HALT-C Screening Phase

Lead-in Group Screening Introduction
To be screened for the HALT-C Trial entering through the Lead-in Phase, patients must have chronic hepatitis C and have been non-responders to their most recent course of interferon treatment prior to entry into the Screening Phase. The treatment must have lasted at least 12 weeks. For detailed information on inclusion/exclusion criteria, please see sections E, F, and G of the HALT-C protocol.

The Screening Phase is divided into Pre-Screening, Screening Visit 1, and Screening Visit 2. The purpose of these visits is to collect information to ensure that the patient is eligible to participate in the study. Further information on the screening phase can be found in Section G of the HALT-C protocol.

Lead-in Group Pre-Screening:
All patients with the above criteria should be screened for eligibility for the HALT-C Trial. The documentation of all potentially eligible patients is important for the HALT-C Trial database. It will provide a comparison of patients enrolled in the HALT-C Trial with those patients with hepatitis C and a history of previous interferon treatment that failed to induce a response.

Patients considered for the HALT-C Trial should be documented on the Screening Log and assigned the next sequential HALT-C patient ID number. The Screening Log also provides space for the patient's name, initials, and date of birth. The Screening Log sheet is the only document which links the patient's name to the HALT-C patient ID number. Therefore, the Screening Log is not data entered. Keep this document in a locked storage compartment (such as a file cabinet or desk drawer) and limit access to appropriate study personnel.

HALT-C patient ID numbers consist of six digits. The first two identify the clinical site. The next three represent the specific patient at that site. The final digit is a computer assigned check digit designed to catch data entry errors.

The following forms are used during Pre-Screening:

- Form #1: Trial ID Assignment. This form is used to enter a new patient into the HALT-C Data Management System, and assigns the patient ID from the screening log to the patient, thus linking the assigned ID number with the patient initials. If the patient is eligible for the trial, store Form #1 with the other data forms, which will be entered for screening. If the patient is not eligible, Form #1 can be stored separately. For re-screened patients, complete a second Form #1 using the newly assigned patient ID number.

- Form #5: Trial Ineligibility. This form must be completed for all patients found to be ineligible for the HALT-C Trial during the pre-screening and/or screening phase. Store these forms with their appropriate form #1.

Lead-in Group Screening Visit 1 (S00):
Once it is determined that the patient should be screened for eligibility, proceed to Screening Visit 1.

Informed consent
Prior to collecting any information for Screening Visits 1 and 2, the patient **MUST** sign the screening consent form (or the main trial consent form if there is no separate screening

consent form). Data collected prior to the signing of the consent will be considered invalid. The exception will be tests which may have been done for clinical reasons or other research studies, and are specifically identified by the protocol as being acceptable if done prior to the start of the study, such as liver biopsy, ultrasound and endoscopy.

The appropriate medical personnel must sign all consent forms. All signatures should be dated. Offer the patient a copy of the consent according to your institutional procedure. Also follow institutional procedure regarding the placement of the consents in the medical or other record. Keep all signed consents forms together in a binder labeled HALT-C Consent Forms or with the patient's data forms as long as the data form binders are kept in a storage area that can be locked and to which access is limited. These consent forms should be made available to Data Coordinating Staff (DCC) during site visits.

Packets of data forms for each screening visit and patient ID number labels will be provided by the DCC. Each patient should have a binder notebook for forms. The binder should be labeled with the patient ID. There should be nothing on the data forms, or source documents (which will be sent outside the clinical site) with any information (such as patient name or medical record number) that could identify the patient. Binders should be stored in a room or other storage space that can be locked. Access should be limited to appropriate personnel.

Visit Control Sheet

A Visit Control Sheet (VCS) should be printed prior to the first screening visit and will detail all the required tests and forms for both screening visits. For information on how to print the VCS, please see the Data Management section.

