# CSCC Arginine Protocol CRF

The following pages will be used at Screening ("Week – 4") visit only.

Some forms in this section will be used at other visits as well, as indicated in the protocol:

- Urinalysis
- Pregnancy

| *Comprehensive Sickle Cell Centers* | **Inclusion Criteria** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Questions 1-7** | • All questions must be answered 'Yes'. For question 1, fill in the date the informed consent was signed in the dd/mmm/yy format (ex. 25SEP04).<br>• Subjects MUST be excluded from the study if any questions are 'No'. |
| **Question 5** | Question #5 may be 'NA' if subject is under 10 years of age. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Inclusion Criteria** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

*For the subject to be considered eligible for this study, Questions 1 through 7 must be answered Yes. Question 5 may be NA.*

1. Has the subject signed the informed consent? Yes ☐ No ☐

   Date of informed consent: ☐☐ / ☐☐☐ / ☐☐
   Day Month Year

2. Does the subject have an established diagnosis of Hb SS or S-beta0 thalassemia? Yes ☐ No ☐

3. Does the subject have a history of at least one documented vaso-occlusive pain event in the last 12 months? Yes ☐ No ☐

4. Does the subject have a regular compliance with comprehensive care? Yes ☐ No ☐

5. Does the subject have a history of a retinal exam in the last year? Yes ☐ No ☐ NA ☐
   ***(For subjects 10 years of age or more)***

6. Is the subject at least 5 years of age? Yes ☐ No ☐

7. Is the subject in his/her steady state and not in the midst of any acute complication due to sickle cell disease at enrollment? Yes ☐ No ☐

# Exclusion Criteria

| Item | Instructions |
|---|---|
| **Questions 1-4**<br>**Questions 7-11** | • All questions must be answered 'No'. Subjects MUST be excluded from the study if any are marked 'Yes'. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Exclusion Criteria** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

*For the subject to be considered eligible for this study, Questions 1 through 4 and 7 through 11 must be answered No.*

| | | |
|---|---|---|
| 1. Does the subject have an inability to take or tolerate oral capsule medications? | Yes ☐ | No ☐ |
| 2. Does the subject have a hepatic dysfunction (SGPT ≥ 2X normal OR albumin ≤ 3.2)? | Yes ☐ | No ☐ |
| 3. Does the subject have a renal dysfunction (Creatinine ≥ 1.2 for children, ≥ 1.4 for adults)? | Yes ☐ | No ☐ |
| 4. Is the subject allergic to arginine? | Yes ☐ | No ☐ |
| 5. Has the subject had a history of priapism requiring treatment within the last year? | **No longer exclusion criteria. (28NOV2005 protocol amendment)** | |
| 6. Has the subject had a history of retinopathy requiring treatment? | **No longer exclusion criteria. (28NOV2005 protocol amendment)** | |
| 7. Is the subject pregnant? | Yes ☐ | No ☐ |
| 8. Has the subject had a transfusion within the last 90 days? | Yes ☐ | No ☐ |
| 9. Has the subject had ≥ 10 hospital admissions (overnight stay) for pain in the last 12 months, or is he/she currently using narcotics daily (adult who takes narcotics everyday, not meant for those who take narcotics for several days due to a crisis)? | Yes ☐ | No ☐ |
| 10. Has the subject had treatment with hydroxyurea within the last 90 days? | Yes ☐ | No ☐ |
| 11. Has the subject had treatment with any investigational drug within the last 90 days? | Yes ☐ | No ☐ |

| *Comprehensive Sickle Cell Centers* | **Demographics** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Weight** | Record the subject's weight in kilograms. |
| **Height** | Record the subject's height in centimeters. |
| **Date of Birth** | Record the subject's date of birth in the dd/mmm/yyyy format (ex. 25SEP1970). |
| **Gender** | Check the appropriate gender. |
| **Diagnosis** | Check the appropriate diagnosis. Either SS **or** $SB^{0.}$ |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Demographics** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Weight: ☐☐☐.☐ (kg)  Height: ☐☐☐.☐ (cm)

Date of Birth: ☐☐ / ☐☐☐ / ☐☐☐☐
Day Month Year

Gender: ☐ Male ☐ Female

Diagnosis:
*(choose one)*

☐ **SS**

☐ **SB$^0$**

| *Comprehensive Sickle Cell Centers* | **Baseline Health History** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Have you been transfused in the last 2 weeks?** | • If 'Yes', record dates in the dd/mmm/yy format (ex. 25SEP04) for all transfusions that occurred ***in the last 2 weeks***. Also, be sure to record the number of units or the number of cc's for each transfusion.<br>• If more than one transfusion occurred, use the 'Add' button to record additional visits. |
| **Questions** | • Answer either 'Yes' of 'No' to each question on the page. Not sure may be recorded for the question about being unusually tired.<br>• Each question refers to **the past 2 weeks**. |
| **Have you had any unusual headaches?** | If 'Yes', choose the <u>one</u> choice that best describes the frequency of the headaches being experienced by the subject. |
| **Have you taken any new medications?** | If 'Yes', be sure to record each new medication on the Concomitant Medications form. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Baseline Health History** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

