mild Impairment
06 Mild to Moderate Impairment
07 Moderate Impairment
08 Moderate to Severe Impairment
09 Severe Impairment

For every score, put one of the above two digit codes in the corresponding space. Example:

B1. General Intellect
Shipley Scores 02

When the rating cannot be determined, then use the special value "-8". Please use this value only on rare occasions.

The signature of neuropsychologist filling out the form is required to consider the form as completed and to use it as a source documentation according to the FDA regulations.

HALT-C Trial Q x Q

Cytotoxic T Lymphocyte Assay - Immunology/Virology AS

Form # 170 Version A: 06/15/2000

Purpose of Form #170: This form is used to record the results of the Cytotoxic T Lymphocyte (CTL) assay tested at the University of Massachusetts laboratory of Dr. Alan Rothman and the Beth Israel Deaconess Medical Center Boston laboratory of Dr. Margaret Koziel.

When to complete Form #170: This form is completed for all patients participating in the Cytotoxic T Lymphocyte sub-study of the Immunology/Virology Ancillary Study at the following clinical sites. Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible for the Immunology/Virology Ancillary Study.

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 12 (Saint Louis University).
- Site 16 (University of Texas Southwestern).
- Site 17 (University of Southern California).

The CTL laboratories should complete form #170 for patients at the following study visits:

- **Screening Phase:** Screening (S00) visit for Lead-In patients.
- **Lead-In Phase:** Form not completed during this phase.
- **Responder Phase**: Form not completed during this phase.
- **Randomized Phase:** Month 24 (M24) and Month 48 (M48) visit for Lead-In, Breakthrough, and Relapser patients.

How to access Form #170: Data entry of this form will take place at the CTL laboratories. In order to data enter Form #170, NERI must set up a special data entry account for your user name.

In order to access Form #170, log on to the HALT-C Production Data Management System (DMS). From the main menu, select "Central Lab D E". Then select "Enter Form 170". Enter the HALT-C patient ID number and the visit number in the appropriate boxes. Click the "Submit" button. A data entry screen for Form #170 will appear.

→ The patient ID will begin with 11 (UMASS/UCONN), 12 (SLU), 16 (UTSW), or 17 (USC).
→ Valid visit numbers are S00, M24, and M48.

After you have data entered the entire form, it will be saved in the system. You may perform edits to the form by following the same directions above for the given patient.

Note on form completion and data entry:

- Forms must be competed in black ink. Pencil is not acceptable. Blue ink does not photocopy well.

- Corrections are made by drawing a single line through the errant data and writing in the correct data. You must initial and write the date you make any change.

- When a result will not completely fill the blank spaces, use a "0" to fill the space.
  → If a result of 592 has space for 4 digits, write in: 0 5 9 2
  → If a result of 3.647 has space for 5 digits, write in: 3 . 6 4 7 0

- If data was not collected or not analyzed, write in “ND” or “not done” on the hard copy of the form. When data entering the form, enter the special value “-9” in the DMS. An error message will now appear on your screen.

  - If the value will never be obtained in the future, type a concise explanation in the "Reason” box. Enter your initials in the space provided and click on the “Set Override” button.

  - If the value may be obtained in the future, click on the “Ignore Value” button. An edit report will be generated after the rest of the form is entered. The form will have a “Pending Edits” status until the value is completed and data entered, or determines to be unobtainable and an override "Reason" provided.

SECTION A: GENERAL INFORMATION

A1. Record the ID number legibly.

A2. Enter the patient’s initials exactly.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed in MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: ASSAY LAB AND STATUS

B1. Record the laboratory that is performing this CTL assay. Enter “1” for Dr. Margaret Koziel’s lab and “2” for Dr. Alan Rothman’s lab.

B2. Record whether it was possible to perform the CTL assay. If it was possible to perform the assay, circle “1” and skip to question C1. If it was not possible to perform the CTL assay, circle “2” and continue to question B3.

B3. Record why it was not possible to perform the CTL assay. If the two reasons provided do not adequately explain why the assay could not be performed, then circle “99” and specify the reason in the space provided. 60 characters (including spaces and punctuation) are available. The form is complete.

SECTION C: ASSAY RESULTS

C1. Enter the date the assay was done in MM/DD/YYYY format.

C2. Target 1: vvLacZ.
- C2a. Record if Target 1: vvLacZ was included in the CTL assay. If "yes", then answer questions C2b, C2c, C2d, and C2e. If "no", then skip to question C3a.

C3. Target 2: 9A(CE-1).
- C3a. Record if Target 2: 9A(CE-1) was included in the CTL assay. If "yes", then answer questions C3b, C3c, C3d, and C3e. If "no", then skip to question C4a.

C4. Target 3: vsc11(c-NS2).
- C4a. Record if Target 3: vsc11(c-NS2) was included in the CTL assay. If "yes", then answer questions C4b, C4c, C4d, and C4e. If "no", then skip to question C5a.

C5. Target 4: 1H(E2-NS2).
- C5a. Record if Target 1: 1H(E2-NS2) was included in the CTL assay. If "yes", then answer questions C5b, C5c, C5d, and C5e. If "no", then skip to question C6a.

C6. Target 5: vsc-59(E2-NS3).
- C6a. Record if Target 5: vsc-59(E2-NS3) was included in the CTL assay. If "yes", then answer questions C6b, C6c, C6d, and C6e. If "no", then skip to question C7a.

C7. Target 6: vv-827-3011.
- C7a. Record if Target 6: vv-827-3011 was included in the CTL assay. If "yes", then answer questions C7b, C7c, C7d, and C7e. If "no", then skip to question D1.

SECTION D: ADDITIONAL COMMENTS

Please use the space provided to record any additional comments or findings. 200 characters (including punctuation and spaces) are available. Please be sure to write legibly and provide as much detail as possible. If there are no additional comments, record "not applicable" on the paper form and data enter a code of "-1" in the DMS.

HALT-C Trial Q x Q

Neutralizing Antibody Test Results – Immunology/Virology AS

Form # 171 Version A: 06/15/2000 (Rev. 05/23/2001)

Purpose of Form #171: This form is used to record the results of the Neutralizing Antibody (NA) assay at the Saint Louis University laboratory of Dr. Ranjit Ray.

When to complete Form #171: This form is completed for all patients participating in the Neutralizing Antibody sub-study of the Immunology/Virology Ancillary Study at the following clinical sites. Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible for the Immunology/Virology Ancillary Study.

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 12 (Saint Louis University).
- Site 16 (University of Texas Southwestern).
- Site 17 (University of Southern California).

The NA laboratory should complete form #171 for patients at the following study visits:

- **Screening Phase:** Form not completed during this phase.
- **Lead-In Phase:** Baseline (W00) visit.
- **Responder Phase**: Form not completed during this phase.
- **Breakthrough/Relapser Patients**: Randomization (R00) visit.
- **Randomized Phase:** Month12 (M12), Month 24 (M24), Month 36 (M36), and Month 48 (M48) for Lead-In, Breakthrough, and Relapser patients.

Data entry of Form #171: Data entry of Form # 171 will take place at the DCC. Retain the original of the completed form and a photocopy of each form to:

HALT-C Trial
New England Research Institutes Inc.
9 Galen Street
Watertown, MA 02472

Note on form completion:

- Forms must be competed in black ink. Pencil is not acceptable. Blue ink does not photocopy well.

- Corrections are made by drawing a single line through the errant data and writing in the correct data. You must initial and write the date you make any change.

- When a result will not completely fill the blank spaces, use a "0" to fill the space.
  → If a result of 592 has space for 4 digits, write in: 0 5 9 2
  → If a result of 3.647 has space for 5 digits, write in: 3 . 6 4 7 0

- If data was not collected or not analyzed, write in "ND" or "not done" on the hard copy of the form.

SECTION A: GENERAL INFORMATION

A1. Record the ID number legibly.

A2. Enter the three-digit code corresponding to this visit.

A3. Record the date the form was completed in MM/DD/YYYY format.

A4. Enter the initials of the person filling out the form.

SECTION B: BSI ID

B1. Record the BSI ID from the aliquot tube. The BSI ID begins with the letter “D”, followed by a second letter corresponding to the study site, followed by six numbers. The BSI ID is used by NERI and BBI to identify specimens by patient and study visit.

The BSI ID also appears on the shipping manifest received from the BBI Repository in the column named “bsi_id”. On the shipping manifest, the BSI ID is followed by a three-digit sequence number, which does not need to be recorded on the paper form.

SECTION C: ASSAY STATUS

C1. Record whether it was possible to perform the Neutralizing Antibody assay. If it was possible to perform the assay, circle “1” and continue to question D1. If it was not possible to perform the assay, circle “2” and the form is complete.

SECTION D: NEUTRALIZING ANTIBODY TITER (reciprocal serum dilution)

D1. Enter the date the E1 assay was performed in MM/DD/YYYY format.

D2. If the E1 titer was at or above set detectable limits [1:20], circle "1" for YES and continue to question D3. If the E1 titer was not at or above set detectable limits [1:20], circle "2" for NO and skip to question D4.

D3. Record the titer of E1.

D4. Enter the date the E2 assay was performed in MM/DD/YYYY format.

D5. If the E2 titer was at or above set detectable limits [1:20], circle "1" for YES and continue to question D6. If the E2 titer was not at or above set detectable limits [1:20], circle "2" for NO and skip to Section E.

D6. Record the titer of E2.

SECTION E: ADDITIONAL COMMENTS

Please use the space provided to record any additional comments or findings. 200 characters (including punctuation and spaces) are available. If there are no additional comments, then write “Not applicable” and the DCC will record a “-1” in the DMS.

HALT-C Trial QxQ

HCV Quasispecies: HTA Immunology/Virology AS

Form # 172 Version A: 06/15/2000

Purpose of Form #172: This form is used to record the results of the HCV Quasispecies Heteroduplex Tracking Analysis at the University of Washington (Central Laboratory).

