# Public Review
# Cure Sickle Cell Initiative
# Common Data Elements (CDE)
# Monitoring Side Effects Working Group

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CURE SICKLE CELL.

**CureSCi CDE Project**
**Monitoring Side Effects Working Group Summary**

The goal of the Monitoring Side Effects Working Group (WG) has developed recommendations for data collection in genetic studies with curative intent in sickle cell disease (SCD). The standard data form recommendations are to facilitate harmonized data collection that will reduce study start-up time, reduce trial costs, and improve data quality and data sharing. The Cure Sickle Cell Initiative (CureSCi) library of recommendations or common data elements (CDE) will facilitate the preparation of data collection tools and present the current state of science through a hierarchical presentation of data elements to collect along with any guidelines for clinical research genetic studies in sickle cell disease.

The Monitoring Side Effects WG defines the following time periods in regards to side effects:

- **Acute** as being first 100 days after infusion (gene therapy/gene editing)
- **Mid** being 100 days to 2 years post-infusion; and,
- **Late** as being 2-15 years.

After some deliberation, the WG defined their scope (see **Table A**) with understanding that there would be some overlap with Physical Examination/Medical History and Genetics/Assays working groups. In addition, side effects were identified when possible to fit into three categories: SCD related (disease-related); conditioning-related; or therapy-related.

**Table A**

| Timeline | Acute | | | Mid | | | Late | | |
|---|---|---|---|---|---|---|---|---|---|
| Cause | Therapy Related | Conditioning Related | Disease Related | Therapy Related | Conditioning Related | Disease Related | Therapy Related | Conditioning Related | Disease Related |
| Infections | X | X | X | X | X | X | X | X | X |
| Liver toxicity | X | X | X | X | X | X | X | X | X |
| Mucositis | X | X | X | X | X | X | X | X | X |
| Transfusion support duration | X | X | X | X | X | X | X | X | X |
| Genotoxicity (off-target effects and insertional mutagenesis, conditioning related clonal proliferation) | X | X | NA | X | X | NA | X | X | NA |
| Presence and Durability of gene modified HSC graft | X | X | NA | X | X | NA | X | X | NA |
| Endocrine insufficiency, infertility, growth | X | X | X | X | X | X | X | X | X |

CURE SICKLE CELL.

| Timeline | Acute | | | Mid | | | Late | | |
|---|---|---|---|---|---|---|---|---|---|
| Cause | Therapy Related | Conditioning Related | Disease Related | Therapy Related | Conditioning Related | Disease Related | Therapy Related | Conditioning Related | Disease Related |
| delay and osteoporosis/avascular necrosis | | | | | | | | | |
| Neurological side effects (e.g., seizures, stroke, hemorrhage) | X | X | X | X | X | X | X | X | X |
| Neuropsychological effects | X | X | X | X | X | X | X | X | X |
| Iron Overload | X | X | X | X | X | X | X | X | X |
| Secondary malignancy | X | X | NA | X | X | NA | X | X | NA |
| Immune function and/or responses | X | X | X | X | X | X | X | X | X |
| Pulmonary Function | X | X | X | X | X | X | X | X | X |
| Infusional toxicity (acute) | X | NA | NA | NA | NA | NA | NA | NA | NA |
| Cytopenia (duration of neutropenia, thrombocytopenia) | X | X | X | X | X | X | X | X | X |
| Serious AEs – Hospitalization (duration) | X | X | X | X | X | X | X | X | X |
| Organ specific toxicities (supplemental) – liver, lung, kidney, heart, brain, GI | X | X | X | X | X | X | X | X | X |
| Mortality and survival | X | X | X | X | X | X | X | X | X |

CURE SICKLE CELL.

**Summary Table:**

| Domain/Subdomain | CRF | Classification | Notes |
|---|---|---|---|
| Safety Data | Genotoxicity Module | TBD | Related to Genetically Modified HSC Infusion. This module was reviewed also by the Genetics/Assays WG. |
| Safety Data | Infusional Toxicity | Supplemental-Highly Recommended | For genetically modified cells – required elements |
| Treatment and Intervention Data | Genetic Persistence | TBD | Baseline and Post therapy monitoring. This module was reviewed also by the Genetics/Assays WG. |
| Treatment and Intervention Data | HCT Infusion | Supplemental | Form used for autologous back up |
| Safety Data | Cytopenia Module | Supplemental | Form modified from CIBMTR |
| Safety Data | Immune function and/or responses Module | Supplemental | CIBMTR Form 2031 revision 2 June 2009 |
| Safety Data | Infections Module | Supplemental | Modified from BMT CTN Infection Form. This module was reviewed also by the Physical Examination/Medical History WG. |

CURE SICKLE CELL.

| Domain/Subdomain | CRF | Classification | Notes |
|---|---|---|---|
| Safety Data | Iron Overload Module | Core and Supplemental | |
| Safety Data | Spleen Toxicities | Supplemental | |
| Safety Data | Toxicity Form | Supplemental | BMT CNT form |
| Safety Data | Malignant Neoplasm Module | Supplemental | Secondary/new malignancy form was drafted new by WG members. |
| Treatment and Intervention Data | Cellular Therapy Essential Data Follow-Up Form | Supplemental | |
| Assessments and Examinations / Chronic Conditions | Endocrine, Fertility and Bone | Core and Supplemental | Core elements on Avascular necrosis and fertility preservation questions. This was also presented in the Physical Examination/Medical History WG public review files. |
| Safety Data | Mortality and survival Module (Death Form) | Supplemental | |
| Safety Data | Serious Adverse Events | Core and Supplemental Elements | Standard form adopted from National Institute of Neurological Disorders and Stroke CDEs |

CURE SICKLE CELL.

# Infection Form

[Study Name/ID pre-filled]

Site Name:
Subject ID:

1. Infection start date:
2. Infection site:
3. Is the infection a nonmicrobiologically defined infection?

   ☐ Yes ☐ No
4. Did the patient have evidence of pneumonia or bronchopneumonia related to an infection?

   ☐ Yes ☐ No
5. Did the patient require mechanical ventilation?

   ☐ Yes ☐ No
6. Did the patient have typhlitis?

   ☐ Yes ☐ No
7. Did the patient have severe sepsis without an identified organism?

   ☐ Yes ☐ No
8. Type of infection (answer following questions for each infection):

   ☐ Bacterial ☐ Fungal ☐ Viral ☐ Protozoal ☐ SARS Covid 2 ☐ Other
9. Organism: (see code list)
   a. Specify other organism:
10. Severity of infection:

    ☐ Grade 2 ☐ Grade 3
11. Was there evidence of sepsis?

    ☐ Yes ☐ No
12. Was there evidence of new or worsening infiltrates at the tie of the infection?

    ☐ Yes ☐ No
13. Was an agent(s) administered to treat the infection?

    ☐ Yes ☐ No
14. Provide agent(s) administered to treat the infection(s): (see code list)
15. Were additional agents administered for the infection(s):
    a. Specify other agent:
16. Did any of the events reported above lead to an advanced care intervention or Intensive Care Unit admission/transfer?