**All questions refer to the past 2 weeks.**

Have you been transfused in the last 2 weeks? Yes ☐ No ☐

**If yes**, record date and number of units or cc's for each transfusion.

Date transfused: ☐☐ / ☐☐☐ / ☐☐ (Day Month Year)

Number of units: _____
**OR**
cc's for pediatrics: _____

**ADD**

Have you had leg ulcers? Yes ☐ No ☐

Have you had blood in the urine? Yes ☐ No ☐

Have you had chronic pain in the hips or shoulders? Yes ☐ No ☐

Have you had chronic pain in other locations? Yes ☐ No ☐

Have you had any increase in problems with painful erections? Yes ☐ No ☐

Have you had a fever 101° or higher? Yes ☐ No ☐

Have you had vision problems? Yes ☐ No ☐

Have you had any problems with breathing, including asthma? Yes ☐ No ☐

Have you been unusually tired, or more tired than you usually are? Yes ☐ No ☐ Not sure ☐

Have you had any unusual headaches? Yes ☐ No ☐

**If yes**, frequency of headaches.

☐ Everyday ☐ 2-3 times/week ☐ Once a week ☐ More than once a week

Have you taken any new medications? Yes ☐ No ☐

**If yes, add each to the CMED form.**

| *Comprehensive Sickle Cell Centers* | **History of Hospital, Clinic, & ED Visits** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **ALL FIELDS** | All information for this page is to be obtained from the subject's medical record. |
| **List all Hospital Admissions…** | • Record all Hospital Admissions that occurred during the last year. Hospital Admission requires an overnight stay.<br>• If more than one Hospital Admission occurred, use the 'Add' button to record additional admissions. |
| **Date of admission/discharge** | • Record the date of hospital admission in the dd/mmm/yy format (ex. 25SEP04).<br>• Record the date of hospital discharge in the dd/mmm/yy format (ex. 25SEP04). |
| **Reason** | • Record the reason for hospital admission from the list provided. More than one reason may be checked for a given date.<br>• If 'Other, specify' is chosen, be sure to specify in the space provided. |
| **List all ED or Day Hospital visits** | • Record all Emergency Department or "Day Hospital" visits that occurred during the last year.<br>• If more than one visit occurred, use the 'Add' button to record additional visits. |
| **Date of visit and location of visit** | • Record the date of visit in the dd/mmm/yy format (ex. 25SEP04).<br>• For each date, check whether the visit was to an Emergency Department or Day Hospital. |
| **Reason** | • Record the reason for the visit from the list provided. More than one reason may be checked for a given date.<br>• If 'Other, specify' is chosen, be sure to specify in the space provided. |
| **List all Clinic visits…** | Record all clinic visits ***for acute pain*** that occurred during the last year. If more than one clinic visit ***for acute pain*** occurred, use the 'Add' button to record additional visits. |
| **Date of clinic visit** | Record the date of all clinic visits in the dd/mmm/yy format (ex. 25SEP04). For multiple dates, click the 'Add' button to enter a new row of data. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **History of Hospital, Clinic, & ED Visits** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Information for these questions is to be obtained from the subject's medical records.

**List all Hospital Admissions that happened during the last year.**

Date of admission: ☐☐ / ☐☐☐ / ☐☐ (Day / Month / Year)

Date of discharge: ☐☐ / ☐☐☐ / ☐☐ (Day / Month / Year)

**Reason:** *(check all that apply)* ☐ ACS ☐ VOC ☐ Non-Sickle Pain ☐ Other, specify _____

**ADD**

**List all Emergency Department visits or "Day Hospital" visits that happened during the last year.**

Date of visit: ☐☐ / ☐☐☐ / ☐☐ (Day / Month / Year)

Location: ☐ Emergency Department ☐ Day Hospital

**Reason:** *(check all that apply)* ☐ ACS ☐ VOC ☐ Non-Sickle Pain ☐ Other, specify _____

**ADD**

**List all Clinic visits *for acute pain* that happened during the last year.**

Date of clinic visit: ☐☐ / ☐☐☐ / ☐☐ (Day / Month / Year)

**ADD**

| *Comprehensive Sickle Cell Centers* | **Medication History** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Medication** | • Check 'Yes' if the medication was used by the subject **in the past year**.<br>• Check 'No' if the medication was *never* used by the subject **in the past year**.<br>• If 'Yes' and the medication is followed by 'If yes, specify' or 'If yes, type', be sure to specify in the space provided.<br>• Use the subject's medical record for all medication information. |
| **Length of Time Used** | • Record the ***approximate*** number of months the medication was used by the subject in the past year.<br>• Record the ***approximate*** number of days the medication was used by the subject in the past year. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Medication History** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Check all medications used by this subject in the **past year.** Information for these questions is to be obtained from the subject's medical records.