Once the screening consent is signed, the patient may begin Screening Visit 1. The patient should be fasting for required lab tests. The following tests, interviews, and forms are done during Screening Visit 1:

Patient administered questionnaires

- QOL (Form #40)
- Symptoms (Form #43)

Interviews

- Screening Medical History (Form #3) Question E1, answer Lead-in.
- Baseline History (Form #6)

Tests

- History and physical (Form #11)

Local Lab tests (Forms #30, 34)

- Fasting serum chemistries (BUN, creatinine, glucose, uric acid, triglycerides)
- Liver chemistries (AST, ALT, alkaline phosphatase, total bilirubin, albumin, and globulin [or total protein])
- Complete blood count with differential (WBC, neutrophils, hematocrit, hemoglobin, platelets
- Prothrombin time (INR)
- AFP (Form #34)

Central Lab tests (Form #31, 70)

- HCV-RNA (sent to the Central Repository for shipping to the Central Virology lab. See Section E, Specimen Collection, Processing and Shipping for further details.) An email will be sent to the site automatically, once the results are available from the Central Virology Lab. Results can also be seen in the DMS under Form #31.

Eligibility Worksheet (optional)
The Eligibility Worksheet may be used to assist clinicians in ensuring that patients meet the eligibility criteria for the trial. It lists each inclusion/exclusion criteria. This is not data entered, but strongly recommended as a guide.

Pre-existing Conditions (optional)
The Pre-existing Conditions Form may be used to assist clinicians in keeping track of those medical conditions that the patient had before the trial started. Knowing the pattern of a condition, such as migraine headaches, will be helpful when determining if an event is a pre-existing condition or an adverse event.

Forms
- Form #3, Screening Medical History
- Form #6, Baseline History
- Form #11, Physical Exam
- Form #15, CTP score (or can be done at Screening Visit 2)
- Form #30, Local Lab
- Form #31, Central Lab (results sent via email to clinical center; form data entered at the Central Virology Lab).
- Form #34, AFP
- Form #40, Quality of Life
- Form #43, Symptoms
- Form #70, Screening 1 Aliquot Form
- Form #121 Glycosylated Hemoglobin (patients with diabetes mellitus, only)
- Form #181 Histopathology

Special considerations for patients with previous neuropsychiatric issues:
Any eligible patients who have had a history of severe or dose limiting neuropsychiatric toxicity during prior interferon treatment will be referred to a consulting psychologist or psychiatrist for further evaluation and possible treatment. Patients who have had a suicide attempt and/or hospitalization for depression more than 5 years ago and any patients who have had severe or poorly controlled psychiatric disorders (e.g. depression, schizophrenia, bipolar illness, obsessive-compulsive disorder, severe anxiety, personality disorder) more than 6 months ago but less than 5 yeas ago must be assessed and followed (if recommended) by a psychiatrist or other mental health professional. (See Section B4, Management Guidelines for further details).

Lead-in Group Screening Visit 2 (S00):
The patient may proceed to the Screening Visit 2 if the criteria for Screening Visit 1 were met. The patient should be fasting for the liver biopsy and ultrasound. The following tests, interviews, and forms are used during Screening Visit 2:

Patient administered questionnaires
- Composite International Diagnostic Interview (CIDI): This survey asks questions regarding the patient's history of drug and alcohol use, anxiety and depression. See Section Q for

further details. The CIDI is optional at sites that have limited clinical resources or if the patient is unable to read or understand English.
- Block Food Frequency Questionnaire: This questionnaire should be given to patients to take home with them following the Screen 2 visit. It should be brought back to the W00 visit. It must be filled out with a #2 pencil. See Section P for further details.

Interview Forms
- Skinner (Form #41)

Tests
- Liver biopsy (Forms #14, 50). The liver biopsy must have been done within the last 12 months before the baseline visit (W00). Ten unstained biopsy slides must be obtained from Pathology and shipped to the Data Coordinating Center. Please see Section G, Pathology for further information.

- Ultrasound (MRI, CT) (Form #22). The ultrasound must have been done in the last 6 months. If an MRI, or CT has been done within the last 6 months, these tests may be substituted for the ultrasound using the same Form #22. Please see Section R of the MOO for further information.

Local Lab Tests (Form #35, #4)
- Pregnancy test (dipstick) for all women of child bearing potential
- Urine dip for protein and heme
- Liver chemistries (AST, ALT, alkaline phosphatase, total bilirubin, albumin, globulin [or total protein])
- Thyroid stimulating hormone (TSH)
- HIV test
- Hepatitis B surface antigen
- ANA
- Ceruloplasmin
- Alpha-1 antitrypsin

Central Lab Tests (Form #71)
- 20 cc in ACD vacutainer tube for EBV to be shipped overnight. (Not to be drawn if patient does not consent to genetic testing.)
- 20 cc in ACD vacutainer tube for PBMC to be shipped overnight.