    ☐ Yes ☐ No
17. Infection site: (see code list)

# Infection CRF Module Instructions

## General Instructions

## Specific Instructions

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

**Organism** list of values: Staphylococcus (coag-);Staphylococcus (coag +);Staphylococcus (NOS);Stomatococcus mucilaginosis;Streptococcus (all species except Enterococcus);Treponema (syphilis);Tuberculosis (NOS, AFB, acid fast bacillus, Koch bacillus);Typical Tuberculosis (TB, Tuberculosis);Vibrio (all species);Other Bacteria;Herpes Simplex (HSV1, HSV2);Herpes Zoster (Chicken Pox, Varicella);Cytomegalovirus (CMV);Adenovirus;Enterovirus (Coxsackie, Echo, Polio);Hepatitis A (HAV);Hepatitis B (HBV, Australian antigen);Hepatitis C (includes non-A and non-B, HCV);HIV-1, HITLV-III;Influenza (Flu);Measles (Rubeola);Mumps;Papovavirus;Respiratory Syncytial virus (RSV);Rubella (German Measles);Parainfluenza;HHV-6 (Human Herpes Virus);Epstein-Barr Virus (EBV);Polyomavirus;Rotavirus;Rhinovirus (Common Cold);Other Viral;Pneumoncystis (PCP);Toxoplasma;Giardia;Cryptosporidium;Amebiasis;Echinoco ocalcyst;Trichomonas (either vaginal or gingivitis);Other Protozoal (parasite);Mycobacterium Tuberculosis;Other Mycobacterium;Mycoplasma;Other Organism;Candida Albicans;Candida Krusei;Candida Parasilosis;Candida Tropicalis;Torulopsis Galbrata (a subspecies of Candida);Candida (NOS);Asperguillus Flavus;Asperguillus Fumigatus;Asperguillus Niger;Asperguillus (NOS);Cryptococcus Species;Fusarium Species;Mucormycosis (Zygomycetes, Rhizopus);Yeast (NOS);Other Fungus;Acinetobacter (baumanii, calcoaceticus, lwoffi, other species);Agrobacterium radiobacter;Alcaligenes xylosoxidans;Anaerobic bacteria (NOS, except for Bacteroides, Clostridium);Bacillus (cereus, other species);Bacteroides (gracillis, uniformis, vulgaris, other species);Borrelia (Lyme Disease);Branhamelia or Moraxella catarrhalis (other species);Campylobacter (all species);Chlamydia;Citrobacter (freundii, other species);Clostridium (all species except difficile);Clostridium diificile;Corynebacterium (all non-diptheria species);Coxiella;Enterobacter;Enterococcus (all species);Escherichia (also E. coli);Flavimonas oryzihabitans;Flavobacterium;Fusobacterium nucleatum;Gram Negative Diplococci (NOS);Gram Negative Rod (NOS);Gram Positive Cocci (NOS);Gram Positive Rod (NOS);Haemophilus (all species including influenzae);Helicobacter pylori;Klebsiella;Lactobacillus (bulgaricus, acidophilus, other species);Legionella;Leptospira;Leptotrichia buccalis;Leuconostoc (all species);Listeria;Methylobacterium;Micrococcus (NOS);Mycobacteria (avium, bovium, haemophilum, intercellulare);Mycoplasma;Neisseria (gonorrhoea, meningitidis, other species);Nocardia;Pharyngeal/Respiratory Flora;Propionbacterium (acnes, avidum, granulosum, other species);Pseudomonas (all species except cepacia and maltophilia);Pseudomonas or Burkholderia cepacia;Pseudomonas or Stenotrophomonas or Xanthomonas maltophilia;Rhodococcus;Rickettsia;Salmonella (all species);Serratia marcescens;Shigella

**Agent**: Abacavir (Ziagen);Acyclovir (Zovirax);Albendazole (Albenza);Amantadine (Symmetrel, Symadine);Amikacin (Amikin);Amoxicillin/clavulanate (Augmentin);Amphotericin b (Abelcet, Amphotec, Fungizone);Ampicillin (Omnipen, Polycillin);Ampicillin/Sulbactam (Unasyn);Amprenavir (Agenerase);Atovaquone (Meprone);Azithromycin (Zithromax, Z-Pack);Cefaclor (Ceclor);Cefadroxil (Duricef, Ultracef);Cefazolin (Ancef, Kefzol);Cefdinir (Omnicef);Cefepime (Maxipime);Cefixime (Suprax);Cefoperazone (Cefobid);Cefotaxime (Claforan);Cefotetan (Cefotan);Cefoxitin (Mefoxin);Cefpodoxime (Vantin);Cefprozil (Cefzil);Ceftazidime (Fortaz, Tazicef);Ceftriaxone (Rocephin);Cefuroxime (Ceftin, Kefurox, Zinacef);Cephalexin (Keflet, Keflex, Keftab);Chloramphenicol (Chloromycetin);Cidofovir (Vistide);Ciprofloxacin (Cipro);Clarithromycin (Biaxin);Clindamycin (Cleocin);Clotrimazole (Mycelex, Lotrimin);Clotrimoxazole/betamethasone (Lotrisone);Co-trimoxazole (Bactrim, Septra, Sulfamethoprim);Dapsone (DDS);Dicloxacillin (Dycill, Dynapen, Pathocil);Didanosine (Videx, ddl);Doxycycline

# Infection CRF Module Instructions

(Vibramycin);Efavirenz (Sustiva);Erythromycin (Ery-Tab, llosone, Pediamycin);Erythromycin ethyl/sulfisoxazole (Pediazole);Erythromycin topical (Akne-mycin, Eryderm);Ethambutol (Myambutol);Famciclovir (Famvir);Fluconazole (Diflucan);Flucytosine (Ancobon);Foscarnet (Foscavir);Ganciclovir (Cytovene);Gatifloxican (Tequin);Gentamicin (Garamycin, Gentacidin);Grepafloxacin (Raxar);Hepatitis A Vaccine (Havrix, Vaqta);Hepatitis B Vaccine (Recombivax HB, Energix-B);Hepatitis C Vaccine;Imipenem/Cilastatin (Primaxin);Imiquimod (Aldara);Indinavir (Crixivan);Interferon Alfacon-1 (Infergen);Interferon beta-1a (Avonex);Interferon beta-1b (Betaseron);Isoniazid (INH, Lanizid, Nydrazid);Itraconazole (Sporonox);Ivermectin (Stromectol);Kanamycin (Kantrex);Ketoconazole (Nizoral);Lamivudine (Epivir, 3TC);Levofloxacin (Levaquin);Linezolid (Zyvox);Lopinavir/Ritonavir (Kaletra);Mefloquine (Larium);Meropenem (Merrem I.V.);Metronidazole (Flagyl, Protostat);Minocycline (Arestin);Moxifloxacin hydrochloride (Avelox);Mupirocin (Bactroban);Nafcillin (Nallpen, Unipen);Nelfinavir (Viracept);Neomycin (Mycifradin, Myciguent);Neomycin/Polymxin/Hydrocortisone (Cortisporin);Nevirapine (Viramune);Nitrofurantoin (Macrobid);Nystatin (Mycostatin);Oseltamivir (Tamiflu);Oxacillin (Bactocill);Palivizumab (Synagis);Penicillin G (Bicillin);Penicillin vk (V-Cillin K, Veetids);Pentamidine (Pentam 300);Piperacillin (Pipracil);Piperacillin/Tazobactam (Zosyn);Podofilox (Condylox);Polymyxin (Ak-Spore H.C., Cortisporin Opthalmic Suspension);PPD Skin test (Mantoux Test, Tine Test);Pyrazinamide (Rifater);Pyrimethamine (Daraprim);Quinidine gluconate (Duraquin, Cardioqiuin);Quinupristin/Dalfopristin (Synercid);Respiratory syncytial immune globulin (Respigam);Ribavirin (Virazole);Rifampin (Rifadin, Rimactane);Rifampin/Isoniazid (Rifamate, Rimactane/INH);Rifampin/isoniazid/Pyrazinamide (Rifater);Rimantadine (Flumadine);Ritonavir (Norvir);Saquinavir mesylate (Fortovase, Invirase);Stavudine (d4T, Zerit);Streptomycin (Streptomycin sulfate);Sulfamethoxazole/Trimethoprim (Bactrim);Terbinafine (Lamisil);Terconazole (Terazol);Tetracycline (Achromycin);Ticarcillin/Clavulanate (Ticar, Timentin);Tobramycin (Nebcin, Tobrex, TobraDex);Trimethoprim/Sulfamethoxazole (Bactrim, Spetra, Co-trimoxazole);Valganciclovir (Valtrex);Valganciclovir (Valcyte);Vancomycin (Vancocin);Zidovudine (AZT, Retrovir);Other