| **Medication**<br>**If yes, record the total approximate length of time used** | | | **Length of Time Used** | |
|---|---|---|---|---|
| | | | Months | Days |
| Hydroxyurea | Yes ☐ | No ☐ | | |
| Prophylactic Penicillin | Yes ☐ | No ☐ | | |
| Any other antibiotic<br>**If yes,specify:** _____ | Yes ☐ | No ☐ | | |
| Folic Acid | Yes ☐ | No ☐ | | |
| Narcotics<br>**If yes, type:** _____ | Yes ☐ | No ☐ | | |
| NSAIDS | Yes ☐ | No ☐ | | |
| Desferal | Yes ☐ | No ☐ | | |
| Oxygen | Yes ☐ | No ☐ | | |
| Any other pain medication<br>**If yes,specify:** | Yes ☐ | No ☐ | | |
| **Specify 1:** _____ | | | | |
| **Specify 2:** _____ | | | | |
| Psychiatric medications | Yes ☐ | No ☐ | | |
| Other, or intravenous meds<br>**If yes, specify:** _____ | Yes ☐ | No ☐ | | |

| *Comprehensive Sickle Cell Centers* | **Pain History** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Number of Times** | • Check the best response, as reported by the subject, *to the best of the subject's knowledge*, **in the past year**.<br>• If any of the lead questions are yes, be sure to record the number of times in the space provided.<br>• **Do not** record a range.<br>• ***To avoid double-counting***, if an event could be reported in more than one category, report this event in the most serious category. (For example, if a subject had a painful event that was treated at home, but then went to the emergency room, this event should be recorded in the 'Visited an emergency room, not admitted to hospital' category.) If a subject called a doctor but did not go to the office, emergency room or hospital, this event should be recorded in 'Was treated at home'. |
| **Information provided by** | For each category, check the appropriate response on how the information for that category was obtained. |
| **Usual Treatment** | For each category, describe the usual treatment given to the subject in order to treat the painful episode **in the past year**. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Pain History** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Record the number of **painful episodes in the past year**, **as reported by the subject to the best of their knowledge**, for which the subject:

| | **Information provided by** | **Usual Treatment** |
|---|---|---|
| Was treated at home?<br>Yes ☐ No ☐ Declined ☐<br>*If yes, specify number of times* _____ | ☐ Patient<br>☐ Parent/Guardian<br>☐ Proxy | |
| Was treated in a clinic or doctor's office, not hospital?<br>Yes ☐ No ☐ Declined ☐<br>*If yes, specify number of times* _____ | ☐ Patient<br>☐ Parent/Guardian<br>☐ Proxy | |
| Visited an emergency room, not admitted to hospital?<br>Yes ☐ No ☐ Declined ☐<br>*If yes, specify number of times* _____ | ☐ Patient<br>☐ Parent/Guardian<br>☐ Proxy | |
| Was admitted to hospital?<br>Yes ☐ No ☐ Declined ☐<br>*If yes, specify number of times* _____ | ☐ Patient<br>☐ Parent/Guardian<br>☐ Proxy | |

| *Comprehensive Sickle Cell Centers* | **Chemistry Labs** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Collection date** | Record the collection date in the dd/mmm/yy format (ex. 25SEP04). |
| **Test/Value** | Record a value for each test in the units provided on the form. |
| **Normal Ranges / Lower Limit** | Record the lower limit of the range that is considered normal for each test, as displayed on the lab report. |
| **Normal Ranges / Upper Limit** | Record the upper limit of the range that is considered normal for each test, as displayed on the lab report. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Chemistry Labs** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Collection date: ☐☐ / ☐☐☐ / ☐☐
Day Month Year

| TEST | VALUE | NORMAL RANGES (Please record the lower & upper limit for each lab value) | |
|---|---|---|---|
| | | LOWER LIMIT | UPPER LIMIT |
| Sodium (mEq/L) | ☐☐☐ | | |
| Potassium (mEq/L) | ☐.☐ | | |
| Chloride (mEq/L) | ☐☐☐ | | |
| $CO_2$ (mEq/L) | ☐☐.☐ | | |
| Calcium (mg/dL) | ☐☐.☐ | | |
| Creatinine (mg/dL) | ☐☐.☐ | | |
| Glucose (mg/dL) | ☐☐☐ | | |
| BUN (mg/dL) | ☐☐☐ | | |
| ALT (IU/L) | ☐☐☐☐ | | |
| Alk phosphatase (IU/L) | ☐☐☐☐ | | |
| Total bilirubin (mg/dL) | ☐☐.☐ | | |
| Total protein (gm/dL) | ☐☐.☐ | | |
| Albumin (g/dL) | ☐☐.☐ | | |
| LDH (u/L) | ☐☐☐☐ | | |