Forms
- Form #4, Screening Checklist (should not be entered until all data is collected and screening is complete)
- Form #14, Specimen Collection (to be completed even if liver biopsy is not done during Screening)
- Form #15, CTP score (or can be done at Screening Visit 1)
- Form #22, Ultrasound, MRI, CT (or can be done at Screening Visit 1)
- Form #35, Screening Visit 2 Local Lab
- Form #41, Skinner
- Form #50, Screening Biopsy Evaluation
- Form #51, Central Review of Biopsy (data entered at the Data Coordinating Center)
- Form #71, Screening 2 Aliquot Form
- Beck Depression Inventory (BDI II) (Form #44) See Depression Management Guidelines, Section B4 for details.

Adequate contraception

All patients enrolled in the HALT-C Trial must be willing to use contraception as indicated by the protocol. Please see Section D5, Adequate Contraception, for details.

Lead-in Group Screening Phase Completion:
If the Lead-In Group patient completes Screening Visit 1 and Screening Visit 2 and is eligible for the trial, the following should be done:

Sign informed consent for HALT-C Trial
The informed consent for participation in the HALT-C Trial must be signed and stored in the manner described above.

Genetic testing
The informed consent for participation in Genetic Testing must be signed and stored in the manner described above. If a patient does not wish to participate in this part of the HALT-C Trial, do not collect the EBV specimens at Screen Visit 02. If, by error, the EBV is collected and the patient did not consent, contact the DCC so that the Repository can be notified to destroy that specimen. A record of verification of destruction of said sample should be kept in the patient's notebook.

Ancillary studies
Discuss appropriate ancillary studies with the patient and have them sign consent forms as appropriate. Consents should be stored in the manner described above. Please see Section K for more information on ancillary studies.

Forms
- Form #4: Screening Checklist. This is the final form completed during the Screening Phase. This form provides a formal check off for the study personnel, verifying that the required steps have been taken prior to enrolling a patient into the Lead-in Phase of the HALT-C Trial and ensuring patient eligibility for enrollment into the HALT-C Trial.

- Form #5: Trial Ineligibility. If a patient has been deemed ineligible for any reason, complete this form. Indicate the reason for ineligibility. This form ends the screening process. This form should be completed at any time the patient becomes ineligible after entry of Form #1: Trial ID Assignment through the Baseline visit (W00), prior to the dispensation of trial medication. **Do not use this form if the patient has taken trial medication.**

Next phase: Lead-in Phase
If a Lead-in Group patient is eligible for the trial, the informed consent has been signed, and the Screening Checklist (Form #4) completed, the patient may proceed to the Lead-in Phase. The baseline visit must be within 14 weeks of the Screening Visit 1.

Lead-in Group Re-Screening:
If the patient has a SINGLE aberrant laboratory value, that test may be repeated within 4 weeks of the initial test. If the new test result meets the eligibility criteria, it may be used for screening purposes. If the repeated test does not meet eligibility criteria, an Exemption Request may be submitted to the Exemption Committee or follow the re-screening procedures outlined below. Patients with more than one aberrant laboratory value must go through the re-screening procedures. Patients can be re-evaluated no more than twice at intervals of no less than 2 months (i.e., a patient may go through the Screening process 3 times.) Patients who have received trial medication are eligible for re-screening, at the PI's discretion, only after the mandatory washout period.

Procedures for Re-screening

ID numbers

- At re-screening, patients are assigned a new ID number.
- Complete Form #1 (Version B or higher), using the new ID number in Section A. Question B0 asks for the old ID number. This will link the two numbers in the DMS.
- The patient's initials may change at this time. If the patient's initials have changed since the previous screening visit, use the new initials.

Informed Consent

Prior to collecting any information for re-screening visits 1 and 2, the patient **MUST** sign a new consent form, even if they have already done so during the previous screening.

Re-Screening Visit 1
Re-screening tests should be performed and forms filled out according to the same schedule as those at original screening visits. Exceptions and special cases are noted with an asterisk below.