**Infection Site:** Blood/Buffy Coat;Disseminated - Generalized, Isolated at 2 or More Distinct Sites;Brain;Spinal Cord;Meninges and CSF;Central Nervous System Unspecified;Lips;Tongue, Oral Cavity, and Oro-Pharynx;Esophagus;Stomach;Gallbladder and Billary Tree (Not Hepatitis), Pancreas;Small Intestine;Large Intestine;Feces/Stool;Peritoneum;Liver;Gastrointestinal Tract Unspecified;Upper Airway and Nasopharynx;Larynx;Lower Respiratory Tract (Lung);Pleural Cavity, Pleural Fluid;Sinuses;Respiratory Tract Unspecified;Kidneys, Renal Pelvis, Ureters and Bladder;Prostate;Testes;Fallopian Tubes, Uterus, Cervix;Vagina;Genito-Urinary Tract Unspecified;Genital Area;Rash, Pustules, or Abscesses Not Typical of Any of the Above;Skin Unspecified;Woundsite;Catheter Tip;Eyes;Ears;Joints;Bone Marrow;Bone Cortex (Osteomyelitis);Muscle (Excluding Cardiac);Cardiac (Endocardium, Myocardium, Pericardium);Lymph Nodes;Spleen;Other Unspecified

Reference: BMT CTN CRFs used to develop this template

# Cytopenia

[Study Name/ID pre-filled] Site Name:

Subject ID:

## POST THERAPY DATA FORM

**Visit:**

☐ 3 month
☐ 6 month
☐ 9 month
☐ 12 month
☐ 15 month
☐ 18 month
☐ 21 month
☐ 24 month
☐ 30 month
☐ 36 month
☐ 42 month
☐ 48 month
☐ 5 years or greater. Number of Years: _____

Report all findings SINCE DATE OF LAST REPORT

__ __ / __ __ / __ __ __ __

Date of examination: __ __ / __ __ / __ __ __ __

Physical assessments:
(to be decided)

Date of initial gene therapy: __ __ / __ __ / __ __ __ __

Has the patient received additional gene therapy since the last report?

☐ Yes
☐ No
If yes, date: __ __ / __ __ / __ __ __ __

### NEUTROPHIL RECOVERY

*To report dates in this section, use the first of 3 consecutive laboratory values obtained on different days.*

Was there evidence of initial granulopoietic recovery?

☐ Yes (ANC ≥ 500/mm3 achieved and sustained for 3 lab values)
☐ No (ANC ≥ 500/mm3 was not achieved)

Not applicable (ANC never dropped below 500/mm3 at any time after the start of the preparative regimen)

# Cytopenia

[Study Name/ID pre-filled] Site Name:

Subject ID:

Date ANC ≥ 500/mm³ (first of 3 lab values):

Following the initial granulopoietic recovery, was there subsequent decline in ANC to < 500/mm3 for ≥ 3 days since the date of last report?

☐ Yes
☐ No

Date of decline in ANC to < 500/mm3 for ≥ 3 days (first of 3 days that the ANC declined):

__ __ / __ __ / __ __ __ __

Did recipient recover and maintain ANC ≥ 500/mm3 following the decline?

☐ Yes
☐ No

Date of ANC recovery (first of 3 lab values): __ __ / __ __ / __ __ __ __

**PLATELET RECOVERY**

*This section relates to initial platelet recovery. All dates should reflect no transfusions in the previous 7 days. To report dates in this section, use the first of 3 consecutive laboratory values obtained on different days.*

Was there evidence of initial thrombopoietic recovery?

☐ Yes (PLT ≥ 50 x $10^9$/L achieved untransfused for 7 days and sustained for 3 lab values)
☐ No (PLT ≥ 50 x $10^9$/L was not achieved)
☐ Not applicable (PLT never dropped below 50 x $10^9$/L at any time after the start of the preparative regimen)

Date PLT ≥ 50 x $10^9$/L (first of 3 lab values): __ __ / __ __ / __ __ __ __

Following the initial thrombopoietic recovery, was there subsequent decline in PLT < 50 x $10^9$/L for ≥ 3 days since the date of last report?

☐ Yes
☐ No

Date of decline in PLT < 20 x $10^9$/L for ≥ 3 days (first of 3 days that the PLT declined):

__ __ / __ __ / __ __ __ __

Did recipient recover and maintain PLT ≥ 20 x $10^9$/L following the decline?

# Cytopenia



__ __ / __ __ / __ __ __ __

Date of PLT recovery (first of 3 lab values):

__ __ / __ __ / __ __ __ __

Date PLT ≥ 50 x $10^9$/L (first of 3 lab values):

__ __ / __ __ / __ __ __ __

Following thrombopoietic recovery PLT ≥ 50 x $10^9$/L, was there subsequent decline in PLT to < 50 x $10^9$/L for ≥ 3 days since the date of last report?

☐ Yes (PLT ≥ 50 x $10^9$/L achieved and sustained for 3 lab values)

☐ No (PLT ≥ 50 x $10^9$/L was not achieved)

☐ Not applicable (PLT never dropped below 50 x $10^9$/L at any time after the start of the preparative regimen)

Date of decline in PLT < 50 x $10^9$/L for ≥ 3 days (first of 3 days that the PLT declined):

__ __ / __ __ / __ __ __ __

Did recipient recover and maintain PLT ≥ 50 x $10^9$/L following the decline?

☐ Yes (PLT ≥ 50 x $10^9$/L achieved and sustained for 3 lab values)

☐ No (PLT ≥ 50 x $10^9$/L was not achieved)

Date of PLT recovery (first of 3 lab values):

Date PLT ≥ 100 x $10^9$/L (first of 3 lab values):

Following thrombopoietic recovery PLT ≥ 100 x $10^9$/L, was there subsequent decline in PLT to
< 100 x $10^9$/L for ≥ 3 days since the date of last report?

☐ Yes (PLT ≥ 100 x $10^9$/L achieved and sustained for 3 lab values)

☐ No (PLT ≥ 100 x $10^9$/L was not achieved)

☐ Not applicable (PLT never dropped below 100 x $10^9$/L at any time after the start of the preparative regimen)

Date of decline in PLT < 100 x $10^9$/L for ≥ 3 days (first of 3 days that the PLT declined):

__ __ / __ __ / __ __ __ __

Did recipient recover and maintain PLT ≥ 100 x $10^9$/L following the decline?

__ __ / __ __ / __ __ __ __Date of PLT recovery (first of 3 lab values):

__ __ / __ __ / __ __ __ __

# Cytopenia

[Study Name/ID pre-filled] Site Name:

Subject ID:

## ERYTHROCYTE RECOVERY

*This section relates to initial hemoglobin recovery. All dates should reflect no transfusions in the previous 90 days. To report dates in this section, use the first of 3 consecutive laboratory values obtained on different days.*

Was there evidence of initial erythropoietic recovery?

☐ Yes (Hb ≥ 10 g/dL achieved and sustained for 3 lab values without transfusion)

☐ No (Hb ≥ 10 g/dL was not achieved)

☐ No Patient continues to receive RBC transfusions

☐ Not applicable (Hb never dropped below 10 g/dL at any time after the start of the preparative regimen)

Date Hb ≥ 10 g/dL (first of 3 lab values) without transfusion:

__ __ / __ __ / __ __ __ __

Hemoglobin _____

Erythrocyte count: _____

Absolute reticulocyte count: _____

Lactate dehydrogenase: _____

Bilirubin (indirect) _____

Following the initial erythropoietic recovery, was there subsequent decline in Hb < 10 g/dL for ≥ 3 days since the date of last report?

☐ Yes

☐ No

Date of decline in Hb < 10 g/dL for ≥ 3 days (first of 3 days that the Hgb declined):

MCV: __ __ / __ __ / __ __ __ __

Erythrocyte count: __ __ / __ __ / __ __ __ __

Absolute reticulocyte count: __ __ / __ __ / __ __ __ __

Lactate dehydrogenase: __ __ / __ __ / __ __ __ __

Bilirubin (indirect) _____

Did recipient recover and maintain Hb ≥ 10 g/dL following the decline?

☐ Yes

☐ No

Date of Hb recovery (first of 3 lab values): __ __ / __ __ / __ __ __ __

MCV: __ __ / __ __ / __ __ __ __

# Cytopenia



Erythrocyte count: __ __ / __ __ / __ __ __ __

Absolute reticulocyte count: __ __ / __ __ / __ __ __ __

Lactate dehydrogenase: __ __ / __ __ / __ __ __ __

Bilirubin (indirect) _____

## GROWTH FACTOR AND CYTOKINE SUPPORT

Did the recipient receive hematopoietic growth factors or cytokines after the start of the preparatory regimen?