When to complete Form #172: This form is completed for all patients participating in the Quasispecies sub-study of the Immunology/Virology Ancillary Study at the following clinical sites. Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible for the Immunology/Virology Ancillary Study.

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 12 (Saint Louis University).
- Site 16 (University of Texas Southwestern).
- Site 17 (University of Southern California).

The Quasispecies laboratory should complete form #172 for patients at the following study visits:

- **Screening Phase:** Form not completed during this phase.
- **Lead-In Phase:** Week 24 (W24) visit.
- **Responder Phase**: Form not completed during this phase.
- **Breakthrough/Relapser Patients**: Randomization (R00) visit.
- **Randomized Phase:** Month12 (M12), Month 24 (M24), Month 36 (M36), Month 48 (M48), and Month 54 (M54) for Lead-In, Breakthrough, and Relapser patients.

How to access Form #172: Data entry of this form will take place only at the University of Washington (Central Laboratory). In order to data enter Form #172, NERI must set up a special data entry account for your user name.

In order to access Form #172, log on to the HALT-C Production Data Management System (DMS). From the main menu, select "Central Lab D E". Then select "Enter Form 172". Enter the HALT-C patient ID number and the visit number in the appropriate boxes. Click the "Submit" button. A data entry screen for Form #172 will appear.

→ The patient ID will begin with 11 (UMASS/UCONN), 12 (SLU), 16 (UTSW), or 17 (USC).
→ Valid visit numbers are W24, R00, M12, M24, M36, M48, and M54.

After you have data entered the entire form, it will be saved in the system. You may perform edits to the form by following the same directions above for the given patient.

Note on form completion and data entry:

- Forms must be competed in black ink. Pencil is not acceptable. Blue ink does not photocopy well.

- Corrections are made by drawing a single line through the errant data and writing in the correct data. You must initial and write the date you make any change.

- When a result will not completely fill the blank spaces, use a "0" to fill the space.
  → If a result of 592 has space for 4 digits, write in: 0 5 9 2
  → If a result of 3.647 has space for 5 digits, write in: 3 . 6 4 7 0

- If data was not collected or not analyzed, write in “ND” or “not done” on the hard copy of the form. When data entering the form, enter the special value “-9” in the DMS. An error message will now appear on your screen.

  - If the value will never be obtained in the future, type a concise explanation in the "Reason” box. Enter your initials in the space provided and click on the “Set Override” button.

  - If the value may be obtained in the future, click on the “Ignore Value” button. An edit report will be generated after the rest of the form is entered. The form will have a “Pending Edits” status until the value is completed and data entered, or determines to be unobtainable and an override "Reason" provided.

SECTION A: GENERAL INFORMATION

A1. Record the ID number legibly.

A2. Enter the three-digit code corresponding to this visit.

A3. Record the date the form was completed in MM/DD/YYYY format.

A4. Enter the initials of the person filling out the form.

SECTION B: BSI ID

B1. Record the BSI ID from the aliquot tube. The BSI ID begins with the letter “D”, followed by a second letter corresponding to the study site, followed by six numbers. The BSI ID is used by NERI and BBI to identify specimens by patient and study visit.

The BSI ID also appears on the shipping manifest received from the BBI Repository in the column named “bsi_id”. On the shipping manifest, the BSI ID is followed by a three-digit sequence number, which does not need to be recorded on the paper form.

SECTION C: ASSAY STATUS

C1. Record whether it was possible to perform the HCV Quasispecies Heteroduplex Tracking Analysis. If it was possible to perform the assay, circle “1” for YES and skip to question D1. If it was not possible to perform the assay, circle “2” for NO and continue to question C2.

C2. Record why it was not possible to perform the HCV quasispecies assay. If the two reasons provided do not adequately explain why the assay could not be performed, then circle “99” and specify the reason in the space provided. 60 characters (including spaces and punctuation) are available. The form is complete.

SECTION D: RESULTS OF HCV QUASISPECIES HTA TESTING

D1. Enter the date the assay was done in MM/DD/YYYY format.

D2. Enter the Heteroduplex Mobility Ratio (HMR) as per HTA in the space provided.

SECTION E: ADDITIONAL COMMENTS

Please use the space provided to record any additional comments or findings. 200 characters (including punctuation and spaces) are available. Please be sure to write legibly and provide as much detail as possible. If there are no additional comments, record "not applicable" on the paper form and enter a code of "-1" in the Data Management System.

HALT-C Trial Q x Q

Lymphoproliferation - Immunology/Virology AS

Form # 173 Version D: 02/12/2004

Purpose of Form #173: This form is used to record the results of the Lymphoproliferation (LP) assay at the University of Washington (Central Laboratory).

When to complete Form #173: This form is completed for patients participating in the Lymphoproliferation sub-study of the Immunology/Virology Ancillary Study at the following clinical sites. Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible for the Immunology/Virology Ancillary Study.

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 12 (Saint Louis University).
- Site 16 (University of Texas Southwestern).
- Site 17 (University of Southern California).

Form #173 should be completed for participating patients at the following study visits:

- **Screening Phase:** Form not completed during this phase.
- **Lead-In Phase:** Baseline (W00) and Week 24 (W24) visits.
- **Responder Phase**: Form not completed during this phase.
- **Breakthrough/Relapser Patients**: Randomization (R00) visit.
- **Randomized Phase:** Month12 (M12), Month 24 (M24), Month 36 (M36), Month 48 (M48), and Month 54 (M54) for Lead-In, Breakthrough, and Relapser patients.

How to access Form #173: Data entry of this form will take place only at the University of Washington (Central Laboratory). In order to data enter Form #173, NERI must set up a special data entry account for your user name.

In order to access Form #173, log on to the HALT-C Production Data Management System (DMS). From the main menu, select "Central Lab D E". Then select "Enter Form 173". Enter the HALT-C patient ID number and the visit number in the appropriate boxes. Click the "Submit" button. A data entry screen for Form #173 will appear.

→ The patient ID will begin with 11 (UMASS/UCONN), 12 (SLU), 16 (UTSW), or 17 (USC).
→ Valid visit numbers are W00, W24, R00, M12, M24, M36, M48, and M54.

After you have data entered the entire form, it will be saved in the system. You may perform edits to the form by following the same directions above for the given patient.

Note on form completion and data entry:

- Forms must be competed in black ink. Pencil is not acceptable. Blue ink does not photocopy well.

- Corrections are made by drawing a single line through the errant data and writing in the correct data. You must initial and write the date you make any change.

- When a result will not completely fill the blank spaces, use a "0" to fill the space.
  → If a result of 592 has space for 4 digits, write in: 0 5 9 2
  → If a result of 3.647 has space for 5 digits, write in: 3 . 6 4 7 0

- If data was not collected or not analyzed, the data collector should write a concise explanation including her/his initials and the date on the hard copy of the form. When data entering the form, enter the special value “-9” in the DMS. An error message will now appear on your screen.

  - If the value will never be obtained in the future, type the explanation in the "Reason" box. Enter the data collector’s initials in the space provided and click on the “Set Override” button.

  - If the value may be obtained in the future, click on the “Ignore Value” button. An edit report will be generated after the rest of the form is entered. The form will have a “Pending Edits” status until the value is completed and data entered, or determines to be unobtainable and an override "Reason" provided.

SECTION A: GENERAL INFORMATION

A1. Record the ID number legibly.

A2. Enter the patient’s initials exactly.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed in MM/DD/YYYY format.

A5. Enter the initials of the person filling out the form.

SECTION B: ASSAY LAB AND STATUS

B1. If the LP assay was attempted within one day, circle "1" for YES and skip to question B2. If the LP assay was not attempted within one day, circle "2" for NO and continue to question B1a.

B1a. Record the number of days between the blood draw and the assay setup (must be >1 day).

B2. If it was possible to perform the LP assay, circle "1" for YES and skip to question B4. If it was not possible to perform the LP assay, circle "2" for NO and contine to question B3.

B3. Record a reason why it was not possible to perform the LP assay. If you circle "Other" or “99”, specify a reason in the space provided. 60 characters (including spaces and punctuation) are available. The form is complete.

B4. Record the percent viability in the space provided. The range is 0-99%.

B5. Record the total cell yield in the spaces provided. The range is 10 - 95 cells.

B5a. Record the total cell yield exponent . The range is 4-9.

SECTION C: ASSAY RESULTS

C1a. Enter the date the assay was performed in MM/DD/YYYY format.

C1b. Enter the batch number of the assay. Batch numbers can range from 001 to 999.

C2 – C13. Record Mean cpm Incorporated in the spaces provided.

Note on Mean cpm Incorporated values: The DMS has been set up to expect a range of 100 – 999,999 for Mean cpm Incorporated. If the obtained value falls outside of this range, it should still be recorded on the paper form and data entered. Upon entering an out of range value in the DMS, a data entry validation error screen will appear. If the data entered value is the actual obtained value recorded on the paper form, then this out-of-range value may be overridden. Type a concise explanation in the "Reason" box (e.g., "Confirmed, correct value"). Enter your initials in the space provided and click the "Set Override" button.

SECTION D: ADDITIONAL COMMENTS

D1. Please use the space provided to record any additional comments or findings. 200 characters (including punctuation and spaces) are available. Please be sure to write legibly and provide as much detail as possible. If there are no additional comments, record "not applicable" on the paper form and enter a code of "-1" in the Data Management System.

HALT-C Trial Q x Q

Replication - Immunology/Virology AS

Form # 174 Version A: 06/15/2000

Purpose of Form #174: This form is used to record the Replication results of in situ detection and quantification of HCV RNAs as part of the Immunology/Virology Ancillary Study.

When to complete Form #174: This form is completed for patients participating in the Replication sub-study of the Immunology/Virology Ancillary Study at the following clinical sites. Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible for the Immunology/Virology Ancillary Study.

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 12 (Saint Louis University).
- Site 16 (University of Texas Southwestern).
- Site 17 (University of Southern California).