Tests

- Local Labs:
- LFTs (AST, ALT, alkaline phosphatase, total bilirubin, total protein or globulin, albumin)
- Fasting chems (BUN, creatinine, glucose, triglycerides)
- CBC with differential and platelets
- Uric acid
- Serum ferritin, serum iron, serum iron binding capacity
- *Serological assays--if the results of these assays are not available (ANA, ceruloplasmin, alpha 1 antitrypsin)
- *HIV and Hepatitis B surface antigen--if they have not been done within the past year of this present screen visit #1.
- Prothrombin time
- AFP
- Glycosylated hemoglobin (for diabetic patients only)
- Central Labs: HCV-RNA
  *Whole blood for EBV transformation does not need to be collected at Screen #1 if previously collected.
- Physical Exam: Must be repeated

Forms

- Form #1: Trial ID Assignment: Must be repeated. Use Version B or higher.
- Form #3: Screening Medical History: Must be repeated
- Form #11: Physical Exam: Must be repeated
- Form #15: CTP Score: Must be repeated

- Form #30: Local Labs: Must be repeated
- Form #31: Central Lab-HCV RNA: Must be repeated (Sites receive email of results and form is entered by Central Lab into DMS.)
- Form #34: AFP: Must be repeated
- Form #40: QOL: Must be repeated
- Form #43: Symptoms: Must be repeated
- Form #70: Screening Visit 1 Aliquot: Must be repeated

Re-Screening Visit 2

Tests

- Local Labs:
- LFTs (AST, ALT, alkaline phosphatase, total bilirubin, total protein or globulin, albumin)
- TSH
- Urinalysis for heme and protein
- Pregnancy test (for women of childbearing potential)
- *Biopsy: Must be repeated if outside the screening window [12 months prior to re-screening baseline visit (W00)]
- *Ultrasound (MRI, CT): Must be repeated if outside the screening window (6 months prior to re-screening visit 1) or previously led to the patient's exclusion.

Forms

- Form #4: Screening Checklist: Must be repeated
- *Form #6: Baseline History: Does not need to be repeated.
- Form #14: Specimen Collection: Must be repeated if liver biopsy is needed.
- *Form #22: Ultrasound (MRI, CT): Must be repeated if test was outside the screening window (6 months prior to screening visit 1) or previously led to the patient's exclusion.
- Form #35: Screening Visit 2-Local Labs: Must be repeated.
- *Form #41: Skinner: Does not need to be repeated if previously data entered in patient's Screen #2 visit. The DMS will automatically transfer the previous results to the new ID.
- *Form #50: Screening Biopsy: Must be repeated if outside the screening window (12 months prior to re-screening baseline visit).
- Form #71: Screening Visit 2 Aliquot: Must be repeated (except for EBV) PBMC must be repeated.
- Beck Depression Inventory (BDI II) must be repeated.
- *CIDI: Does not need to be repeated (results from previous screening must be entered on the new Form #4: Screening Checklist.
- *The Block Food Questionnaire: Does not need to be repeated.

* Starred items indicate that this particular item does not need to be repeated if certain stipulations are adhered to.

Express Group Screening Introduction

To be screened for the HALT-C Trial, patients must have chronic hepatitis C, with a history of previous interferon treatment that has failed to induce a virological response. Express patients are will bypass the Lead-in Phase of the trial because they have received parallel, or had intended to receive parallel, treatment with pegylated interferon and ribavirin (180 mcg or 1.5 MU with at least 800 mg of ribavirin) for at least 24 weeks. The pre-treatment liver biopsy must be available and performed within 18 months of randomization. Express patients may enter the Screening Phase of HALT-C Trial while still on pegylated interferon and ribavirin provided they have been treated for at least 20 weeks and have had a positive HCV-RNA after week 20 of treatment. However, these patients must not be receiving the drugs as part of participation in another clinical trial. For more detailed information on inclusion/exclusion criteria, please see section E, F, and G of the main HALT-C protocol.

The Screening Phase is divided into Pre-Screening, Screening Visit 1, and Screening Visit 2. The purpose of these visits is to collect information to ensure that the patient is eligible to participate in the study. Further information on the screening phase can be found in Section G of the HALT-C protocol.

Express Group Pre-Screening:

All patients with the above criteria should be screened for eligibility for the HALT-C Trial. The documentation of all potentially eligible patients is important for the HALT-C Trial database. It will provide a comparison of patients enrolled in the HALT-C Trial with those patients with hepatitis C and a history of previous interferon treatment that failed to induce a response.