Specify granulopoietic agent:

- ☐ G-CSF
- ☐ Peg G-CSF
- ☐ GM-CSF
- ☐ Other

Date started: __ __ / __ __ / __ __ __ __

Indication: _____

- ☐ Planned therapy per protocol
- ☐ Intervention for delay in cell count recovery
- ☐ Intervention for decline in cell count
- ☐ Other

Date ended __ __ / __ __ / __ __ __ __:

Specify thrombopoietic agent:

- ☐ Romiplostim
- ☐ Eltrombopag
- ☐ Avatrombopag
- ☐ Lusutrombopag
- ☐ Oprelvekin
- ☐ Other

Date started: __ __ / __ __ / __ __ __ __

Indication: __ __ / __ __ / __ __ __ __

- ☐ Planned therapy per protocol
- ☐ Intervention for delay in cell count recovery
- ☐ Intervention for decline in cell count
- ☐ Other

Date ended: __ __ / __ __ / __ __ __ __

# Cytopenia

[Study Name/ID pre-filled] Site Name:

Subject ID:

Specify erythropoietic agent:

- ☐ Epoetin alfa
- ☐ Darbepoetin
- ☐ Other

Date started: __ __ / __ __ / __ __ __ __

Indication: __ __ / __ __ / __ __ __ __

- ☐ Planned therapy per protocol
- ☐ Intervention for delay in Hb recovery
- ☐ Intervention for decline in Hb count
- ☐ Other

Date ended: __ __ / __ __ / __ __ __ __

**CURRENT HEMATOLOGICAL INDICES**

Date drawn: __ __ / __ __ / __ __ __ __

- ☐ White Blood Cell (WBC)
- ☐ Red Blood Cell (RBC)
- ☐ Hemoglobin (Hb)
- ☐ Hematocrit (HCT)
- ☐ Mean Cell Volume (MCV)
- ☐ Mean Cell Hemoglobin (MCH)
- ☐ Mean Cell Hb Conc (MCHC)
- ☐ Red Cell Dist Width (RDW)
- ☐ Reticulocyte %
- ☐ Absolute reticulocyte count
- ☐ Platelet count
- ☐ Mean Platelet Volume
- ☐ WBC Differential
  - ☐ Neutrophil %
  - ☐ Lymphocyte %
  - ☐ Monocyte %
  - ☐ Eosinophil %
  - ☐ Basophil %
  - ☐ Neutrophil, Absolute
  - ☐ Lymphocyte, Absolute
  - ☐ Monocyte, Absolute
  - ☐ Eosinophil, Absolute
  - ☐ Basophil, Absolute

# Cytopenia

[Study Name/ID pre-filled] Site Name:

Subject ID:

## HEMOGLOBIN ELECTROPHORESIS

Was hemoglobin electrophoresis performed? *(do not include results if an RBC transfusion occurred within 4 weeks of the electrophoresis study)*

☐ Yes

Date: __ __ / __ __ / __ __ __ __

☐ No

☐ Not Applicable (transfused within the last month)

Method:

☐ Gel based electrophoresis
☐ High-pressure liquid chromatography
☐ Capillary zone electrophoresis
☐ Isoelectric focusing
☐ Other

Specify the allele types:

HbA1
☐ Yes _____%
☐ No

HbA2
☐ Yes _____%
☐ No

HbC
☐ Yes _____%
☐ No

HbS
☐ Yes _____%
☐ No

HbF
☐ Yes _____%
☐ No

Other (specify)
☐ Yes _____%
☐ No

Other (specify)
☐ Yes _____%
☐ No

# Cytopenia

[Study Name/ID pre-filled] Site Name:

Subject ID:

**General Instructions**

All these CDEs are Supplemental. From CIBMTR form – needs reference

**Specific Instructions**

Bulleted List/Text

# Genotoxicity

[Study Name/ID pre-filled] Site Name:

Subject ID:

Date of Genetically Modified HSC Infusion_____

Time since autologous transplant and Genetically Modified HSC Infusion):

☐ Day 0

☐ 3 month ☐ 6 months ☐ 1 /1.5 yr ☐ 2 /2.5 yr ☐ 3/3.5 yr ☐ 4/4.5yr ☐ 5yr
☐ 6yr ☐ 7yr ☐ 8 yr ☐ 9 yr ☐ 10 yr ☐ 11yr ☐ 12yr
☐ 13yr ☐ 14yr ☐ 15yr

Type of Hematopoietic Stem and Progenitor Cell (HSPC) Product: see DP CRF

**Hematological Status since the date of last report:** ☐ Non-concerning ☐ Concerning*

The latest Complete Blood Count

Hb _____

WBC_____

Plt_____

Neutrophils %_____

Lymphocytes%_____

Retic Count_____

-***If concerning and clinically significant, complete AE form**

**Is there evidence of Premalignant/Malignant Hematopoiesis**

☐ No ☐ Yes

Dysplastic Cells ☐ No ☐ Yes

If Yes, Lineages affected_____

Blasts ☐ Yes ☐ No.

If Yes, type_____ Percentage_____

# Genotoxicity

[Study Name/ID pre-filled] Site Name:

Subject ID:

**What best describes the abnormal hematopoiesis**

☐ MDS

☐ Leukemia/lymphoma

Date of onset_____

Is the event being treated? ☐ Yes ☐ No

Treatment: ☐ Transfusions Blood Product_____ frequency_____

☐ Chemotherapy

☐ HSC Transplant

Has analysis been performed to determine probably cause of hematological toxicity ? ☐ Yes ☐ No

**Is it related or likely due to the genetic manipulation** ☐ Yes ☐ No

If yes, specify relationship:

☐ definitely related ☐ probably related ☐ possibly related ☐ unrelated

**Is it related to the conditioning regimen** ☐ Yes ☐ No

If yes, specify relationship:

☐definitely related ☐probably related ☐possibly related ☐unrelated

**Bone Marrow Aspirate Performed?**

☐ Yes ☐ No

☐ Normal Morphology ☐ Dysplastic Morphology ☐ Malignant morphology

☐ Normal Cytogenetics ☐ Abnormal Cytogenetics

Cytogenetic Abnormalities_____(describe)

**Has the abnormal hematopoeisis resolved?** ☐ Yes ☐ No

Date of resolution_____

Survival Status

☐ Alive

☐ Dead Date Expired_____

# Genotoxicity

[Study Name/ID pre-filled] Site Name:

Subject ID:

## SECTION A: FOR INTEGRATING VIRAL VECTOR PRODUCTS

**Complete this Portion if Trial Involves Genetic Manipulation of HSPC using Integrating Viral Vectors (e.g. Lentiviruses)**

**Vector Specifics:** Transgene in the vector_____

Promoter/Enhancers in Vector _____

**Vector Copy Number (VCN) performed in**

☐ Blood VCN_____ **CD3 depleted?:** ☐ Yes ☐ No

☐ VCN in Specific Lineages: CD3+_____ CD19+_____ CD15+_____GPA+_____ CD14+_____

☐Percentage of Blood Cells Positive for Integrating Vector: PBMC _____ BFU-E_____

☐ Bone Marrow VCN: BMMC_____ CD34+_____ CFC_____

☐ Percentage of Bone Marrow Cells Positive for Integrating Vector: BMMC_____ CD34+_____ CFC_____

**Vector Integration Site Analysis (VISA) performed in**

☐ Blood

☐ Bone Marrow

☐ Sorted/fractionated Cell Populations

(specify lineages)_____

**Is there evidence of Polyclonal ("Rich") Gene-Modified Hematopoiesis?**

Is there a "Rich" (polyclonal population with ≥1000 unique integrations) of minimally fractionated cell specimens (whole Bone Marrow, CD34+ cell product, whole blood)

☐ Yes ☐ No

| Time Point* | Specimen Type | Number of unique integrants | Rich (Y/N) | VCN |
|---|---|---|---|---|
| _____ | _____` | _____ | _____ | ____ |
| _____ | _____` | _____ | _____ | ____ |
| _____ | _____` | _____ | _____ | ____ |