| *Comprehensive Sickle Cell Centers* | **Hematology Labs** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Collection date** | Record the collection date in the dd/mmm/yy format (ex. 25SEP04). |
| **Test/Value** | • Record a value for each test in the units provided on the form.<br>• Record information for Absolute Retic Count ***or*** % Retic. |
| **Normal Ranges / Lower Limit** | Record the lower limit of the range that is considered normal for each test, as displayed on the lab report. |
| **Normal Ranges / Upper Limit** | Record the upper limit of the range that is considered normal for each test, as displayed on the lab report. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Hematology Labs** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Collection date: ☐☐ / ☐☐☐ / ☐☐
Day Month Year

| TEST | VALUE | NORMAL RANGES (Please record the lower & upper limit for each lab value) | |
|---|---|---|---|
| | | LOWER LIMIT | UPPER LIMIT |
| Hemoglobin (mg/dL) | ☐☐.☐ | | |
| Hematocrit (%) | ☐☐ | | |
| RBC ($X10^3/mm^3$) | ☐☐.☐ | | |
| WBC ($X10^3/mm^3$) | ☐☐.☐ | | |
| MCV (fl) | ☐☐☐.☐ | | |
| MCHC (gm/dL) | ☐☐.☐ | | |
| Platelet count ($X10^3/mm^3$) | ☐☐☐ | | |
| Absolute Retic Count | ☐☐☐ | | |
| **OR** | | | |
| % Retic | ☐☐.☐ | | |

| *Comprehensive Sickle Cell Centers* | **Met Hb** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Collection date** | Record the collection date in the dd/mmm/yy format (ex. 25SEP04). |
| **Test/Value** | Record a value in the units provided on the form. |
| **Normal Ranges / Lower Limit** | Record the lower limit of the range that is considered normal for the test, as displayed on the lab report. |
| **Normal Ranges / Upper Limit** | Record the upper limit of the range that is considered normal for the test, as displayed on the lab report. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Met Hb** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Collection date: ☐☐ / ☐☐☐ / ☐☐
Day Month Year

| TEST | VALUE | NORMAL RANGES (Please record the lower & upper limit) | |
|---|---|---|---|
| | | LOWER LIMIT | UPPER LIMIT |
| Met Hb (%) | ☐☐.☐ | | |

| *Comprehensive Sickle Cell Centers* | **Urinalysis** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Specify gravity, pH, Microscopic RBC, and WBC** | • Record the result for each test in the units provided on the form. If units are not provided, use the standard unit for that test.<br>• For Microscopic RBC and WBC check only one response. For lab results that are in the 20-30 range, check the 25-50 box. |
| **Protein** | Select the one choice as reported by your lab. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Urinalysis** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Specific gravity: ☐.☐☐☐

pH: ☐☐.☐

Protein *(Select the one choice, as reported by your lab)*:

☐ Negative ☐ Trace ☐ 100 ☐ 200 ☐ 300 ☐ 1+ ☐ 2+ ☐ 3+

Microscopic RBC (#/$mm^3$): ☐ 0-5 ☐ 5-10 ☐ 10-25 ☐ 25-50 ☐ 50+

WBC (#/$mm^3$): ☐ 0-5 ☐ 5-10 ☐ 10-25 ☐ 25-50 ☐ 50+

| *Comprehensive Sickle Cell Centers* | **Pregnancy Test** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Pregnancy Test** | • Check ***one*** of the following three choices:<br><br>'Not done, subject male'<br>'Not done, female subject not of menstruating age'<br>'Not done, female subject not of child-bearing potential'<br><br>• If 'Not done, female subject not of child-bearing potential', check ***all*** reasons that apply.<br><br>• If 'Other, specify' is chosen, be sure to specify.<br><br>• If pregnancy test is not done, omit the rest of this page. |
| **Date of Collection** | Record the date of collection in the dd/mmm/yy format (ex. 25SEP04). |
| **Result** | Check the result of the pregnancy test, either 'Positive' or 'Negative'. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Pregnancy Test** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

| | |
|---|---|
| ☐ Not done, subject male<br>☐ Not done, female subject not of menstruating age<br>☐ Not done, female subject not of child-bearing potential **(check reason below)**<br>☐ Postmenopausal<br>☐ Hysterectomy<br>☐ Tubal ligation<br>☐ Other, specify:<br>_____ | Date of Collection: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year<br><br>Result: ☐ Positive ☐ Negative |

The following pages will be used at Visit Week – 2, and later, as indicated in the protocol.