Patients considered for the HALT-C Trial should be documented on the Screening Log and assigned the next sequential HALT-C patient ID number. The Screening Log also provides space for the patient's name, initials, and date of birth. The Screening Log sheet is the only document which links the patient's name to the HALT-C patient ID number. Therefore, the Screening Log is not data entered. Keep this document in a locked storage compartment (such as a file cabinet or desk drawer) and limit access to appropriate study personnel.

HALT-C patient ID numbers consist of six digits. The first two identify the clinical site. The next three represent the specific patient at that site. The final digit is a computer assigned check digit designed to catch data entry errors.

<u>The following forms are used during Pre-Screening:</u>

- Form #1: Trial ID Assignment. This form is used to enter a new patient into the HALT-C Data Management System, and assigns the patient ID from the screening log to the patient, thus linking the assigned ID number with the patient initials. If the patient is eligible for the trial, store Form #1 with the other data forms, which will be entered for screening. If the patient is not eligible, Form #1 can be stored separately. For re-screened patients, complete a second Form #1 using the newly assigned patient ID number.

- Form #5: Trial Ineligibility. This form must be completed for all patients found to be ineligible for the HALT-C Trial during the pre-screening and/or screening phase. Store these forms with their appropriate form #1.

<u>Pre-treatment Medical Information</u>

Express patients have by definition been treated outside of the Lead-in Phase of the HALT-C Trial with pegylated interferon and ribavirin for at least 24 weeks. The following information

should be obtained from the patient's medical record regarding their pre-treatment status and recorded on Forms #38 and #50:

- Liver biopsy (Form #50). The liver biopsy must have been performed before the current treatment and within the last 18 months before randomization. Ten unstained biopsy slides must be obtained from Pathology and shipped to the Data Coordinating Center. Please see Section G, Pathology for further information.
- Fasting serum chemistries (BUN, creatinine, glucose, uric acid, triglycerides)
- Liver chemistries (AST, ALT, alkaline phosphatase, total bilirubin, albumin, and globulin [or total protein])
- Complete blood count with diff (WBC, neutrophils, hematocrit, hemoglobin, platelets
- Prothrombin time (INR)

All of these laboratory tests may not be available. Essential values are ANC, platelets, Hct or Hemoglobin and a liver biopsy.

Forms

- Form #1: Trial ID Assignment. This form is used to enter a new patient into the Trial Data Management System, and assigns the patient ID from the screening log to the patient, thus linking the assigned ID number with the patient initials. If the patient is eligible for the trial, store Form #1 with the other data forms, which will be entered for screening. If the patient is not eligible, they should be kept separately.

- Form #5: Trial Ineligibility. This form must be completed for all patients found to be ineligible for the HALT-C Trial during the pre-screening and/or screening phase. Store these forms with their appropriate Form #1.

Express Group Screening Visit 1 (S00):

Once it is determined that the patient should be screened for eligibility, proceed to Screening Visit 1.

Informed consent

Prior to collecting any information for Screening Visits 1 and 2, the patient **MUST** sign the screening consent form (or the main trial consent form if there is no separate screening consent form). Data collected prior to the signing of the consent will be considered invalid. The exception will be tests which may have been done for clinical reasons or other research studies, and are specifically identified by the protocol as being acceptable if done prior to the start of the study, such as liver biopsy, ultrasound and endoscopy (see below for further details). Patients may not be screened if they are currently in another clinical trial.

The appropriate medical personnel must sign all consent forms. All signatures should be dated. Offer the patient a copy of the consent according to your institutional procedure. Also follow institutional procedure regarding the placement of the consents in the medical or other record. Keep all signed consents forms together in a binder labeled HALT-C Consent Forms or with the patient's data forms as long as the data form binders are kept in a storage area that can be locked and to which access is limited. These consent forms should be made available to Data Coordinating Staff (DCC) during site visits.

Packets of data forms for each screening visit and patient ID number labels will be provided by the DCC. Each patient should have a binder notebook for forms. The binder should be labeled with the patient ID. There should be nothing on the data forms, or source documents (which will be sent outside the clinical site) with any information (such as patient name or

medical record number) that could identify the patient. Binders should be stored in a room or other storage space that can be locked. Access should be limited to appropriate personnel.