Form #174 should be completed for participating patients at the following study visits:

- **Screening Phase:** Screening (S00) visit for Lead-In patients.
- **Lead-In Phase:** Form not completed during this phase.
- **Responder Phase**: Form not completed during this phase.
- **Randomized Phase:** Month 24 (M24) and Month 48 (M48) visit for Lead-In, Breakthrough, and Relapser patients.

How to data enter Form #174: Data entry of this form will take place only at the University of Washington (Central Laboratory). In order to data enter Form #174, NERI must set up a special data entry account for your user name.

In order to access Form #174, log on to the HALT-C Production Data Management System (DMS). From the main menu, select "Central Lab D E". Then select "Enter Form 174". Enter the HALT-C patient ID number and the visit number in the appropriate boxes. Click the "Submit" button. A data entry screen for Form #174 will appear.

→ The patient ID will begin with 11 (UMASS/UCONN), 12 (SLU), 16 (UTSW), or 17 (USC).
→ Valid visit numbers are S00, M24, and M48.

After you have data entered the entire form, it will be saved in the system. You may perform edits to the form by following the same directions above for the given patient.

Note on form completion and data entry:

- Forms must be competed in black ink. Pencil is not acceptable. Blue ink does not photocopy well.

- Corrections are made by drawing a single line through the errant data and writing in the correct data. You must initial and write the date you make any change.

- When a result will not completely fill the blank spaces, use a "0" to fill the space.
  → If a result of 592 has space for 4 digits, write in: 0 5 9 2
  → If a result of 3.647 has space for 5 digits, write in: 3 . 6 4 7 0

- If data was not collected or not analyzed, write in “ND” or “not done” on the hard copy of the form. When data entering the form, enter the special value “-9” in the DMS. An error message will now appear on your screen.

  - If the value will never be obtained in the future, type a concise explanation in the "Reason” box. Enter your initials in the space provided and click on the “Set Override” button.

  - If the value may be obtained in the future, click on the “Ignore Value” button. An edit report will be generated after the rest of the form is entered. The form will have a “Pending Edits” status until the value is completed and data entered, or determines to be unobtainable and an override "Reason" provided.

SECTION A: GENERAL INFORMATION

A1. Record the ID number legibly.

A2. Enter the three-digit code corresponding to this visit.

A3. Record the date the form was completed in MM/DD/YYYY format.

A4. Enter the initials of the person completing the form.

SECTION B: BSI ID

B1. Record the BSI ID from the aliquot tube. The BSI ID begins with the letter “D”, followed by a second letter corresponding to the study site, followed by six numbers. The BSI ID is used by NERI and BBI to identify specimens by patient and study visit.

The BSI ID also appears on the shipping manifest received from the BBI Repository in the column named “bsi_id”. On the shipping manifest, the BSI ID is followed by a three-digit sequence number, which does not need to be recorded on the paper form.

SECTION C: In Situ Negative-Strand RNA Detection

C1. Record whether it was possible to perform in situ detection of HCV negative-strand RNA.
- If it was possible to perform the assay, circle "1" for YES and continue to question C2.
- If it was not possible to perform the assay, circle "2" for NO and skip to question C4.

C2. Record the date of HCV negative-strand assay in MM/DD/YYYY format.

C3. Record the Average IU negative-strand RNA per ml of liver tissue. Then skip to question D1.

- For the first field, enter a value between 1 and 9.
- For the second field, enter a value between 02 and 12.
- The upper limit is 1×10^{12}.

C4. Record a reason why it was not possible to perform the HCV negative-strand assay. If you circle "Other" or “99”, specify a reason in the space provided. 60 characters (including spaces and punctuation) are available. Continue to question D1.

SECTION D: Total HCV RNA in Liver Tissue

D1. Record if it was possible to measure the total HCV RNA by the Roche Monitor.
- If it was possible to measure the HCV RNA, circle "1" for YES and continue to question D2.
- If it was not possible to measure the HCV RNA, circle "2" for NO and skip to question D4.

D2. Enter the date the total HCV RNA was measured in MM/DD/YYYY format.

D3. Record the IU HCV RNA (positive & negative-strand) per ml of liver tissue. Then skip to question D1.

- For the first field, enter a value between 1 and 9.
- For the second field, enter a value between 02 and 12.
- The upper limit is 1×10^{12}.

D4. Record a reason why it was not possible to perform the HCV RNA assay. If you circle "Other" or “99”, specify a reason in the space provided. 60 characters (including spaces and punctuation) are available.

SECTION E: ADDITIONAL COMMENTS

Please use the space provided to record any additional comments or findings. 200 characters (including punctuation and spaces) are available. If there are no additional comments, then record "NA” or “Not Applicable” on the hard copy of the form and enter the special value “-1” in the DMS.

HALT-C Trial Q x Q

Immunology/Virology AS Aliquot Form

Form # 175 Version A: 06/15/2000 (Rev. 04/07/2003)

Purpose of Form #175: This form lists the specimens collected for the Immunology/Virology Ancillary Study that are being sent to the Central Repository (BBI). This form should be filled out when blood specimens for the Neutralizing Antibody and Quasispecies sub-studies and liver specimens for the Replication sub-study are collected.

When to complete Form #175: This form is completed following processing and aliquoting of Immunology/Virology Ancillary Study specimens at the following clinical sites. Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible.

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 12 (Saint Louis University).
- Site 16 (University of Texas Southwestern).
- Site 17 (University of Southern California).

Form #175 should be completed for specimens collected at the following study visits:

- Serum for the Neutralizing Antibodies sub-study. One 1 ml aliquot (sequence number 301) at the Baseline (W00), Breakthrough/Relapse Randomization Visit (R00), Month 12 (M12), Month 24 (M24), Month 36 (M36), and Month 48 (M48) study visits.

- Serum for the Quasispecies sub-study. Two 1 ml aliquots (sequence numbers 302 and 303) at the Baseline (W00), Week 24 (W24), Breakthrough/Relapse Randomization Visit (R00), Month 12 (M12), Month 24 (M24), Month 36 (M36), Month 48 (M48), and Month 54 (M54) study visits.

- Liver tissue for the Replication sub-study. 2.5 cm size (sequence number 320) collected in OCT at the Screening (S00), Month 24 (M24), and Month 48 (M48) study visits.

Form #175 is data entered at the clinical sites. Data entry of this form for a patient visit is the first step of the shipping and tracking procedures for HALT-C. All of the specimens will go into a database of specimens available for shipment to the Central Repository for your clinical center. Entry of this form also allows NERI to link the HALT-C Trial ID's and study visits with the Sample ID assigned by the Central Repository.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Record the visit number for this visit.

A4. Record the date the form was completed in the MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: BSI ID

B1. Record the BSI ID from the aliquot tube. The BSI ID begins with the letter “D”, followed by a second letter corresponding to the study site, followed by six numbers. The BSI ID is used by NERI and BBI to identify specimens by patient and study visit.

The BSI ID also appears on the shipping manifest received from the BBI Repository in the column named “bsi_id”. On the shipping manifest, the BSI ID is followed by a three-digit sequence number, which does not need to be recorded on the paper form.

B2. Record the date of the blood draw using the MM/DD/YYYY format. This must be the same date that the blood was aliquotted into cryovials and frozen.

SECTION C: SPECIMEN INFORMATION

C1. Please indicate if there were any problems or delays in specimen processing in C1.
- If there was a delay of > 4 hours or problems with specimen processing, circle 1 for "Yes".
- If serum was separated within 2-4 hours of collection with no problems, circle 2 for “No”.

C2. If the answer for C2a is “No”, circle 2 and skip to the sequence number in the next row. If the answer for C2a is “Yes”, circle 1 and follow the directions below.

<u>If C1 = 1 (Yes) and C2a = 1 (Yes)</u>
- Columns C2b, C2c, and C2d must be completed.
- Column C2b must list the total volume in ml of the sample in the cryovial.
- Column C2c must list one of the codes for specimen processing listed in the box below.
- Column C2d must list the data that processing of the sample was completed.

<u>If C1 = 2 (No) and C2a = 1 (Yes)</u>
- Only Column C2b must be completed. Enter the total volume in ml of the sample in the cryovial.

SECTION D: LIVER TISSUE

D1. Please record the date the biopsy was performed in MM/DD/YYYY format. This must be the date the liver was frozen in OCT.

D2. Please indicate if there were any problems or delays in liver specimen processing in D1.
- If there was a delay or problems with specimen processing, circle 1 for "Yes".
- If there were no delays or problems, circle 2 for “No”.

D3. If the answer for D3a is “No”, circle 2. The form is complete.

<u>If D2 = 1 (Yes) and D3a = 1 (Yes)</u>
- Columns D3b, D3c, and D3d must be completed.
- Column D3b must list the length of the liver sample in cm.
- Column D3c must list one of the codes for specimen processing listed in the box below.
- Column D3d must list the data that processing of the liver sample was completed.

<u>If D2 = 2 (No) and D3a = 1 (Yes)</u>
- Only Column D3b must be completed. List the length of the liver sample in cm.

Codes for specimen processing

1. okay
2. hemolysis
3. delay in processing-processed within 4-6 hours of collection
4. delay in processing-processed within 6-8 hours of collection
5. delay in processing-processed within 8-12 hours of collection
6. delay in processing-processed within 12-18 hours of collection
7. delay in processing-processed within 18-24 hours of collection
8. delay in processing-processed within 24-48 hours of collection
9. delay in processing-processed 48+ hours after collection
10. delay in shipping
11. collected in incorrect tube-plasma collected instead of serum
12. delay in snap freezing liver tissue
13. Vacutainer tube stored in refrigerator
99. Other-please specify

HALT-C Trial

Immunology / Virology Withdrawal Form

Form # 176 Q x Q Version B: 01/30/2003

Purpose of Form #176: This form records that a patient has withdrawn from the entire Immunology / Virology Ancillary Study or from one or more of the five Immunology / Virology sub-studies:

- Cytotoxic T Lymphocyte (CTL)
- Replication
- Neutralizing Antibody (NA)
- Quasispecies
- Lymphoproliferation (LP)

When to complete Form #176: This form should be completed when a patient has withdrawn from any or all of the Immunology / Virology sub-studies. Lead-In patients were eligible for the Immunology / Virology Ancillary Study. Express patients were not eligible. Participating sites are listed below:

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 12 (Saint Louis University).
- Site 16 (University of Texas Southwestern).
- Site 17 (University of Southern California).