| *Comprehensive Sickle Cell Centers* | **Chemistry Labs** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Collection date** | Record the collection date in the dd/mmm/yy format (ex. 25SEP04). |
| **Test/Value** | Record a value for each test in the units provided on the form. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Chemistry Labs** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Collection date: ☐☐ / ☐☐☐ / ☐☐
Day Month Year

| TEST | VALUE |
|---|---|
| Sodium (mEq/L) | ☐☐☐ |
| Potassium (mEq/L) | ☐.☐ |
| Chloride (mEq/L) | ☐☐☐ |
| $CO_2$ (mEq/L) | ☐☐.☐ |
| Calcium (mg/dL) | ☐☐.☐ |
| Creatinine (mg/dL) | ☐☐.☐ |
| Glucose (mg/dL) | ☐☐☐ |
| BUN (mg/dL) | ☐☐☐ |
| ALT (IU/L) | ☐☐☐☐ |
| Alk phosphatase (IU/L) | ☐☐☐☐ |
| Total bilirubin (mg/dL) | ☐☐.☐ |
| Total protein (gm/dL) | ☐☐.☐ |
| Albumin (g/dL) | ☐☐.☐ |
| LDH (u/L) | ☐☐☐☐ |

| *Comprehensive Sickle Cell Centers* | **Hematology Labs** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Collection date** | Record the collection date in the dd/mmm/yy format (ex. 25SEP04). |
| **Test/Value** | • Record a value for each test in the units provided on the form.<br>• Record information for Absolute Retic Count ***or*** % Retic. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Hematology Labs** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Collection date: ☐☐ / ☐☐☐ / ☐☐
Day Month Year

| TEST | VALUE |
|---|---|
| Hemoglobin (mg/dL) | ☐☐.☐ |
| Hematocrit (%) | ☐☐ |
| RBC ($X10^3/mm^3$) | ☐☐.☐ |
| WBC ($X10^3/mm^3$) | ☐☐.☐ |
| MCV (fl) | ☐☐☐.☐ |
| MCHC (gm/dL) | ☐☐.☐ |
| Platelet count ($X10^3/mm^3$) | ☐☐☐ |
| Absolute Retic Count<br>**OR** | ☐☐☐ |
| % Retic | ☐☐.☐ |

| *Comprehensive Sickle Cell Centers* | **Met Hb** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Collection date** | Record the collection date in the dd/mmm/yy format (ex. 25SEP04). |
| **Test/Value** | Record a value in the units provided on the form. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Met Hb** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Collection date: ☐☐ / ☐☐☐ / ☐☐
Day Month Year

| TEST | VALUE |
|---|---|
| Met Hb (%) | ☐☐.☐ |

| *Comprehensive Sickle Cell Centers* | **Echocardiogram** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Date of most recent echocardiogram** | Record the date of the **most recent** echocardiogram in the dd/mmm/yy format (ex. 25SEP04). |
| **TR Jet**<br>**Ejection Fraction**<br>**Shortening Fraction**<br>**LVH**<br>**RVH** | • Check 'Yes' or 'No' where applicable.<br>• Record a value for each in the units provided on the form.<br>• The TR Jet is a velocity. If TR Jet is undetectable, be sure to check that box.<br>• The Ejection Fraction should be measured by the Simpsons method.<br>• For Ejection Fraction and Shortening Fraction, not reported may be checked. |
| **Right Ventricular to Right Atrial Difference** | • If two values are received, subtract them. The subtracted value should then be entered into this field.<br>• Not reported may be marked. |
| **Has ECHO ever been abnormal?** | • **If the values recorded in the first section are considered to be normal**, answer the questions 'has ECHO **ever** been abnormal?", Yes or No.<br>• If 'Yes', answer the remaining questions on the page.<br>• If 'No', skip the rest of the page. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Echocardiogram** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Date of most recent echocardiogram: ☐☐ / ☐☐☐ / ☐☐
Day Month Year