*Time since infusion (0/0.5/1/1.5/2/2.5/3/3.5/4/4.5/5/6/7/8/9/10/11/12/13/14/15 yrs)

**Is there evidence of oligoclonal gene modified hematopoiesis?**

# Genotoxicity

[Study Name/ID pre-filled] Site Name:

Subject ID:

☐ Yes ☐ No

**Is there evidence of Clonal Dominance? i.e., Do any cell clone/s or integrant/s account for ≥20% of all clones?**

☐ Yes ☐ No

If Yes, List the site of integration of dominant (≥20% representation) clone/s [e.g. gene location or flanking gene location]

| Gene Location | Percent Representation/Relative Abundance |
|---|---|
| _____ | _____ |
| _____ | _____ |
| _____ | _____ |
| _____ | _____ |

Is the location of the dominant integrant/s

☐ within or < 50Kb of a known oncogene

☐ Within or <50Kb of a Transcriptional Unit of any gene

☐ Within or < 50Kb of Cell signaling/proliferation Gene

☐ Within or near the following genes known to be associated with insertional oncogenesis

- ☐ LMO2
- ☐ IKZF1
- ☐ CCND2
- ☐ HMGA2
- ☐ MECOM

**Is there evidence of clonal expansion/Are any cell clones increasing in proportion over the last two analyses?**

| Clone | Last % representation/abundance | Current % Abundance |
|---|---|---|
| _____ | _____ | _____ |

**Based on VCN and VISA, what best describes the gene-modified hematopoiesis?**

☐ Clonal Dominance ☐ Oligoclonal hematopoiesis ☐ MDS

# Genotoxicity

[Study Name/ID pre-filled] Site Name:

Subject ID:

☐ Leukemia/lymphoma

**SECTION B: FOR GENE EDITED CELLULAR PRODUCTS**

Complete this portion if Gene Edited HSPC product

Gene editing frequency performed:

Blood:

**CD3 depleted?:** ☐ Yes ☐ No

Percent Conversion _____ or On-target Indels_____

☐ Percent conversion in Specific Blood Lineages: CD3+_____ CD19+_____ CD15+_____GPA+_____ CD14+_____

☐ On-target Indels in Specific Blood Lineages: CD3+_____ CD19+_____ CD15+_____GPA+_____ CD14+_____

Bone Marrow:

☐ BMMC Percent Conversion _____ or On-target Indels_____

☐ CD34+ Percent Conversion _____ or On-target Indels_____

☐ CFC Percent Conversion _____ or On-target Indels_____

Off Target Interrogation: Bioinformatic: ☐ CRISPOR ☐ CRISTA

☐ Other: list _____

Number of off-target editing sites screened: _____

Number of off-target editing sites confirmed: _____

Checked by GUIDE-seq? ☐ Yes ☐ No

Confirmed by NGS? ☐ Yes ☐ No

Confirmed by other method: ☐ Yes ☐ No If yes, list: _____

Acceptable editing rate confirmed for each off-target editing site:

What is the location of the dominant off-target site(s):

# Genotoxicity

[Study Name/ID pre-filled] Site Name:

Subject ID:

Is the editing site location: ☐ inter-genic ☐ intra-genic

Translocations between on-target and off-target editing sites detected by:

Cytogenetics: ☐ Yes ☐ No

If yes, summarize: _____

Droplet Digital PCR: ☐ Yes ☐ No

If no, what is the limit of detection:_____

If yes, what is the frequency of detection: _____

What method was used to monitor clonality:

☐ on-target indels ☐ Whole exome sequencing ☐ other_____

Do any cell clone/s associated with an editing event account for ≥20% of all clones?

☐ Yes ☐ No

If Yes, List the site of off-target gene editing of dominant (≥20% representation) clone/s [e.g. gene location or flanking gene location], if known

| Gene Location | Percent Representation/Relative Abundance |
|---|---|
| _____ | _____ |
| _____ | _____ |
| _____ | _____ |
| _____ | _____ |

Is the location of the dominant gene editing site

☐ within or < 50Kb of a known oncogene

☐ Within or <50Kb of a Transcriptional Unit

☐ Within or < 50Kb of Cell signaling/proliferation Gene

Are any cell clones increasing in proportion over the last two analyses?

| Clone | Last % representation | Current % representation |
|---|---|---|

# Genotoxicity

[Study Name/ID pre-filled] Site Name:

Subject ID:

If genotoxic event detected was an Oncogene panel used? ☐ Yes ☐ No

Was whole exome sequencing used? ☐ Yes ☐ No WGS? ☐ Yes ☐ No

If yes, state results:

If genotoxicity developed, were pre-manipulated cells genetically analyzed for ChIP? ☐ Yes ☐ No

How?

State results:

FROM FDA DOCUMENT:

Since drug product infusion has there been?

New malignancy(ies) ?
☐ Yes ☐ No If yes, describe_____

New incidence or exacerbation of a pre-existing neurologic disorder

☐ Yes ☐ No If yes, describe_____

New incidence or exacerbation of a prior rheumatologic or other autoimmune disorder

☐ Yes ☐ No If yes, describe_____

New incidence of a hematologic disorder.
☐ Yes ☐ No If yes, describe_____

New incidence of infection (potentially product-related)
☐ Yes ☐ No If yes, describe_____

# Genetic Persistence

[Study Name/ID pre-filled]

Site Name:

Subject ID:

BASELINE DATA

Autologous stem cell collection strategy

- ☐ Bone marrow harvest
- ☐ Cytokine mobilization
  - ☐ G-CSF
  - ☐ Plerixafor
  - ☐ G-CSF and Plerixafor
  - ☐ Other
- ☐ Chemotherapy mobilization
  - ☐ Cyclophoshamide
  - ☐ Other
- ☐ Gene modification technique
  - ☐ Viral transduction
  - ☐ Y-Retroviral
    - ☐ Lentiviral
    - ☐ Other
    - ☐ Vector construct (Gene Cassette, Insulator)
- ☐ Gene editing
  - ☐ CRISPER-Cas9
  - ☐ TALEN
  - ☐ ZFN
  - ☐ RGEN
  - ☐ Other
  - ☐ Gene target
    - ☐ γ-globin
    - ☐ β-globin
    - ☐ BCL11A

# Genetic Persistence

[Study Name/ID pre-filled]

Site Name:

Subject ID:

Transduction/Editing efficiency (%cells)

Cryopreservation

☐ y/n

☐ %DMSO

POST THERAPY MONITORING

(same frequency as reporting forms? To be included on each form? – 3 monthly intervals for the first 2 years, then 6 monthly until year 5, then annually)

Date sample drawn:

Tissue monitoring site:

☐ Peripheral blood

☐ Bone marrow

- ☐ Cells sorted?
  - ☐ Yes ☐ No
  - ☐ Immunophenotype

Method

☐ RFLP

☐ Sanger sequencing

☐ Western Blot

☐ NGS

☐ TIDE3

☐ Reporter gene assay

- ☐ Specify

☐ Other

Determination of immunogenicity

☐ [further discussion]

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

**PRE_INFUSION_BASELINE_FEMALE**

**This form captures data up until transplant ("Baseline")[1]**
PATIENT AGE AT INFUSION
PUBERTY STAGE[2] AT INFUSION
Height (cm)
Weight (kg)[3]
HYDROXYUREA USE: DURATION (years)

**BONES**

Have there ever been bone fractures? ☐ Yes ☐ No ☐ Unknown

If Yes, specify:

History of osteomyelitis ☐ Yes ☐ No ☐ Unknown

Have you ever been diagnosed with any condition or abnormality of the spine or skeleton? ☐ Yes ☐ No ☐ Unknown

If Yes, specify:

Has a DEXA scan ever been performed? ☐ Yes ☐ No ☐ Unknown

If Yes, specify indication and results:

Have you ever been told that you had rickets? ☐ Yes ☐ No ☐ Unknown

Do you get steroid injections for joints?