In the HALT-C Data Management System (DMS), Form #176 can be added to any study visit by clicking the "Additional Forms" button on the study visit screen. Data entry of this form by the clinical site removes relevant study forms and samples from future visits in the DMS and on applicable Visit Control Sheets (VCS).

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Record the date the form was completed in MM/DD/YYYY format.

A4. Enter the initials of the person filling out the form.

SECTION B: WITHDRAWAL INFORMATION

Possible Reasons for Withdrawal from the entire Immunology / Virology Ancillary Study:

- A patient withdraws consent to participate in the Immunology / Virology Ancillary Study.

B1. If the patient is being withdrawn from the entire Immunology / Virology Ancillary Study (all five sub-studies), circle 1 for "Yes" and continue to Question B2.

If the patient is not being withdrawn from the entire Immunology / Virology Ancillary Study (all five sub-studies), circle 2 for "No" and skip to Question B4.

B2. Record the date of withdrawal from the entire Immunology / Virology Ancillary Study in MM/DD/YYYY format. If the patient withdrew consent, record the date the patient made the request. If there was a problem with the initial samples, record the date the samples were not collected, damaged, or lost.

B3. Circle the primary reason why the patient is being withdrawn from the entire Immunology / Virology Ancillary Study. If the reason is not listed, circle 99 for “Other” and specify a reason. 60 characters including spaces and punctuation are available. Skip to question B14.

Possible Reasons for Withdrawal from one or more of the five Immunology / Virology sub-studies:

- A patient withdraws consent to participate in one (or more) of the five sub-studies at any time.
- The *initial* samples for the NA, Quasispecies, or LP sub-study were not collected. For example, if an adequate serum specimen was not obtained for the LP sub-study at the W00 visit, the patient should be withdrawn from only the LP sub-study.
- The *initial* samples for the NA, Quasispecies, or LP sub-study were destroyed or lost in shipping.
- If *initial* samples for the CTL or Replication sub-study were not collected, the patient may *remain* in the CTL or Replication sub-study.

→ **NOTE.** Even if all required samples for the CTL or Replication sub-study were not collected at the initial visit (S00 or W00), the patient is still eligible for continuing in that sub-study. Incomplete sample collection at the initial visit does not require withdrawal from the CTL or Replication sub-study. For example, if specimens for the CTL sub-study were not at the S00visit, but the M24 specimen was collected, the patient can remain in the CTL sub-study. Samples should be also collected at the M48 visit.

Cytotoxic T Lymphocyte sub-study

B4. If the patient is being withdrawn from the CTL sub-study, circle 1 for "Yes" and continue to Question B4a.

If the patient is not being withdrawn from the CTL sub-study, circle 2 for "No" and skip to Question B6.

B4a. Record the date of withdrawal from the CTL sub-study, in MM/DD/YYYY format. If the patient withdrew consent, record the date the patient made the request. If there was a problem with the initial samples, record the date the samples were not collected, damaged, or lost.

B5. Circle the primary reason why the patient is being withdrawn from the CTL sub-study. If the reason is not listed, circle 99 for “Other” and specify a reason. 60 characters including spaces and punctuation are available.

Replication sub-study

B6. If the patient is being withdrawn from the Replication sub-study, circle 1 for "Yes" and continue to Question B6a.

If the patient is not being withdrawn from the Replication sub-study, circle 2 for "No" and skip to Question B8.

B6a. Record the date of withdrawal from the Replication sub-study, in MM/DD/YYYY format. If the patient withdrew consent, record the date the patient made the request. If there was a problem with the initial samples, record the date the samples were not collected, damaged, or lost.

B7. Circle the primary reason why the patient is being withdrawn from the Replication sub-study. If the reason is not listed, circle 99 for “Other” and specify a reason. (60 characters including spaces and punctuation are available.)

→ **NOTE.** If all required samples for the NA, Quasispecies, or LP sub-study were collected at the initial visit (S00 or W00), the patient is eligible for continuing in that sub-study. Incomplete sample collection at a later visit does not require withdrawal from the LP, Quasispecies, or NA sub-study. For example, if specimens for the LP sub-study were collected at the W00, W24, and M12 visits, but the M24 specimen was not collected, the patient can remain in the LP sub-study. Samples should be collected at the M36, M48, and M54 visits.

Neutralizing Antibody sub-study

B8. If the patient is being withdrawn from the NA sub-study, circle 1 for "Yes" and continue to Question B8a.

If the patient is not being withdrawn from the NA sub-study, circle 2 for "No" and skip to Question B10.

B8a. Record the date of withdrawal from the NA sub-study, in MM/DD/YYYY format. If the patient withdrew consent, record the date the patient made the request. If there was a problem with the initial samples, record the date the samples were not collected, damaged, or lost.

B9. Circle the primary reason why the patient is being withdrawn from the NA sub-study. If the reason is not listed, circle 99 for “Other” and specify a reason. 60 characters including spaces and punctuation are available.

Quasispecies sub-study

B10. If the patient is being withdrawn from the Quasispecies sub-study, circle 1 for "Yes" and continue to Question B10a.

If the patient is not being withdrawn from the Quasispecies sub-study, circle 2 for "No" and skip to Question B12.

B10a. Record the date of withdrawal from the Quasispecies sub-study, in MM/DD/YYYY format. If the patient withdrew consent, record the date the patient made the request. If there was a problem with the initial samples, record the date the samples were not collected, damaged, or lost.

B11. Circle the primary reason why the patient is being withdrawn from the Quasispecies sub-study. If the reason is not listed, circle 99 for “Other” and specify a reason. 60 characters including spaces and punctuation are available.

Lymphoproliferation sub-study

B12. If the patient is being withdrawn from the LP sub-study, circle 1 for "Yes" and continue to Question B12a.

If the patient is not being withdrawn from the LP sub-study, circle 2 for "No" and skip to Question B14.

B12a. Record the date of withdrawal from the LP sub-study, in MM/DD/YYYY format. If the patient withdrew consent, record the date the patient made the request. If there was a problem with the initial samples, record the date the samples were not collected, damaged, or lost.

B13. Circle the primary reason why the patient is being withdrawn from the LP sub-study. If the reason is not listed, circle 99 for “Other” and specify a reason. 60 characters including spaces and punctuation are available.

B14. Please enter any additional information regarding the patient’s withdrawal. 250 characters including spaces and punctuation are available.

HALT-C Trial Q x Q

HCV Quasispecies: CFA

Immunology/Virology AS

Form # 177 Version A: 06/15/2000

Purpose of Form #177: This form is used to record the results of the HCV Quasispecies Clonal Frequency Analysis.

When to complete Form #177: This form is completed at the Baseline visit (W00) for all Lead-In patients participating in the Quasispecies sub-study of the Immunology/Virology Ancillary Study at the following clinical sites. Express patients are not eligible for the Immunology/Virology Ancillary Study.

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 12 (Saint Louis University).
- Site 16 (University of Texas Southwestern).
- Site 17 (University of Southern California).

The Quasispecies laboratory should complete form #177 for patients at the following study visit:

- **Lead-In Phase:** Baseline (W00) visit.

How to access Form #177: Data entry of this form will take place at the Quasispecies laboratories. In order to data enter Form #177, NERI must set up a special data entry account for your user name.

In order to access Form #177, log on to the HALT-C Production Data Management System (DMS). From the main menu, select "Central Lab D E". Then select "Enter Form 177". Enter the HALT-C patient ID number and the visit number in the appropriate boxes. Click the "Submit" button. A data entry screen for Form #177 will appear.

→ The patient ID will begin with 11 (UMASS/UCONN), 12 (SLU), 16 (UTSW), or 17 (USC).
→ Valid visit numbers are W00.

After you have data entered the entire form, it will be saved in the system. You may perform edits to the form by following the same directions above for the given patient.

Note on form completion and data entry:

- Forms must be competed in black ink. Pencil is not acceptable. Blue ink does not photocopy well.

- Corrections are made by drawing a single line through the errant data and writing in the correct data. You must initial and write the date you make any change.

- When a result will not completely fill the blank spaces, use a "0" to fill the space.
  → If a result of 592 has space for 4 digits, write in: 0 5 9 2
  → If a result of 3.647 has space for 5 digits, write in: 3 . 6 4 7 0

- If data was not collected or not analyzed, write in "ND" or "not done" on the hard copy of the form. When data entering the form, enter the special value "-9" in the DMS. An error message will now appear on your screen.

- If the value will never be obtained in the future, type a concise explanation in the "Reason" box. Enter your initials in the space provided and click on the "Set Override" button.

- If the value may be obtained in the future, click on the "Ignore Value" button. An edit report will be generated after the rest of the form is entered. The form will have a "Pending Edits" status until the value is completed and data entered, or determines to be unobtainable and an override "Reason" provided.

SECTION A: GENERAL INFORMATION

A1. Record the ID number legibly.

A2. Enter the three-digit code corresponding to this visit.

A3. Record the date the form was completed in MM/DD/YYYY format.

A4. Enter the initials of the person filling out the form.

SECTION B: BSI ID

B1. Record the BSI ID from the aliquot tube. The BSI ID begins with the letter "D", followed by a second letter corresponding to the study site, followed by six numbers. The BSI ID is used by NERI and BBI to identify specimens by patient and study visit.

The BSI ID also appears on the shipping manifest received from the BBI Repository in the column named "bsi_id". On the shipping manifest, the BSI ID is followed by a three-digit sequence number, which does not need to be recorded on the paper form.