Visit Control Sheet
A Visit Control Sheet (VCS) should be printed prior to the first screening visit and will detail all the required tests and forms for both screening visits. For information on how to print the VCS, please see the Data Management section of the MOO.

Once the screening consent is signed, the patient may begin Screening Visit 1. The patient should be fasting for required lab tests. The following tests, interviews, and forms are done during Screening Visit 1:

Patient administered questionnaires
- QOL (Form #40)
- Symptoms (Form #43)

Interviews
- Screening Medical History (Form #3) Question E1, answer Express.
- Pre-existing Conditions (if applicable)

Tests
- History and physical (Form #11)

Local Lab tests (Forms #30, #34)
- Fasting serum chemistries (BUN, creatinine, glucose, uric acid, triglycerides)
- Liver chemistries (AST, ALT, alkaline phosphatase, total bilirubin, albumin, and globulin [or total protein])
- Complete blood count with diff (WBC, neutrophils, hematocrit, hemoglobin, platelets
- Prothrombin time (INR)
- AFP

Central Lab tests (Form #31, 70)
- HCV-RNA (sent to the Central Repository for shipping to the Central Virology lab. See Section E, Specimen Collection, Processing and Shipping for further details.)

Screening Eligibility Worksheet (optional)
The Eligibility Worksheet may be used to assist clinicians in ensuring that patients meet the eligibility criteria for the trial. It lists each inclusion/exclusion criteria. This is **NOT** data entered, but strongly recommended only as a guide. Criteria specific to Express patients is indicated by a box – Express Group.

Pre-existing Conditions (optional)
The Pre-existing Conditions Form may be used to assist clinicians in keeping track of those medical conditions that the patient had before the trial started. Knowing the pattern of a condition, such as migraine headaches, will be helpful when determining if an event is a pre-existing condition or an adverse event.

Forms
- Form #3, Screening Medical History
- Form #11, Physical Exam
- Form #15, CTP score (must be done for Express patients at both S01 & S02)

- Form #30, Local Lab
- Form #31, Central Lab (results sent via email to clinical center; data form entered at the Central Virology Lab).
- Form #34, AFP
- Form #38, Pre-treatment Lab Work
- Form #40, Quality of Life
- Form #43, Symptoms
- Form #70, Screening 1 Aliquot Form
- Pre-existing Conditions Form (optional)
- Screening Eligibility Worksheet (optional)

Special considerations for patients with previous neuropsychiatric issues:
Any eligible patients who have had a history of severe or dose limiting neuropsychiatric toxicity during prior interferon treatment will be referred to a consulting psychologist or psychiatrist for further evaluation and possible treatment. Patients who have had a suicide attempt and/or hospitalization for depression more than 5 years ago and any patients who have had severe or poorly controlled psychiatric disorders (e.g. depression, schizophrenia, bipolar illness, obsessive-compulsive disorder, severe anxiety, personality disorder) more than 6 months ago but less than 5 yeas ago must be assessed and followed (if recommended) by a psychiatrist or other mental health professional. (See Section B4, Management Guidelines for further details).

Special considerations for patients with AFP >200.
If an Express patient has a Screening AFP of between 200 and 1000 ng/L, an ultrasound must be normal and an MRI or CT must be normal for the patient to be eligible for enrollment.

Express Group Screening Visit 2 (S00):
The patient may proceed to the next screening visit if the criteria for Screening Visit 1 are met. The patient should be fasting for the liver biopsy and ultrasound. The following tests, interviews, and forms are done during Screening Visit 2:

Patient administered questionnaires
- Composite International Diagnostic Interview (CIDI). This survey asks questions regarding the patient's history of drug and alcohol use, anxiety and depression. See Section Q for further details. The CIDI is optional at sites that have limited clinical resources or if the patient is unable to read or understand English.
- Block Food Frequency. This questionnaire should be given to patients to take home with them following the Screen 2 visit. It should be brought back to the W00 visit. It must be filled out with a #2 pencil. See Section P for further details.
- Beck Depression Inventory (Form #44)

Interview Forms
- Baseline History (Form #6)
- Skinner (Form #41)

Tests
- Ultrasound (MRI, CT) (Form #22). The ultrasound must have been done in the last 6 months. If an MRI, or CT has been done within the last 6 months, these tests may be substituted for the ultrasound using the same Form #22. If the AFP was > 200 at Screen Visit 01, follow instructions under III G above. See Section R of MOO for further information.