For adults between the ages of 40 – 90, World Health Organization (WHO) Fracture Risk Assessment tool (FRAX) score:

*AVASCULAR NECROSIS AT/BEFORE CURE

*If yes, where:

*If yes, stage (1-4) of Lesion 1___ Lesion 2 ___ OR Unknown/Unavailable

BONE TREATMENTS [ ] Vit D [ ] Calcium [ ] Bisphosphonates
Surgery for AVN ☐ Yes ☐ No ☐ Unknown

**ENDOCRINE**

[1] Confirmation that preparative regimen details are captured elsewhere

[2] Balasubramanian R, Crowley WF Jr. Isolated Gonadotropin-Releasing Hormone (GnRH) Deficiency. 2007 May 23 [Updated 2017 Mar 2]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Table 1. [Tanner Staging]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1334/table/kms.T.tanner_staging/

[3] Suggest REDCap fields for automatically generating percentiles for pediatric subjects

*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

## Short Stature/Growth Hormone Deficiency

Have you ever been diagnosed with short stature?

1.

☐ Yes ☐ No ☐ Unknown

2. *Have you ever been diagnosed with growth hormone deficiency?

☐ Yes ☐ No ☐ Unknown

a. *If Yes, did you receive growth hormone? ☐ Yes ☐ No ☐ Unknown

## Other Endo

3. Any other known hormone-related/endocrine syndromes or disorders?

☐ Yes ☐ No ☐ Unknown

a. If Yes, indicate all that apply:

☐ Polycystic ovary syndrome: Age at diagnosis:

☐ Constitutional delay of growth and puberty: Age at diagnosis:

☐ *Hypogonadotropic hypogonadism: Age at diagnosis:

☐ Hyperthyroidism: Age at diagnosis:

☐ Hypothyroidism: Age at diagnosis:

☐ Cushing's syndrome: Age at diagnosis:

☐ Hypoparathyroidism: Age at diagnosis: ☐ Adrenal insufficiency: Age at diagnosis:

☐ Dyslipidemia: Age at diagnosis:

☐ Exocrine pancreatic insufficiency: Age at diagnosis:

☐ Diabetes (see separate diabetes-specific CRF) : Age at diagnosis:

☐ Other, specify: Age at diagnosis

Identify any pre-existing endocrine abnormalities pre-infusion

**FERTILITY**

**To be answered by patient/parent**

Have you had menarche: Yes/No
If yes, age at menarche:
If yes, regular/irregular periods:
If no, why don't you get regular menses

- Menstrual suppressing contraception?

*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

- History of chemotherapy causing premature menopause
- Anatomic, endocrinologic or genetic cause unrelated to sickle cell disease, explain _____

Fertility assessments[4] performed: Yes/No
If no, why not (check all that apply): [ ] family / patient refused [ ] inappropriate for age [ ] not available at Center [ ] costs associated with testing
Was testing performed in relation to a menstrual cycle? Yes / No

*Fertility Preservation: Yes/No/Decline
*If no, why (pt may decline to answer)___
*If Yes, how paid for (check all that apply): [] insurance [] self-pay [] grant/foundation support [ ] research study about fertility preservation [ ] paid for by gene therapy study
*If insurance, copay_____
*If Yes, taking hydroxyurea at fertility preservation? Yes/No
If HU has been stopped, please indicate for how long?
*If yes, what is banked: oocytes, ovarian tissue, embryos
*If yes, storage cost for cryopreserved tissue/gametes (per year):
*Storage cost paid by [ ] patient / family [ ] insurance [ ] foundation/grant [ ] research study

**To be reported by Center**

Does your center have access to specialists in reproductive endocrinology/infertility?

- Yes, at our center
- Yes, at a referral center (academic practice)
- Yes, at a referral center (private practice)
- No
- If yes, do the reproductive endocrinology/infertility specialists perform ovarian tissue cryopreservation?
  Yes/ No

Fertility assessment results

[ ] Antimullerian Hormone (AMH): ____ Unit ____
[ ] Name of lab performing AMH
[ ] Follicle Stimulating Hormone
Day 3 – 5: Y/N
[ ] Luteinizing Hormone
Day 3 – 5: Y/N

[4] The fertility assessments need to described to patient in detail

*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

[ ] Estradiol
Day 3 – 5: Y/N
[ ] Total antral follicle count

Fertility preservation results

*Ovarian tissue preserved Y/N
*If oocytes preserved Y/N, If yes, how many?
*If embryos preserved Y/N, If yes, how many?

**Pre-BMT Reproduction History**

Contraception concurrent with infusion Y/N
If yes, name contraception:

**Pregnancy + Outcomes**
Have you been an expectant father before? Y/N
If yes, complete form: PRE_INFUSION_PREGNANCY_MALE

Pre BMT Menstrual History
Regular Y/N
Menorrhagia Y/N
Associated with VOC Y/N



*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

**PRE_INFUSION_BASELINE_MALE**

**BONES (see above)**

**ENDOCRINE (see above)**

**FERTILITY**

**To be answered by patient/parent**

Semen analysis to assess fertility performed: Yes/No
If no, why not (check all that apply): [ ] family / patient refused [ ] inappropriate for age [ ] not available at Center [ ] costs associated with testing

*Fertility Preservation: Yes/No/Decline
*If no, why (pt may decline to answer)___
*If Yes, how paid for (check all that apply): [] insurance [] self-pay [] grant/foundation support [ ] research study about fertility preservation [ ] paid for by gene therapy study
*If insurance, copay_____
*If yes, what is banked: sperm, embryos, testicular tissue
*If yes, storage cost for cryopreserved tissue/gametes (per year):
*Storage cost paid by [ ] patient / family [ ] insurance [ ] foundation/grant [ ] research study

**To be entered by Center**

Does your center have access to specialists in reproductive endocrinology/infertility?

- Yes, at our center
- Yes, at a referral center (academic practice)
- Yes, at a referral center (private practice)
- No

If yes, do the reproductive endocrinology/infertility specialists perform ovarian tissue cryopreservation?
Yes/ No

If semen analysis performed, results:
* Sperm concentration:
* Sperm motility:
* Sperm morphology:

Taking hydroxyurea at time of first semen analysis? Yes/No
If no, how long not taking hydroxyurea (months)
if yes, how long taking hydroxyurea

*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

Was semen analysis performed more than once? Y/N
If yes, why was semen analysis was repeated, why? [ ] testing incomplete [ ] confirm findings [ ] repeat off hydroxyurea [ ] other

If semen analysis was performed, what was result?
* Sperm concentration:
* Sperm motility:
* Sperm morphology:

Fertility preservation results

*Sperm preserved Y/N

Taking hydroxyurea at time of first semen analysis? Yes/No
If no, how long not taking hydroxyurea (months)
if yes, how long taking hydroxyurea

**Pre-BMT Reproduction History**

Contraception concurrent with infusion Y/N
If yes, name contraception:

**Pregnancy + Outcomes**
Have you ever been pregnant? Y/N
If yes, complete form: PRE_INFUSION_PREGNANCY_MALE



*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

**POST_INFUSION_FOLLOW_UP_YEAR_X_FEMALE**

Current age:

Medications

Which medications are you currently using.

- HORMONES (LIST Y/N)
  - INSULINs (expand list)
  - THYROID
  - HORMONE REPLACEMENT (list)
  - CORTICOSTEROIDS
  - VITAMIN D
  - BISPHOSPHONATES

- CONTRACEPTION (circle all that apply)
  - Combined oral contraception (estrogen & progesterone)
  - Progesterone-only pill
  - The patch
  - The shot
  - The implant
  - The hormonal IUD
  - The copper IUD

- CHELATION / PHLEBOTOMY

Which medications have you used in the past X years…

**Bones (see above)**

**Endocrine (see above)**

**Fertility**

**To be answered by patient/parent[5]**

Do you get menses (periods): Yes/No
If yes, are your periods regular or irregular periods:



[5] At 10 or 15 year follow-up visit, may addition how families who couldn't/didn't pursue biological parenthood pursued adoption or other alternative ways.