SECTION C: ASSAY STATUS

C1. Record whether it was possible to perform the HCV Quasispecies Clonal Frequency Analysis. If it was possible to perform the assay, circle 1 for YES and skip to question D1. If it was not possible to perform the assay, circle 2 for NO and continue to question C2.

C2. Record why it was not possible to perform the HCV Quasispecies Clonal Frequency Analysis. If the two reasons provided do not adequately explain why the assay could not be performed, then circle 99 and specify the reason in the space provided. 60 characters (including spaces and punctuation) are available. The form is complete.

SECTION D: RESULTS OF HCV QUASISPECIES CFA TESTING

D1. Enter the date the assay was done in MM/DD/YYYY format.

D2. Enter a value for the Heteroduplex Mobility Ratio (HMR) as per CFA in the space provided. One digit must be entered before the decimal point and three digits must be entered after the decimal point.

D3. Enter a value for Quasispecies complexity in the space provided.

SECTION E: ADDITIONAL COMMENTS

Please use the space provided to record any additional comments or findings. 200 characters (including punctuation and spaces) are available. Please be sure to write legibly and provide as much detail as possible.

If there are no additional comments, record “not applicable” on the paper form and enter a code of “-1” in the Data Management System.

HALT-C Trial Q x Q

Histopathology – Iron & HFE Gene Mutation AS

Form #181 Version A: 06/15/2000 (Rev. 11/11/2003)

Purpose of Form #181: This form documents central determination of iron in hepatocytes, iron in Kupffer cells, and portal triads with stainable iron for the Iron and HFE Gene Mutation Ancillary Study.

When to complete Form #181: This form should be completed at the Screening (S00), Month 24 (M24) and Month 48 (M48) visit on biopsies from all patients participating in the HALT-C Trial. Form #181 is completed by HALT-C study pathologists. Form #181 is data entered at the DCC.

SECTION A: GENERAL INFORMATION

A1. FOR NERI ONLY. After data entering the dummy ID for this form, record the patient ID number legibly in black or blue pen.

A2. Record the Dummy ID found on the slide.

A3. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A5. Record the date the form was completed using MM/DD/YYYY format.

A6. Enter the initials of the person who is completing the form.

SECTION B: HISTOPATHOLOGY SUMMARY – STAINABLE IRON

B1. Record the date the biopsy was read in MM/DD/YYYY format.

B2. Record the initials of the first pathologist reading the biopsy.

B3. If a second pathologist also read the biopsy, circle 1 for YES and continue to question B4. If only one pathologist read the biopsy, circle 2 for NO and skip to question B5.

B4. Record the initials of the second pathologist reading the biopsy.

B5. If the specimen is adequate to perform histopathology, circle 1 for YES and continue to question B6. If the specimen is inadequate to perform histopathology, circle 2 for NO. The form is complete.

B6. Record location of iron in hepatocytes. Circle 1 for ABSENT. Circle 2 for PRESENT IN <50% OF CELLS. Circle 3 for PRESENT IN >50% OF CELLS.

B7. Record location of iron in reticuloendothelial cells. Circle 1 for ABSENT. Circle 2 for PRESENT IN <50% OF CELLS. Circle 3 for PRESENT IN >50% OF CELLS.

B8. Record the total number of Portal Triads.

B9. Record the number of Portal Triads with stainable iron. If the answer is 0, the form is complete. If the answer is >0, continue to question B10.

B10. Record whether there were endothelial cells with stainable iron. Circle 1 for YES, 2 for NO, and 3 for NOT SPECIFIED.

B11. Record whether there were Kupffer and stromal cells with stainable iron. Circle 1 for YES, 2 for NO, and 3 for NOT SPECIFIED. The form is complete.

WHEN THE FORM IS COMPLETED PLEASE MAIL OR FAX TO THE DCC: 617-926-0144.

HALT-C Trial Q x Q

Serum Iron – Iron and HFE Gene Mutation AS

Form #183 Version A: 06/15/2000

Purpose of Form #183: The Serum Iron form records the result of local testing of serum iron, total iron binding capacity, and serum ferritin, for the Iron and HFE Gene Mutation Ancillary Study.

When to complete Form #183: Form #183 should be completed at the following study visits for all randomized patients:

- Randomization phase: Month 24 (M24) and Month 48 (M48).

Form #183 will be data entered at each clinical site.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the patient number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed using MM/DD/YYYY format.

A5. Record the initials of the person completing the form.

SECTION B: SERUM IRON

B1. Record the date of the blood draw using MM/DD/YYYY format.

B2. Serum iron results, reported in μg/dL. Range is 20 to 210.

B3. Total iron binding capacity (TIBC), reported in μg/dL. Range is 190 to 460.

B4. Serum ferritin results, reported in ng/mL. Range is 7 to 360.

HALT-C Trial Q x Q

Iron and HFE Aliquot Form – Iron & HFE Gene Mutation AS

Form #184 Version A: 06/15/2000

Purpose of Form #184: The Iron and HFE aliquot form should be used to document the liver specimen collected at the various visits that will be sent to the University of Connecticut laboratory. Data entry of this form will allow the DCC to track the shipment and receipt of liver specimens collected for the Iron and HFE Ancillary Study.

When to complete Form #184: Form #184 should be completed in addition to the aliquot form specific for the regular study visit. This form should be completed following processing and aliquotting of the liver tissue for the Iron and HFE AS at the appropriate visits. Form #184 should be completed at the Screening (S00), Month 24 (M24), and Month 48 (M48)study visits.

Form #184 will be completed and data entered for patients participating in the Iron and HFE Ancillary Study at the following clinical sites.

- Site 11 (University of Massachusetts and University of Connecticut).
- Site 15 (University of California - Irvine).

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the patient number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed using MM/DD/YYYY format.

A5. Record the initials of the person completing the form.

SECTION B: COLLECTION DATE

B1. Record the date of the biopsy using the MM/DD/YYYY format.

SECTION C: SPECIMEN INFORMATION

A room temperature liver specimen of approximately 0.5 cm in length is requested for this Ancillary Study. The sequence number for the liver specimen is 600. The liver specimen must be batch shipped at ambient temperature to the University of Connecticut laboratory.

If a liver sample was collected for this Ancillary Study, circle 1 for YES under Column a. Record the length of the specimen in centimeters under Column b. The form is complete.

If a liver sample was not able to be collected for this Ancillary Study, circle 2 for NO under Column a. The form is complete.

HALT-C Trial Q x Q

Quantitative Liver Function Test Record – QLFT AS

Form # 190 Version B: 07/06/2001

Purpose of Form #190: This form is used to record the timed administration of study compounds and blood collection for the Quantitative Liver Function Test (QLFT) Ancillary Study.

When to complete Form #190: This form is completed for all patients participating in the QLFT Ancillary Study at the following clinical sites.

- Site 14 (University of Colorado Health Sciences Center).
- Site 15 (University of California - Irvine).
- Site 19 (Virginia Commonwealth University).

The clinical centers should complete and data enter form #190 for patients at the following study visits:

- Lead-In Phase patients: Baseline visit (W00)
- Express patients: Randomization visit (R00)
- Randomized patients: Month 24 (M24) and Month 48 (M48).

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed using MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

Note on dates:

- All dates on this form should be recorded using MM/DD/YYYY format.
- Enter the 2 digit number for the month in the first 2 spaces provided (i.e., January = "01", February = "02", etc.) enter the 2 digit number for the day of the month in the second 2 spaces provided and the 4 digit number for the year in the final 4 spaces provided.

Note on times:

- EXCEPT WHERE OTHERWISE INDICATED, all times should be recorded in 24 hour or military time, to the hour and minute. For example, 1:30 AM would be 01:30 and 1:30 PM would be 13:30. Use 00:00 for midnight.
- To perform this test, a timer and a clock will be required.

Note on blank spaces and missing values:

- When a result will not completely fill the blank spaces, use a "0" to fill the space.
  Examples
  - ➔ If a result of 592 has space for 4 digits, write in: 0 5 9 2 .
  - ➔ If a result of 3.647 has space for 5 digits, write in: 3 . 6 4 7 0.
- If a sample is not collected or is unable to be used, write in "not collected" or "not available for use" in the space provided for the times.

SECTION B: PATIENT INFORMATION

B1. Weight
- Weigh the patient with clothes on and heavy outerwear and shoes off.
- Record the weight in units (kg or lb) that were used on the measuring instrument. It is not necessary to record both kilograms and pounds.
- Record kilograms to 0.1 kg. Round pounds to the nearest pound.

B2. Height
- Measure height with shoes off and all headgear removed.
- Record the height in units (cm or in) that were used on the measuring instrument. It is not necessary to record both centimeters and inches.
- Round centimeters to the nearest cm. Round inches to the nearest inch.

SECTION C: BASELINE SAMPLES

C1. Record the date the test was performed. Use MM/DD/YYYY format.

Section C Table: This section documents samples drawn prior to the administration of the test compounds. These samples should be drawn 30-60 minutes prior to the baseline administration.

- The first column lists the Question number.
- The second column lists the procedure.
- The third column describes the type of tube and the amount of each sample.
- The fourth column lists the time at which the sample should be collected.
- The fifth column should be completed with the time (24-hour clock) the sample was collected.

C2-C5. Record the 24-hour clock time when each baseline sample was collected.

SECTION D: ADMINISTRATION OF TEST COMPOUNDS

Section D Table: This section records the timer and 24-hour clock times the compounds were administered.

- The first column lists the Question number.
- The second column lists the procedure.
- The third column describes the compound (where applicable).
- The fourth column lists the projected time at which the sample should be collected.
- The fifth column (a) should be completed with the actual timer end time in minutes.
- The sixth column (b) should be completed with the time (24-hour clock) the sample was collected.

D1b. Record the 24-hour clock time when the timer was started before administering test compounds.

D2a-D7a. Record the timed minutes when the procedure was completed.

D2b-D7b. Record the 24-hour clock time when the procedure was completed.