Local Lab Tests (Form #35, #94)

- Pregnancy test for all women of child bearing potential
- Urine dip for protein and heme
- Liver chemistries (AST, ALT, alkaline phosphatase, total bilirubin, albumin, globulin [or total protein])
- Thyroid stimulating hormone (TSH)
- Prothrombin time (INR)
- HIV test
- Hepatitis B Surface Antigen
- ANA
- Ceruloplasmin
- Alpha-1 antitrypsin

Central Lab Tests (Form #71)

These are fresh blood specimens.

- 20 cc in ACD vacutainer tube for EBV to be shipped overnight. (Not to be drawn if patient does not consent to genetic testing.)
- 20 cc in ACD vacutainer tube for PBMC to be shipped overnight.

Forms

- Form #6 Baseline History
- Form #15, CTP score (must be done for Express patients at both S01 & S02)
- Form #22, Ultrasound, MRI, CT
- Form #35, Screening Visit 2 Local Lab
- Form #41, Skinner
- Form #50, Screening Biopsy Evaluation
- Form #71, Screening 2 Aliquot Form
- Form #44 Beck Depression Inventory (BDI II) See Depression Management Guidelines, Section B4 for details.
- Block Food Questionnaire
- Form #94, Screening Checklist (should not be entered until all data is collected and screening is complete)
- Form #181, Histopathology

Adequate contraception

All patients enrolled in the HALT-C Trial must be willing to use contraception as indicated by the protocol. Please see Section D5, Adequate Contraception, for details.

Express Group Screening Phase Completion:

If the Express Group patient completes Screening Visit 1 and Screening Visit 2 and is eligible for the trial, the following should be done:

Sign informed consent for HALT-C Trial

The informed consent for participation in the HALT-C Trial must be signed and stored in the manner described above.

Genetic testing

The informed consent for participation in Genetic Testing must be signed and stored in the manner described above. If a patient does not wish to participate in this part of the HALT-C Trial, do not collect the EBV specimens at Screen Visit 02. If, by error, the EBV is collected and the patient did not consent, contact the DCC so that the Repository can be notified to

destroy that specimen. A record of verification of destruction of said sample should be kept in the patient's notebook.

Ancillary studies

The only Ancillary Study that will be available to Express patients is QLFT. Discuss appropriate ancillary study with the patient and have them sign consent forms as appropriate. Consents should be stored in the manner described above. Please see Section K for more information on ancillary studies.

Forms

- Form #94, Express Screening Checklist. This is the final form completed during the screening phase. This form provides a formal check off for the study personnel, verifying that the required steps have been taken prior to assessing an Express patient for entry into the HALT-C Trial.

- Form #1, Trial ID Assignment. For those Express patients who were continuing on a course of interferon and ribavirin during the Screening Phase, go back to the questions on Form #1, regarding the number of weeks and dose adjustments for interferon and ribavirin and complete if applicable at this point in time.

- Form #5, Trial Ineligibility. If a patient has been deemed ineligible for any reason, complete this form. Indicate the reason for ineligibility. This form ends the screening process. This form should be completed at any time the patient becomes ineligible after entry of Form #1, Trial ID Assignment up to the Randomization Visit (R00), prior to the dispensation of trial medication. **Do not use this form if the patient has taken trial medication.**

Next Phase: Assessment for Randomization

By definition, the Express patients will bypass the Lead-in Phase. If the patient is eligible for the trial, the informed consent has been signed, and the Express Screening Checklist (Form #94) completed, the patient may be assessed for eligibility for the Randomization Phase. The following timeframes must be adhered to in bringing an Express patient to the Randomization (R00) visit:

- The patient can not be off pegylated interferon and ribavirin combination for more than 6 months
- The pre-treatment liver biopsy must be within 18 months of the Randomization Visit (R00). For details, see Express Patients Assessment for Randomization Phase, Section D3.
- The Randomization Visit (R00) must be held within 2 weeks of data entering Form #99. For details, see Express Patients Assessment for Randomization Phase, Section D3.