*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

If no, why don't you get regular menses

- Menstrual suppressing contraception?
- History of chemotherapy causing premature menopause
- Anatomic, endocrinologic or genetic cause unrelated to sickle cell disease, explain _____
- Menopause

If menopause, how old were you when you stopped getting periods:
If menopause, did you see a doctor to receive hormones: Y/N
If menopause, did the hormones cause you to resume menstrual cycles: Y/N
Hormone levels to be captured as needed.

Fertility assessments performed: Yes/No
If no, why not (check all that apply): [ ] family / patient refused [ ] inappropriate for age [ ] not available at Center [ ] costs associated with testing
Was testing performed in relation to a menstrual cycle? Yes / No

**To be reported by Center**

Does your center currently have access to specialists in reproductive endocrinology/infertility?

- Yes, at our center
- Yes, at a referral center (academic practice)
- Yes, at a referral center (private practice)
- No
- If yes, do the reproductive endocrinology/infertility specialists perform ovarian tissue cryopreservation?
  Yes/ No

Fertility assessment results

[ ] Antimullerian Hormone (AMH): ____ Units ____
[ ] Name of lab performing AMH
[ ] Follicle Stimulating Hormone
  Day 3 – 5: Y/N
[ ] Luteinizing Hormone
  Day 3 – 5: Y/N
[ ] Estradiol
  Day 3 – 5: Y/N
[ ] Total antral follicle count

Fertility preservation results



*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

If preserved oocytes / ovarian tissue, has it been retrieved: Yes/No
If yes, has patient pursued pregnancy: Yes/No
If yes, complete PREGNANCY FORM

*Are you continuing to preserve your oocytes/ ovarian tissue /embryos
*If yes, what is current cost of preservation:
*If no, why: [ ] cost [ ] family complete [ ] lab accident

Pregnancy

*Have you been pregnant since your last study visit? Y/N
*If yes, complete POST_INFUSION_FOLLOW-UP_YEAR_X_PREGNANCY_FEMALE



*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

**POST_INFUSION_FOLLOW_UP_YEAR_X_MALE**

Current age:

Medications

Which medications are you currently using.

- HORMONES (LIST Y/N)
  - INSULINs (expand list)
  - THYROID
  - HORMONE REPLACEMENT (list)
  - CORTICOSTEROIDS
  - VITAMIN D
  - BISPHOSPHONATES

- CHELATION / PHLEBOTOMY

Which medications have you used in the past X years…

**Bones (see above)**

**Endocrine (see above)**

**Fertility**

**To be answered by patient/parent**

Fertility assessments performed: Yes/No
If no, why not (check all that apply): [ ] family / patient refused [ ] inappropriate for age [ ] not available at Center [ ] costs associated with testing

**To be reported by Center**

Does your center currently have access to specialists in reproductive endocrinology/infertility?

- Yes, at our center
- Yes, at a referral center (academic practice)
- Yes, at a referral center (private practice)
- No

*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

- If yes, do the reproductive endocrinology/infertility specialists perform ovarian tissue cryopreservation?
  Yes/ No

Fertility assessment results

If semen analysis was performed, what was result?
* Sperm concentration:
* Sperm motility:
* Sperm morphology:

Fertility preservation results

If preserved sperm / embryos / testicular tissue, has it been retrieved: Yes/No
If yes, has patient pursued pregnancy: Yes/No
If yes, complete PREGNANCY FORM

Are you continuing to preserve your sperm/ embryos / testicular tissue?
If yes, what is current cost of preservation:
If no, why: [ ] cost [ ] family complete [ ] lab accident

Pregnancy

Have you been pregnant since your last study visit? Y/N
If yes, complete POST_INFUSION_FOLLOW-UP_YEAR_X_PREGNANCY_MALE



*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

**PRE_INFUSION_PREGNANCY_FEMALE**

**Pregnancy 1**

Maternal age at pregnancy:
Paternal age at pregnancy:
Pregnancy conception: “natural”, assisted reproductive technology, miracle, other ____
Outcome of pregnancy: termination, miscarriage, live birth, still birth
If live birth, weight at birth:
Maternal complications of pregnancy:
Fetal complications of pregnancy:



*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

**PRE_INFUSION_PREGNANCY_MALE**

**Pregnancy 1**

Maternal age at pregnancy:
Paternal age at pregnancy:
Pregnancy conception: “natural”, assisted reproductive technology, miracle, other ____
Outcome of pregnancy: termination, miscarriage, live birth, still birth
If live birth, weight at birth:
Maternal complications of pregnancy:
Fetal complications of pregnancy:



*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

**POST_INFUSION_PREGNANCY_FEMALE**

**Pregnancy 1**

Maternal age at pregnancy:
Paternal age at pregnancy:
Pregnancy conception: “natural”, assisted reproductive technology, miracle, other ____
If ART, was this pregnancy the result of oocytes, embryo or ovarian tissue cryopreservation?
If yes, which one:
Outcome of pregnancy: termination, miscarriage, live birth, still birth
If live birth, weight at birth:
Maternal complications of pregnancy:
Fetal complications of pregnancy:



*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

**POST_INFUSION_PREGNANCY_MALE**

**Pregnancy 1**

Maternal age at pregnancy:
Paternal age at pregnancy:
Pregnancy conception: “natural”, assisted reproductive technology, miracle, other ____
If ART, was this pregnancy the result of semen, embryo or testicular tissue cryopreservation?
If yes, which one:
Outcome of pregnancy: termination, miscarriage, live birth, still birth
If live birth, weight at birth:
Maternal complications of pregnancy:
Fetal complications of pregnancy:



*** Core CDE**

# Endocrine Infertility Bones

[Study Name/ID pre-filled] Site Name:

Subject ID:

**INSTRUCTIONS**

This document contains assessments related to **bone health**, **endocrine function**, **fertility**, and **pregnancy**

This module contains the following assessments:

- PRE_INFUSION BASELINE FORM_1_FEMALE
- PRE_INFUSION BASELINE FORM_1_MALE

- PRE_INFUSION PREGNANCY_FEMALE
- PRE_INFUSION PREGNANCY_MALE

- POST-INFUSION FOLLOW-UP_Year X_FEMALE
- POST-INFUSION FOLLOW-UP_Year X_MALE

- POST_INFUSION_PREGNANCY_FEMALE
- POST_INFUSION_PREGNANCY_MALE

Assessments are to be completed using the same follow-up form

- PRE INFUSION (include data up to start of preparative regimen)
- POST_INFUSION_YEAR_2
- POST_INFUSION_YEAR_5
- POST_INFUSION_YEAR_10
- POST_INFUSION_YEAR_15



The items with asterisks (*) are Core and should be collected on all genetic studies in sickle cell disease assessing acute painful episodes. The others are Supplemental and should be collected based on study design.

*** Core CDE**

# Iron Overload CRF Module instructions

Suggested Timeline for Related Laboratory Assessments – every 90-120 days for the first year and every 6 months thereafter for 5 years and then yearly until normal.

Hepatic Assessments

1. Was a liver MRI performed?

   ☐ Yes

   ☐ No

   ☐ Unknown

   *If Yes, what was the liver iron content (LIC)?

   ☐ Known, by ☐ R2* or ☐T2*:

   ☐ Unknown

   *If Known, estimated LIC: __ __ __ * __

   ☐ mg Fe/g liver dry weight

   ☐ g Fe/kg liver dry weigh

   ☐ umol Fe/g liver dry weight

2. Was a liver biopsy performed?

   ☐ Yes

   ☐ No

   ☐ Unknown

   *If Yes, date of most recent liver biopsy: __ __ __ __ / __ __ / __ __
   YYYY MM DD

   If yes, what was LIC? ___ mg Fe/gm liver dry wt

   If the LIC is >22 mg Fe/gm dw, consider cardiac iron assessment by MRI

   IF performed, was cardiac iron: ☐ *T2*>20;* ☐ *T2*>10, <20;* ☐ *T2* <10;*

   Was there evidence of fibrosis?

   ☐ Yes

   ☐ No

   *If Yes, identify type of fibrosis ☐ Bridging ☐ Periportal

   Was there evidence of cirrhosis?

   ☐ Yes

# Iron Overload CRF Module instructions

☐ No

Was there evidence of hepatic inflammatory/hepatitis?