SECTION E: SPECIMEN COLLECTION TIMES

CHOLATE, MEGX, & GALACTOSE (BLOOD)

Section E Table for Blood samples for CHOLATE, MEGX, & GALACTOSE tests: This section documents blood samples drawn following the administration of the test compounds. These samples should be drawn at the defined intervals.

- The first column lists the Question number.
- The second column lists the procedure.
- The third column describes the type of tube and the amount of each sample.
- The fourth column lists the projected time at which the sample should be collected.
- The fifth column (a) should be completed with the actual timer end time in minutes.
- The sixth column (b) should be completed with the time (24-hour clock) the sample was collected.

E1a-E19a. Record the timed minutes when this blood sample was collected.

E1b-E19b. Record the 24-hour clock time when this blood sample was collected.

CAFFEINE & ANTIPYRINE (SALIVA)

Section E Table for Saliva samples for CAFFEINE & ANTIPYRINE tests: This section documents saliva samples to be collected following the administration of the test compounds. These samples should be collected at the defined intervals.

- The first column lists the Question number.
- The second column lists the procedure.
- The third column describes the type of tube and the amount of each sample.
- The fourth column lists the projected time at which the sample should be collected.
- The fifth column (a) should be completed with the projected date in MM/DD/YYYY format for the sample to be collected.
- The sixth column (b) should be completed with the projected time (12-hour clock) for the sample to be collected.
- The sixth column (c) also includes an item to record AM or PM.
- The seventh column (d) should be completed with the actual date in MM/DD/YYYY format that the sample was collected.
- The eighth column (e) should be completed with the actual time (12-hour clock) that the sample was collected.
- The eighth column (f) also includes an item to record AM or PM.

E20a-E25a. Record the projected date the sample should be collected. Use MM/DD/YYYY format.

E20b-E25b. Record the projected time in hours and minutes (12-hour clock) that the sample should be collected. **DO NOT USE MILITARY TIME.**

E20c-E25c. Indicate if this time is AM or PM.
- Circle "1" if this time is from 12:00 Midnight to 11:59 in the morning.
- Circle "2" if this time is from 12:00 Noon to 11:59 in the evening.

E20d-E25d. Record the date the sample was actually collected. Use MM/DD/YYYY format.

E20e-E25e. Record the actual time in hours and minutes (12-hour clock) that the sample was collected. **DO NOT USE MILITARY TIME.**

E20f-E25f. Indicate if this time was AM or PM.
- Circle "1" if this time is from 12:00 Midnight to 11:59 in the morning.
- Circle "2" if this time is from 12:00 Noon to 11:59 in the evening.

SECTION F: BATCH AND LOT NUMBERS

F1-F3. Complete the table using the pharmacy lot and/or batch numbers found on the bottles of solutions B (Galactose), C (Cholate), and the oral compound. If no number is found, write in NA or not applicable.

SECTION G: METHIONINE BREATH TEST – BASELINE SAMPLES

G1. Record the date the test was performed. Use MM/DD/YYYY format.

Section G Table: This section documents breath samples drawn prior to administration of the test compound. These samples should be drawn 5-10 minutes prior to the baseline administration.

- The first column lists the Question number.
- The second column lists the procedure.
- The third column describes the type and number of the breath tube for each sample.
- The fourth column lists the time at which the sample should be collected.
- The fifth column should be completed with the time (24-hour clock) the sample was collected.

G2-G3. Record the 24-hour clock time when each baseline sample was collected.

SECTION H: METHIONINE BREATH TEST – ADMINISTRATION OF TEST COMPOUNDS

Section H Table: This section records the timer and 24-hour clock times the compounds were administered.

- The first column lists the Question number.
- The second column lists the procedure.
- The third column describes the compound (where applicable).
- The fourth column lists the projected time at which the sample should be collected.
- The fifth column (a) should be completed with the actual timer end time in minutes.
- The sixth column (b) should be completed with the time (24-hour clock) the sample was collected.

H1b. Record the 24-hour clock time when the timer was started before administering test compounds.

H2a. Record the timed minutes when the procedure was completed (the time when the patient completed consumption and rinsing of the dose).

H2b. Record the 24-hour clock time when the procedure was completed (the time when the patient completed consumption and rinsing of the dose).

SECTION I: METHIONINE BREATH TEST – SPECIMEN COLLECTION TIMES

Section I Table for Breath samples: This section documents blood samples drawn following the administration of the test compounds. These samples should be drawn at the defined intervals.

- The first column lists the Question number.
- The second column lists the procedure.
- The third column describes the type of tube and the amount of each sample.
- The fourth column lists the projected time at which the sample should be collected.
- The fifth column (a) should be completed with the actual timer end time in minutes.
- The sixth column (b) should be completed with the time (24-hour clock) the sample was collected.

I1a-I16a. Record the timed minutes when this blood sample was collected.

I1b-I16b. Record the 24-hour clock time when this blood sample was collected.

SECTION J: LOT NUMBERS

J1. Complete the table using the lot number found on C-Methionine dose. The lot number can be found on the vial containing the C-Methionine dose located between the caution information and the company address.

HALT-C Trial Q x Q

Quantitative Liver Function Test Results – QLFT AS

Form # 191 Version A: 06/15/2000 (Rev. 11/13/2001)

Purpose of Form #191: This form is used to record the results of the Quantitative Liver Function Tests done for the QLFT Ancillary Study at the University of Colorado Health Sciences Center QLFT Laboratory.

When to complete Form #191: This form is completed for all patients participating in the QLFT Ancillary Study at the following clinical sites.

- Site 14 (University of Colorado Health Sciences Center).
- Site 15 (University of California - Irvine).
- Site 19 (Virginia Commonwealth University).

The QLFT laboratory should complete and data enter form #191 for patients at the following study visits:

- Lead-In Phase patients: Baseline visit (W00)
- Express patients: Randomization visit (R00)
- Randomized patients: Month 24 (M24) and Month 48 (M48).

How to access Form #191: Data entry of this form will take place only at the University of Colorado Health Sciences Center QLFT Laboratory. In order to data enter Form #191, NERI must set up a special data entry account for your user name.

In order to access Form #191, log on to the HALT-C Production Data Management System (DMS). From the main menu, select "Central Lab D E". Then select "Enter Form 191". Enter the HALT-C patient ID number and the visit number in the appropriate boxes. Click the "Submit" button. A data entry screen for Form #191 will appear.

→ The patient ID will begin with 14 (UCHSC), 15 (UCI), or 19 (VCU).
→ Valid visit numbers are W00, R00, M24, and M48.

After you have data entered the entire form, it will be saved in the system. You may perform edits to the form by following the same directions above for the given patient.

Note on form completion and data entry:

- Forms must be competed in black ink. Pencil is not acceptable. Blue ink does not photocopy well.

- Corrections are made by drawing a single line through the errant data and writing in the correct data. You must initial and write the date you make any change.

- When a result will not completely fill the blank spaces, use a "0" to fill the space.
  → If a result of 592 has space for 4 digits, write in: 0 5 9 2
  → If a result of 3.647 has space for 5 digits, write in: 3 . 6 4 7 0

- If data was not collected or not analyzed, the data collector should write a concise explanation including her/his initials and the date on the hard copy of the form. When

data entering the form, enter the special value "-9" in the DMS. An error message will now appear on your screen.

- If the value will never be obtained in the future, type the explanation in the "Reason" box. Enter the data collector's initials in the space provided and click on the "Set Override" button.

- If the value may be obtained in the future, click on the "Ignore Value" button. An edit report will be generated after the rest of the form is entered. The form will have a "Pending Edits" status until the value is completed and data entered, or determines to be unobtainable and an override "Reason" provided.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed using MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: TEST RESULTS

B1. Enter the date the assay was done in MM/DD/YYYY format.
- Indicate the results of the cholate kinetic studies using the following units:
  B1a. K elimination in min-1
  B1b. V distribution in L/kg
  B1c. IV clearance in ml/min
  B1d. PO clearance in ml/min
  B1e. Shunt fraction in %

B2. Enter the date the assay was done in MM/DD/YYYY format.
- Indicate the results of the antipyrine clearance studies using the following units:
  B2a. K elimination in hr-1
  B2b. V distribution in L/kg
  B2c. Clearance in ml/min

B3. Enter the date the assay was done in MM/DD/YYYY format.
- B3a. Indicate the result of the caffeine clearance study in hr-1.

B4. Enter the date the assay was done in MM/DD/YYYY format.
- B4a. Indicate the result of the galactose clearance study in mg/min.kg.

B5. Enter the date the assay was done in MM/DD/YYYY format.
- Indicate the results of the Lidocaine/MEGX study using the following units:
  B5a. 15 Min – Base in ug/L.
  B5b. 30 Min – Base in ug/L.

HALT-C Trial Q x Q

SPECT Scan – QLFT AS

Form # 192 Version A: 06/15/2000 (Rev. 04/04/2003)

Purpose of Form #192: This form is used to record the results of the SPECT liver-spleen scan as determined by the University of California – Irvine SPECT scan reading center.

When to complete Form #192: This form is completed for all patients participating in the QLFT Ancillary Study at the following clinical sites.

- Site 14 (University of Colorado Health Sciences Center).
- Site 15 (University of California - Irvine).
- Site 19 (Virginia Commonwealth University).

The SPECT scan reading center should complete and data enter form #192 for patients at the following study visits:

- Lead-In Phase patients: Baseline visit (W00)
- Express patients: Randomization visit (R00)
- Randomized patients: Month 24 (M24) and Month 48 (M48).

How to access Form #192: Data entry of this form will take place only at the University of California – Irvine SPECT scan reading center. In order to data enter Form #192, NERI must set up a special data entry account for your user name.

In order to access Form #192, log on to the HALT-C Production Data Management System (DMS). From the main menu, select "Central Lab D E". Then select "Enter Form 192". Enter the HALT-C patient ID number and the visit number in the appropriate boxes. Click the "Submit" button. A data entry screen for Form #192 will appear.