TR Jet: ☐☐.☐ ☐ TR Jet Undetectable

Ejection Fraction: ☐☐ (%) ☐ Not reported

Shortening Fraction: ☐☐ (%) ☐ Not reported

Right Ventricular to Right Atrial Difference: ☐☐☐ mm Hg ☐ Not reported

LVH: Yes ☐ No ☐

RVH: Yes ☐ No ☐

If above is normal, has ECHO **ever** been abnormal? Yes ☐ No ☐

If **Yes**, date of most recent **abnormal** ECHO: ☐☐ / ☐☐☐ / ☐☐
Day Month Year

TR Jet: ☐☐.☐ ☐ TR Jet Undetectable

Ejection Fraction: ☐☐ (%) ☐ Not reported

Shortening Fraction: ☐☐ (%) ☐ Not reported

Right Ventricular to Right Atrial Difference: ☐☐☐ mm Hg ☐ Not reported

LVH: Yes ☐ No ☐

RVH: Yes ☐ No ☐

| *Comprehensive Sickle Cell Centers* | **Interim Health History** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Have you had any hospitalizations since your last visit?** | • Check 'Yes' if the subject had any hospitalizations ***since the last study visit***. Otherwise, check 'No'.<br>• If 'Yes', record the date of admission, date of discharge, and reason for admission. If more than one hospitalization occurred ***since the last study visit***, use the 'Add' button to record additional visits.<br>• If 'No', go to the next section on the page. |
| **Date of admission/discharge** | • Record the date of hospital admission in the dd/mmm/yy format (ex. 25SEP04).<br>• Record the date of hospital discharge in the dd/mmm/yy format (ex. 25SEP04). |
| **Reason** | • Record the reason for hospital admission from the list provided. More than one reason may be checked for a given date.<br>• If 'Other, specify' is chosen, be sure to specify in the space provided. |
| **Have you been to the ED or Day Hospital since your last visit?** | • Check 'Yes' if the subject had any visits ***since the last study visit***. Otherwise, check 'No'.<br>• If 'Yes', record the date of visit, reason, and location of visit. If more than one visit occurred ***since the last study visit***, use the 'Add' button to record additional visits.<br>• If 'No', go to the next section on the page. |
| **Date of visit and location of visit** | • Record the date of visit in the dd/mmm/yy format (ex. 25SEP04).<br>• For each date, check whether the visit was to an Emergency Department or Day Hospital. |
| **Reason** | • Record the reason for the visit from the list provided. More than one reason may be checked for a given date.<br>• If 'Other, specify' is chosen, be sure to specify in the space provided. |
| **Have you had any clinic visits for acute pain since the last study visit?** | • If 'Yes', record dates in the dd/mmm/yy format (ex. 25SEP04) for all clinic visits ***for acute pain*** that occurred ***since the last study visit.***<br>• If more than one clinic visit ***for acute pain*** occurred, use the 'Add' button to record additional visits. |
| **Have you been transfused?** | • If 'Yes', record dates in the dd/mmm/yy format (ex. 25SEP04) for all transfusions that occurred ***since the last study visit***. Also, be sure to record the number of units or the number of cc's for each transfusion.<br>• If more than one transfusion occurred, use the 'Add' button to record additional visits. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Interim Health History** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

**All questions relate to changes since the last study visit**

Have you had any hospitalizations since your last study visit? Yes ☐ No ☐

**If yes,** Date admitted: ☐☐ / ☐☐☐ / ☐☐ (Day / Month / Year) Date discharged: ☐☐ / ☐☐☐ / ☐☐ (Day / Month / Year)

**Reason:** *(check all that apply)* ☐ ACS ☐ VOC ☐ Non-Sickle Pain ☐ Other, specify _____

**ADD**

Have you been to the Emergency Department or "Day Hospital" since your last study visit? Yes ☐ No ☐

**If yes**, record date, reason and check the location (emergency department or day hospital).

Date of visit: ☐☐ / ☐☐☐ / ☐☐ (Day / Month / Year)

Location: ☐ Emergency Department ☐ Day Hospital

**Reason:** *(check all that apply)* ☐ ACS ☐ VOC ☐ Non-Sickle Pain ☐ Other, specify _____

**ADD**

Have you had any clinic visits ***for acute pain*** since the last study visit? Yes ☐ No ☐

**If yes**, record date of clinic visit: ☐☐ / ☐☐☐ / ☐☐ (Day / Month / Year)

**ADD**

Have you been transfused? Yes ☐ No ☐

**If yes**, record date and number of units or cc's for each transfusion.

Date transfused: ☐☐ / ☐☐☐ / ☐☐ (Day / Month / Year)

Number of units: _____

**OR**

cc's for pediatrics: _____

**ADD**

| *Comprehensive Sickle Cell Centers* | **Interim Health History** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Questions** | • Answer either 'Yes' of 'No' to each question on the page. Not sure may be recorded for the question about being unusually tired.<br>• Each question relates to changes ***since the last study visit***. |
| **Have you had any unusual headaches?** | If 'Yes', choose the <u>one</u> choice that best describes the frequency of the headaches being experienced by the subject. |
| **Have you taken any new medications?** | If 'Yes', be sure to record each new medication on the Concomitant Medications form. |
| **Have you had any Adverse Events?** | If 'Yes', be sure to record each adverse event on the Adverse Events form. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Interim Health History** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

**All questions relate to changes since the last study visit**

Have you had leg ulcers? Yes ☐ No ☐

Have you had blood in the urine? Yes ☐ No ☐

Have you had any increase in problems with painful erections? Yes ☐ No ☐

Have you had a fever 101° or higher? Yes ☐ No ☐

Have you had vision problems? Yes ☐ No ☐

Have you had any problems with breathing, including asthma? Yes ☐ No ☐

Have you been unusually tired, or more tired than you usually are? Yes ☐ No ☐ Not sure ☐