→ The patient ID will begin with 14 (UCHSC), 15 (UCI), or 19 (VCU).
→ Valid visit numbers are W00, R00, M24, and M48.

After you have data entered the entire form, it will be saved in the system. You may perform edits to the form by following the same directions above for the given patient.

Note on form completion and data entry:

- Forms must be competed in black ink. Pencil is not acceptable. Blue ink does not photocopy well.

- The DMS has been programmed to expect specific ranges for the values of its data. If the obtained value falls outside of this range, however, it should still be recorded on the paper form and data entered. Upon entering an out of range value in the DMS, a data entry validation error screen will appear. If the value originally entered by the user is the actual obtained value and matches the value recorded on the paper, then this problem value may be overridden. In order to override the value, explain your reasons for doing so in the space provided (e.g., "This is the correct value."), and enter your initials in the appropriate box. Then click on the button to "Set Override".

- Corrections are made by drawing a single line through the errant data and writing in the correct data. You must initial and write the date you make any change.

- When a result will not completely fill the blank spaces, use a "0" to fill the space.
  → If a result of 592 has space for 4 digits, write in: 0 5 9 2
  → If a result of 3.647 has space for 5 digits, write in: 3 . 6 4 7 0

- If data was not collected or not analyzed, the data collector should write a concise explanation including her/his initials and the date on the hard copy of the form. When data entering the form, enter the special value "-9" in the DMS. An error message will now appear on your screen.

- If the value will never be obtained in the future, type the explanation in the "Reason" box. Enter the data collector's initials in the space provided and click on the "Set Override" button.

- If the value may be obtained in the future, click on the "Ignore Value" button. An edit report will be generated after the rest of the form is entered. The form will have a "Pending Edits" status until the value is completed and data entered, or determines to be unobtainable and an override "Reason" provided.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed using MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: SPECT SCAN

B1. Enter the date the SPECT scan test was performed in MM/DD/YYYY format.

B2. Record ROI's around the summarized transaxial SPECT LSS for Total Liver Counts.
- The expected range is range is $1.00 \times E^6 – 1.00 \times E^7$ CPM.

B3. Record ROI's around the summarized transaxial SPECT LSS for Total Spleen Counts.
- The expected range is range is $1.00 \times E^5 – 4.00 \times E^7$ CPM.

B4 Record ROI's around the summarized transaxial SPECT LSS for Total BM Counts.
- The expected range is $2.00 \times E^3 – 2.00 \times E^6$ CPM.

B5. Record the number of frames.
- The number of frames can be no fewer than 20 and no greater than 60.

B6. Record the Pixel Counts on the posterior planar LSS for the hottest area over the liver.
- The pixel count can be no fewer than 30 CPM and no greater than 700 CPM.

B7. Record the Pixel Counts on the posterior planar LSS for the hottest area over the spleen.
- The pixel count can be no fewer than 30 CPM and no greater than 700 CPM.

B8. Record the Pixel Counts of Bone Marrow.
- The pixel count can be no fewer than 2 CPM and no greater than 70 CPM.

B9. Record the Liver Right Lobe Length.
- The length can be no fewer than 10.0 CM and no greater than 40.0 CM.

B10. Record the Liver Left Lobe Length.
- The length can be no fewer than 6.0 CM and no greater than 30.0 CM.

B11. Record the Spleen Length.
- The length can be no less than 0.0 CM and no greater than 30.0 CM.

Note on Questions B12 – B17:
The expected range for these questions is 1000 – 5000 CPM/Voxel.

B12. Record the Large ROI Maximum Concentration Liver.

B13. Record the Large ROI Mean Concentration Liver.

B14. Record the Standard Deviation (SD) for Large ROI Liver.

B15. Record the Large ROI Maximum Concentration Spleen.

B16. Record the Large ROI Mean Concentration Spleen.

B17. Record the Standard Deviation (SD) for Large ROI Spleen.

Note on Questions B18 – B23:
The expected range for these questions is 100 – 5000 CPM/Voxel.

B18. Record the Liver Small ROI Mean for probe 1.

B19. Record the Liver Small ROI Max for probe 1.

B20. Record the Liver Small ROI Mean for probe 2.

B21. Record the Liver Small ROI Max for probe 2.

B22. Record the Liver Small ROI Mean for probe 3.

B23. Record the Liver Small ROI Max for probe 3.

Note on Questions B24 – B29:
The expected range for these questions is 50 – 1000 CPM/Voxel.

B24. Record the Spleen Small ROI Mean for probe 1.

B25. Record the Spleen Small ROI Max for probe 1.

B26. Record the Spleen Small ROI Mean for probe 2.

B27. Record the Spleen Small ROI Max for probe 2.

B28. Record the Spleen Small ROI Mean for probe 3.

B29. Record the Spleen Small ROI Max for probe 3.

B30. Record the Voxel length/side (mm).
- The Voxel length/side value can be no less than 0.01 mm and no greater than 9.99 mm.

SECTION C:

The calculations from the SPECT scan data can be accessed through the AS Reports menu item on the DMS by clicking on Main Menu\ AS Reports\QLFT Study\ SPECT Scan Calculations.

HALT-C Trial Q x Q

QLFT AS Aliquot Form

Form # 193 Version A: 06/15/2000 (Rev. 06/30/2004)

Purpose of Form #193: The QLFT AS Aliquot form should be used to detail the specimens collected for the QFLT AS that will be sent to the Central Repository (BBI). This form should be completed in addition to the aliquot form specific for the regular study visit.

Data entry of this form for a patient visit is the first step of the shipping and tracking procedures for HALT-C. All of the specimens will go into a database of specimens available for shipment to the Central Repository for your clinical center. Entry of this form also allows NERI to link the HALT-C Trial ID's and study visits with the Sample ID assigned by the Central Repository.

When to complete Form #193: This form is completed for all patients participating in the QLFT Ancillary Study at the following clinical sites.

- Site 15 (University of California - Irvine).
- Site 19 (Virginia Commonwealth University).

The clinical centers should complete and data enter form #193 for patients at the following study visits:

- Lead-In Phase patients: Baseline visit (W00)
- Express patients: Randomization visit (R00)
- Randomized patients: Month 24 (M24) and Month 48 (M48).

Form #193 is not completed for specimens collected at the Site 14 (University of Colorado Health Sciences Center) because these specimens are not shipped to the BBI Repository.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed using MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: BSI ID

B1. Record the BSI ID from the aliquot tube. The BSI ID begins with the letter "D", followed by a second letter corresponding to the study site, followed by six numbers. The BSI ID is used by NERI and BBI to identify specimens by patient and study visit.

The BSI ID also appears on the shipping manifest received from the BBI Repository in the column named "bsi_id". On the shipping manifest, the BSI ID is followed by a three-digit sequence number, which does not need to be recorded on the paper form.

B2. Record the date of the specimen collection using the MM/DD/YYYY format. This must be the same date that the specimen was aliquotted and frozen.

SECTION C: SPECIMEN INFORMATION

C1. Please indicate if there were any problems or delays in specimen processing in C1.
- If there was a delay of > 4 hours or problems with specimen processing, circle 1 for "Yes".
- If serum was separated within 2-4 hours of collection with no problems, circle 2 for "No".

C2. If the answer for C2a is "No", circle 2 and skip to the sequence number in the next row. If the answer for C2a is "Yes", circle 1 and follow the directions below.

If C1 = 1 (Yes) and C2a = 1 (Yes)
- Columns C2b, C2c, and C2d must be completed.
- Column C2b must list the total volume in ml of the sample in the cryovial.
- Column C2c must list one of the codes for specimen processing listed in the box below.
- Column C2d must list the data that processing of the sample was completed.

If C1 = 2 (No) and C2a = 1 (Yes)
- Only Column C2b must be completed. Enter the total volume in ml of the sample in the cryovial.

Codes for specimen processing

1. okay
2. hemolysis
3. delay in processing-processed within 4-6 hours of collection
4. delay in processing-processed within 6-8 hours of collection
5. delay in processing-processed within 8-12 hours of collection
6. delay in processing-processed within 12-18 hours of collection
7. delay in processing-processed within 18-24 hours of collection
8. delay in processing-processed within 24-48 hours of collection
9. delay in processing-processed 48+ hours after collection
10. delay in shipping
11. collected in incorrect tube-plasma collected instead of serum
12. delay in snap freezing liver tissue
13. Vacutainer tube stored in refrigerator
99. Other-please specify

HALT-C Trial Q x Q

QLFT AS Withdrawal Form

Form # 194 Version A: 06/15/2000

Purpose of Form #194: The QLFT AS Withdrawal form documents which patients have withdrawn from the study and the reason for doing so. Additionally, data entry of this form removes relevant study forms from future visits in the DMS.

When to complete Form #194: This form should be completed upon withdrawal of a patient from the QLFT study. This form can be added to any study visit by clicking on the "Additional Forms" button on the study visit screen.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Record the date the form was completed using MM/DD/YYYY format.

A4. Enter the initials of the person completing the form.

SECTION B: WITHDRAWAL INFORMATION

B1. Record the date that the patient withdrew from the QLFT study using MM/DD/YYYY format.

B2. Circle the primary reason why the patient withdrew from the QLFT ancillary study. If the reason is not listed, circle "99" for OTHER and specify a reason (sixty characters including spaces and punctuation are available).

B3. Please enter any additional information regarding the patient's withdrawal from this study in as much detail as necessary (two hundred fifty characters including spaces and punctuation are available). If there is not additional information, record "Not applicable" on the paper form and data enter "-1" in the HALT-C Data Management System (DMS).

HALT-C Trial Q x Q

QLFT AS – Methionine Breath Test Aliquot Form

Form # 195 Version A: 06/15/2000 (Rev. 06/30/2004)

Purpose of Form #195: This form should be used to record the specimens collected from the Methionine Breath Test for the QFLT AS that will be sent to the Central Repository (BBI).

Data entry of this form for a patient visit is the first step of the shipping and tracking procedures for HALT-C. All of the specimens will go into a database of specimens available for shipment to the Central Repository for your clinical center. Entry of this form also allows NERI to link the HALT-C Trial ID's and study visits with the Sample ID assigned by the Central Repository.

When to complete Form #195: This form is completed for all patients participating in the QLFT Ancillary Study at the following clinical sites.

- Site 14 (University of Colorado Health Sciences Center).
- Site 15 (University of California - Irvine).
- Site 19 (Virginia Commonwealth University).

The clinical centers should complete and data enter form #195 for patients at the following study visits:

- Lead-In Phase patients: Baseline visit (W00)
- Express patients: Randomization visit (R00)
- Randomized patients: Month 24 (M24) and Month 48 (M48).

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the ID number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the form was completed using MM/DD/YYYY format.

A5. Enter the initials of the person completing the form.

SECTION B: SAMPLE ID

B1. Record the BSI ID from the aliquot tube. The BSI ID begins with the letter "D", followed by a second letter corresponding to the study site, followed by six numbers. The BSI ID is used by NERI and BBI to identify specimens by patient and study visit.

The BSI ID also appears on the shipping manifest received from the BBI Repository in the column named "bsi_id". On the shipping manifest, the BSI ID is followed by a three-digit sequence number, which does not need to be recorded on the paper form.

B2. Record the date of the breath specimen collection using the MM/DD/YYYY format.

SECTION C: SPECIMEN INFORMATION: BREATH

For each of the sequence numbers listed on the form (30 – 37), record if the specimen was collected.

- If "YES", then circle 1.
- If "NO", then circle 2.

HALT-C Trial Q x Q

CTL Serum Aliquot Form

Form #270 Version A: 06/15/2000 (Revised 07/10/2003)

Purpose of Form #270: The CTL Serum Aliquot form documents the fresh serum that is being sent to Dr. Margaret Koziel's or Dr. Alan Rothman's CTL laboratories for the Cytotoxic T Lymphocyte sub-study of the Immunology/Virology Ancillary Study.

When to complete Form #270: Form #270 should be completed for serum collected at the Screening (S00) study visit. This form is completed following processing and aliquoting of CTL serum specimens at the following clinical sites. Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible.

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 12 (Saint Louis University).
- Site 16 (University of Texas Southwestern).
- Site 17 (University of Southern California).

Form #270 is data entered at the clinical sites. Data entry of Form #270 must be done prior to shipment of fresh serum to the CTL laboratories. Data entry of this form allows the receiving laboratory and the DCC to track the shipment and receipt of the specimens.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the patient number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit (S00).

A4. Record the date the specimen was collected and shipped in MM/DD/YYYY format.

A5. Record the initials of the person completing the form.

SECTION B: COLLECTION DATE

B1. Record the date of the blood draw in MM/DD/YYYY format. The samples must be processed and shipped on the same date as the blood draw. Shipments must be sent via overnight Federal Express at room temperature.

SECTION C: SPECIMEN INFORMATION

C1. Up to five 10 ml EDTA Vacutainer tubes can be prepared with fresh serum stored at room temperature. For each tube, fill out one row of the table.

If the answer for C1a is "Yes", circle 1 and complete Column C1b. Enter the total volume of the sample in the Vacutainer tube in ml. If the answer for C1a is "No", circle 2 and skip to the next row. If you are on the final row, the Form is complete.

Shipping and Receiving Procedures: When you have data entered Form #270 and are ready to prepare the CTL fresh serum shipment; the specimens will appear in the LP/CTL Shipment Database as being available for shipment. The LP/CTL shipping database is similar to the Main Trail shipping database. Please refer to section C (Specimen Shipping and Tracking) in the Manual of Operations (MOO) for complete information on general use of the HALT-C shipping database. The serum must be batch shipped at ambient temperature to the designated laboratory.

When the CTL shipment has been successfully finalized in the DMS, an automated email is sent to the receiving Laboratory and the DCC. The subject heading for this email will read: ***Site 1X HALTC Automate Specimen Tracking batch#000 type: CTL Serum***.

The receiving laboratory **must Reply All** to the automated email informing NERI and shipping clinical site that the shipment has been received. The subject heading should be changed to read: ***Batch #: 000: type; serum; received MM/DD/YYYY; condition OK***.

HALT-C Trial Q x Q

CTL Liver Aliquot Form

Form #271 Version A: 06/15/2000

Purpose of Form #271: The CTL Liver Aliquot form documents the liver that is being sent to Dr. Margaret Koziel's or Dr. Alan Rothman's CTL laboratories for the Cytotoxic T Lymphocyte sub-study of the Immunology/Virology Ancillary Study.

When to complete Form #271: This form is completed following processing and aliquoting of Immunology/Virology Ancillary Study specimens at the following clinical sites. Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible.

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 12 (Saint Louis University).
- Site 16 (University of Texas Southwestern).
- Site 17 (University of Southern California).

Form #271 should be completed when fresh liver tissue is collected for the CTL sub-study at the Screening (S00), Month 24 (M24), and Month 48 (M48) study visits.

Form #271 is data entered at the clinical sites. Data entry of Form #271 must be done prior to shipment of fresh liver to the CTL laboratories. Data entry of this form allows the receiving laboratory and the DCC to track the shipment and receipt of the specimens.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the patient number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the specimen was collected and shipped in MM/DD/YYYY format.

A5. Record the initials of the person completing the form.

SECTION B: COLLECTION DATE

B1. Record the date of the liver biopsy in MM/DD/YYYY format. The fresh liver sample must be processed and shipped in media on the same date as the biopsy. Shipments must be sent via overnight Federal Express.

SECTION C: SPECIMEN INFORMATION

C1. If liver was collected for the CTL sub-study, the answer for C1a is "Yes". Circle 1 and complete Column C1b. Enter the total length of the sample cm.

If liver was not collected for the CTL sub-study, the answer for C1a is "No". Circle 2 and the Form is complete.

Shipping and Receiving Procedures: When you have data entered Form #271 and are ready to prepare the CTL fresh liver shipment; the specimens will appear in the LP/CTL Shipment Database as being available for shipment. The LP/CTL shipping database is similar to the Main Trail shipping database. Please refer to section C (Specimen Shipping and Tracking) in the Manual of Operations (MOO) for complete information on general use of the HALT-C shipping database. The liver must be batch overnight shipped in media at ambient temperature to the designated laboratory.

When the CTL shipment has been successfully finalized in the DMS, an automated email is sent to the receiving Laboratory and the DCC. The subject heading for this email will read: ***Site 1X HALTC Automate Specimen Tracking batch#000 type: CTL Liver***.

The receiving laboratory **must Reply All** to the automated email informing NERI and shipping clinical site that the shipment has been received. The subject heading should be changed to read: ***Batch #: 000: type; Liver; received MM/DD/YYYY; condition OK***.

HALT-C Trial Q x Q

LP Aliquot Form

Form #273 Version A: 06/15/2000

Purpose of Form #273: The LP Aliquot form documents the blood that is being sent to the Lymphoproliferation laboratory at the University of Washington for the Lymphoproliferation sub-study of the Immunology/Virology Ancillary Study.

When to complete Form #273: This form is completed following processing and aliquoting of Immunology/Virology Ancillary Study specimens at the following clinical sites. Lead-In patients are eligible for this Ancillary Study. Express patients are not eligible.

- Site 11 (University of Massachusetts / University of Connecticut).
- Site 12 (Saint Louis University).
- Site 16 (University of Texas Southwestern).
- Site 17 (University of Southern California).

Form #273 should be completed for fresh blood collected at the following study visits:

- Baseline (W00), Week 24 (W24), Breakthrough/Relapse Randomization Visit (R00), Month 12 (M12), Month 24 (M24), Month 36 (M36), Month 48 (M48), and Month 54 (M54) study visits.

Form #273 is data entered at the clinical sites. Data entry of Form #273 must be done prior to shipment of fresh blood to the LP laboratory. Data entry of this form allows the receiving laboratory and the DCC to track the shipment and receipt of the specimens.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided.
- If the label is not available, record the patient number legibly.

A2. Enter the patient's initials exactly as recorded on the Trial ID Assignment form.

A3. Enter the three-digit code corresponding to this visit.

A4. Record the date the specimen was collected and shipped in MM/DD/YYYY format.

A5. Record the initials of the person completing the form.

SECTION B: COLLECTION DATE

B1. Record the date of the blood draw in MM/DD/YYYY format. The fresh blood samples must be processed and shipped on the same date as the blood draw. Shipments must be sent via overnight Federal Express at room temperature.

SECTION C: SPECIMEN INFORMATION

C1. Up to five 8.5 ml ACD Vacutainer tubes can be prepared with fresh blood stored at room temperature. For each tube, fill out one row of the table.

If the answer for C1a is "Yes", circle 1 and complete Column C1b. Enter the total volume of the sample in the Vacutainer tube in ml. The possible range is 01.0 to 10.0 ml.

If the answer for C1a is "No", circle 2 and skip to the next row. If you are on the final row, the form is complete.

Shipping and Receiving Procedures: When you have data entered Form #273 and are ready to prepare the LP fresh blood shipment; the specimens will appear in the LP/CTL Shipment Database as being available for shipment. The LP/CTL shipping database is similar to the Main Trail shipping database. Please refer to section C (Specimen Shipping and Tracking) in the Manual of Operations (MOO) for complete information on general use of the HALT-C shipping database. The serum must be batch shipped at ambient temperature to the designated laboratory.

When the CTL shipment has been successfully finalized in the DMS, an automated email is sent to the receiving Laboratory and the DCC. The subject heading for this email will read: ***Site 1X HALTC Automate Specimen Tracking batch#000 type: LP Blood***.

The receiving laboratory **must Reply All** to the automated email informing NERI and shipping clinical site that the shipment has been received. The subject heading should be changed to read: ***Batch #: 000: type; LP blood; received MM/DD/YYYY; condition OK***.