Have you had any unusual headaches? Yes ☐ No ☐

**If yes**, frequency of headaches.

☐ Everyday ☐ 2-3 times/week ☐ Once a week ☐ More than once a week

Have you taken any new medications? Yes ☐ No ☐

**If yes, add each to the CMED form.**

Have you had any Adverse Events? Yes ☐ No ☐

**If yes, add each to the AE form.**

| *Comprehensive Sickle Cell Centers* | **Discontinuation Checklist** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Has the subject experienced any of the following events?** | • Check all events that the subject experienced ***since the last study visit***.<br>• If 'Other' is chosen, be sure to specify.<br>**If you believe a subject should be discontinued, please contact Lori Styles @ Children's Hospital Oakland.* |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Discontinuation Checklist** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Since the last visit, has the subject experienced any of the following events:

***check all that apply***

- ☐ Drop in hemoglobin below 5 gm/dL
- ☐ Pulmonary failure requiring intubation
- ☐ Hepatic dysfunction (SGPT $\geq$ 3X normal OR albumin $\leq$ 3.0)
- ☐ Renal dysfunction (Creatinine $\geq$ 1.4 for children, $\geq$ 1.6 for adults)
- ☐ Focal neurological changes
- ☐ Increase in methemoglobin level to > 2X normal level
- ☐ Apparent allergic reaction to arginine
- ☐ Episode of priapism requiring treatment
- ☐ Severe headache
- ☐ Pregnancy
- ☐ Episode of retinopathy requiring treatment
- ☐ Other Specify: _____

**** Please contact Lori Styles @ Children's Hospital Oakland if you believe this subject should be discontinued.***

| *Comprehensive Sickle Cell Centers* | **Study Drug Record** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Randomization Number** | Record the correct randomization number for the subject. The pharmacist will give the randomization number. |
| **Date** | **Each time** pills are dispensed or returned, record the date in the dd/mmm/yy format (ex. 25SEP04). |
| **# of Pills Returned / # of Pills Dispensed** | • On the first day drug is dispensed the date should be recorded. For # returned, 0 should be entered. For number dispensed the number that was dispensed to the subject should be recorded.<br>• For Visit 6 and Visit 7, along with the date, record the number returned and the number dispensed to the subject.<br>• For Visit 8, along with the date, record the number returned and record 0 for the number dispensed.<br>• Visit 3, 6, and 7 should all have the same number for “Number dispensed” since the subject will be receiving a fresh stock. |
| **Add** | Use the ‘Add’ button to record additional dispense or return dates. |
| **Comment** | Record any pertinent comments regarding each date if necessary. |

| *Comprehensive Sickle Cell Centers* | **Study Drug Record** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | **Randomization Number:**<br>☐☐☐☐ | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

*Each time that pills are dispensed or returned, record the date. The number of pills remaining is the number of pills left in the bottle(s) that the subject brought with him/her that day. The number of pills dispensed is the total of new pills plus the pills the subject returned.*

| **Date**<br>**DD / MON / YY** | **# of Pills Returned** | **# of Pills Dispensed**<br>**(on that day)** | **Comment** |
|---|---|---|---|
| ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | | | |

**ADD**

| *Comprehensive Sickle Cell Centers* | **Concomitant Medications** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Medication** | • Record the ***generic*** name for each concurrent medication separately in the space provided. For multiple medications, click the 'Add' button to enter a new row of data.<br>***Hydroxyurea and Arginine require a 90 day washout period prior to study drug dosing.*** |
| **Indication** | Record the indication for each medication. |
| **Start date** | Record start date in dd/mmm/yy format (25SEP04). Record the closest approximation for any portion of a date that is unknown. |
| **Stop date** | Record stop date in dd/mmm/yy format (25SEP04). Record the closest approximation for any portion of a date that is unknown. Leave stop date blank if medication is ongoing. |
| **Ongoing** | Check ongoing if the subject is currently taking the medication.<br>Leave stop date blank. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Concomitant Medications** | |
|---|---|---|
| **CSCC Concomitant Medications Form** | | CSCC ID: ☐☐☐☐☐☐☐ Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

*Record all medications from baseline to termination of study. Include start dates prior to the study **only** if the medication continues to be taken at baseline visit.*

| Medication | Indication | Start Date<br>DD MON YY | Stop Date<br>DD MON YY | Ongoing |
|---|---|---|---|---|
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |
| | | | | |

# Adverse Events

| Item | Instructions |
|---|---|
| **Serious Adverse Event** | Check 'Yes' or 'No' to indicate if the adverse event was considered a serious adverse event. If yes, be sure to submit a SAE report. |
| **Adverse Event** | Record each adverse event separately in the space provided. For multiple events click the 'Add' button to enter a new row of data. |
| **Onset date** | Record the date the adverse event began using the dd/mmm/yy format (ex. 25SEP04). Month and year are required date parts. If day is unknown, please estimate. |
| **Stop date** | • Record the date the adverse event stopped using the dd/mmm/yy format (ex. 25SEP04). Month and year are required date parts. If day is unknown, please estimate.<br>• If the adverse event is ongoing at the end of the study, leave the stop date blank. If the subject dies while an adverse event is ongoing, the stop date should be the date of death. |
| **Outcome** | • If adverse event is ongoing at end of study and subject is alive, outcome should be 3 (ongoing).<br>• If adverse event is present at time of death, but did not contribute to subject's death, outcome should be 4.<br>• If adverse event is present at time of death, and **did** contribute to subject's death, outcome should be 5. |
| **Severity** | Choose 1-5. |
| **Relationship to study drug** | Choose (1-5). ***Refer to section 11.2.2 of the protocol for additional information about relationship to study drug.*** |
| **Action(s) Taken** | Check the action taken for each adverse event recorded. More than one box may be checked. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Adverse Events** | |
|---|---|---|
| **CSCC Adverse Events Form** | | CSCC ID: ☐☐☐☐☐☐☐ Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

| **Serious Adverse Event?** | **Adverse Event** | **Onset Date** DD MON YY | **Stop Date** DD MON YY | **Outcome** 1=Resolved without sequelae 2=Resolved with sequelae 3=Ongoing 4=Present at death, not contributing to death 5=Death due to AE | **Severity** 1=Mild 2=Moderate 3=Severe 4=Life threatening 5=Death | **Relationship to Study Drug** 1=Unrelated 2= Probably not/ remote 3=Possibly related 4=Probably related 5=Definitely related | **Action(s) Taken** No action | Study drug interrupted | Study drug discontinued | Study drug dose adjusted | Medical intervention | Hospitalization |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Yes ☐ Y<br>No ☐ N | | | | | | | | | | | | |
| Yes ☐ Y<br>No ☐ N | | | | | | | | | | | | |
| Yes ☐ Y<br>No ☐ N | | | | | | | | | | | | |
| Yes ☐ Y<br>No ☐ N | | | | | | | | | | | | |
| Yes ☐ Y<br>No ☐ N | | | | | | | | | | | | |

| *Comprehensive Sickle Cell Centers* | **Study Termination** | |
|---|---|---|

| Item | Instructions |
|---|---|
| **Was the study blind broken for this subject?** | • If 'Yes' is checked, record the date the blind was broken in the dd/mmm/yy format (ex. 25SEP04). Also, record the reason for the unblinding in the space provided.<br><br>• If 'No' is checked, proceed to the next question. |
| **Did the subject complete the study?** | • If 'Yes', skip the rest of the page.<br><br>• If 'No', record the date of last dose of study drug AND check one primary reason for study discontinuation.<br><br>• If 'Adverse Event' is chosen, be sure to also check **all** adverse events that contributed to study discontinuation.<br><br>• If 'Other' is chosen, be sure to specify. |
| **Comments for page?** | Record any pertinent comments for this page only. |

| *Comprehensive Sickle Cell Centers* | **Study Termination** | |
|---|---|---|
| **Protocol # 1**<br><br>**Arginine** | Date of Visit: ☐☐ / ☐☐☐ / ☐☐<br>Day Month Year | CSCC ID: ☐☐☐☐☐☐☐<br>Center code: ☐☐☐<br>Hospital code: ☐☐☐ |

Was the study blind broken for this subject? Yes ☐ No ☐

If yes, date blind broken: ☐☐ / ☐☐☐ / ☐☐
Day Month Year

Reason for unblinding: _____

Did the subject complete the study? Yes ☐ No ☐

If no, date of last dose of study drug: ☐☐ / ☐☐☐ / ☐☐
Day Month Year

Check **one** primary reason for study discontinuation:

- ☐ Adverse Event **(check all that apply)**
  - ☐ Drop in hemoglobin below 5 gm/dL
  - ☐ Pulmonary failure requiring intubation
  - ☐ Hepatic dysfunction (SGPT ≥ 3X normal OR albumin ≤ 3.0)
  - ☐ Renal dysfunction (Creatinine ≥ 1.4 for children, ≥ 1.6 for adults)
  - ☐ Focal neurological changes
  - ☐ Increase in methemoglobin level to > 2X normal level
  - ☐ Apparent allergic reaction to arginine
  - ☐ Episode of priapism requiring treatment
  - ☐ Severe headache
  - ☐ Other Specify: _____
- ☐ Pregnancy
- ☐ Non-compliance
- ☐ Withdrew consent
- ☐ Lost-to-follow-up
- ☐ Death
- ☐ Other Specify: _____