☐ Yes

☐ No

Is a copy of biopsy report attached?

☐ Yes

☐ No



| Test | Normal | Result | Value | Significance | Comorbidities/ Comments |
|---|---|---|---|---|---|
| *Iron | | Data to be entered by site | ☐ Normal<br>☐ Abnormal<br>☐ Unknown | ☐ Normal<br>☐ Abnormal<br>☐ Unknown | ☐ Clinically significant<br>☐ Not clinically significant |
| *% Serum transferrin (% saturation) | | Data to be entered by site | ☐ Normal<br>☐ Abnormal<br>☐ Unknown | ☐ Normal<br>☐ Abnormal<br>☐ Unknown | ☐ Clinically significant<br>☐ Not clinically significant |
| Soluble transferrin receptor | | Data to be entered by site | ☐ Normal<br>☐ Abnormal<br>☐ Unknown | ☐ Normal<br>☐ Abnormal<br>☐ Unknown | ☐ Clinically significant<br>☐ Not clinically significant |
| Hepcidin | | Data to be entered by site | ☐ Normal<br>☐ Abnormal<br>☐ Unknown | ☐ Normal<br>☐ Abnormal<br>☐ Unknown | ☐ Clinically significant<br>☐ Not clinically significant |
| TIBC | | Data to be entered by site | ☐ Normal<br>☐ Abnormal<br>☐ Unknown | ☐ Normal<br>☐ Abnormal<br>☐ Unknown | ☐ Clinically significant<br>☐ Not clinically significant |
| Serum ferritin | | Data to be entered by site | ☐ Normal<br>☐ Abnormal<br>☐ Unknown | ☐ Normal<br>☐ Abnormal<br>☐ Unknown | ☐ Clinically significant<br>☐ Not clinically significant |

# Iron Overload CRF Module instructions

General Instructions
This form contains data elements that are collected to measure iron overload.

**Specific Instructions**

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

*Core Elements

…..

# New Malignancy

[Study Name/ID pre-filled

Site Name:

Subject ID:

New malignancy

1. Did a new malignancy develop (excluding non-melanoma skin cancer)?
    a. Yes / No
    b. If yes, date of diagnosis
    c. Was biopsy done to confirm diagnosis?
        i. Yes / No
        ii. If yes, indicated if copy of pathology report was submitted Yes/No
    d. Type of malignancy:
        i. Acute myeloid leukemia
            1. Was a genetic mutational (myeloid) panel done?
                a. Yes / No / unknown; if yes, attach results
                b. Date of test
        ii. Myelodysplastic syndrome
            1. Was a genetic mutational (myeloid) panel done?
                a. Yes / No / unknown; if yes, attach results
                b. Date of test
        iii. Lymphoma including post-transplant lymphoproliferative disorder (PTLD)
            1. Was there EBV reactivation in the blood?
                a. Yes / No /unknown
        iv. Other malignancy
            1. Acute lymphoblastic leukemia
                a. Yes/No, if Yes, date of diagnosis, attach copy of pathology report
            2. Other acute leukemia
                a. Yes/No, if Yes, date of diagnosis, attach copy of pathology report

2. If patient developed acute leukemia or myelodysplastic syndrome
    a. is there evidence of a unique vector insertion site in the malignant clone?
        i. Yes / No
        ii. if yes, is there an adjacent oncogene?
            1. Yes / No
            2. Is there evidence of a unique on-target gene modification in the malignant clone?
                a. Yes / No
    b. Is there evidence of a unique off-target gene mediation in the malignant clone?
        i. yes or no,
            1. if yes, is the off-target modification linked to an adjacent oncogene?
                a. Yes/No
    c. Is there an evidence of a unique chromosomal rearrangement in the malignant clone?
        i. Yes / No
            1. if yes, is it related to an off or on-target genomic modification?
                a. Yes / No

3. Was there loss of engraftment of gene-modified cells?
    a. Yes / No
        i. If Yes
            1. Date of event
            2. Vector copy number:
                a. 50% - 75% genetically corrected RBC

# New Malignancy

[Study Name/ID pre-filled

Site Name:

Subject ID:

   b. 25% - 50% genetically corrected RBC
   c. 0% - 25% genetically corrected RBC
3. Engraftment of genetically modified product
   a. ≤20%
4. Rescue with back-up autologous cells
   a. Yes / No

# Malignant Neoplasm Module Instructions

## General Instructions

This form is created to capture malignancies developed by patient during and after therapy and may be related or unrelated to sickle cell disease. Data elements on this form are Supplemental (recommended based on study design) unless indicated otherwise.

## Specific Instructions

# Immune Function Form

[Study Name/ID pre-filled]

Site Name:
Subject ID:

1. **Laboratory Studies at Diagnosis**

   Date CBC tested: (testing done within 6 weeks of diagnosis)
   WBC: ☐ Not tested

   Lymphocytes: % ☐ Not tested

   Polymorphonuclear leukocytes (PMN): % ☐ Not tested

   Hemoglobin: ☐ Not tested ☐ Transfused RBC < 30 days from date of test

   Immunoglobulin Analysis
   Specify the following quantitative immunoglobulins measured prior to any disease treatment:
   IgG: ☐ Not tested

   IgM: ☐ Not tested

   IgA: ☐ Not tested

   Did the recipient receive supplemental intravenous immunoglobulins (IVIG)?

   ☐ Yes

   ☐ No

   ☐ Unknown

2. **Lymphocyte Analysis**

   Were lymphocyte analyses performed?

   ☐ Yes

   ☐ No

   Date of most recent testing performed:
   Absolute lymphocyte count: cells / µL (cells / mm3)
   CD3 (T cells): value
   CD4 (T helper cells): value
   CD8 (cytotoxicT cells): value
   CD20 (B lymphocyte cells): value
   CD56 (natural killer (NK) cells): value
   CD4+ / CD45RA+(naive T cells): value
   CD4+ / CD45RO+(memory T cells): value
   Specify units
   ☐ x 109/L(x 1 03/mm3)
   ☐ x 106/L
   ☐ Not tested

3. **Antibody Response**

   Date antibody responses were assessed: *(date closest to diagnosis, before any IVIG)*

# Immune Function Form

[Study Name/ID pre-filled]

Site Name:
Subject ID:

| Absent | Low | Normal | Not tested | |
|---|---|---|---|---|
| ☐ | ☐ | ☐ | ☐ | Bacteriophage phi X-174 or other neoantigen |
| ☐ | ☐ | ☐ | ☐ | Diptheria |
| ☐ | ☐ | ☐ | ☐ | Isohemagglutinin anti-A |
| ☐ | ☐ | ☐ | ☐ | Isohemagglutinin anti-B |
| ☐ | ☐ | ☐ | ☐ | Protein conjugated HIB or pneumococcal vaccine |
| ☐ | ☐ | ☐ | ☐ | Tetanus |

Unconjugated pneumococcal polysaccharide: _____/ _____

Number of serotypes producing a protective level / Total serotypes tested from vaccine

4. **Lymphocyte Function**

Date lymphocyte function was assessed:

| | Absent (< 10% of control) | Low (10-30% of control) | Normal (> 30% of control) | Not Tested |
|---|---|---|---|---|
| Anti-CD3 | | | | |
| Candida antigen | | | | |
| Concavalin A (ConA) | | | | |
| Phytohemagglutinin (PHA) | | | | |
| Pokeweed mitogen (PWM) | | | | |
| Tetanus antigen | | | | |

# Immune Function Form

[Study Name/ID pre-filled]

Site Name:
Subject ID:

5. **Clinical Features Assessed between Diagnosis and the Start of the Preparative Regimen**

Infections (See Infection CRF) Identified between Diagnosis and the Start of the Preparative Regimen.

Specify the presence of all clinically significant infections identified between diagnosis and the start of the preparative regimen. If any given infection was identified, use the Codes for Commonly Reported Organisms on the following page to report the organism present.

Only report an organism once, even if it was identified at the same site in subsequent infections.

Hepatitis ☐ Yes ☐ No

If yes, indicate:

First organism

Second organism

Third organism

Specify other organism

If hepatitis was present, was it a prominent feature of ID?

☐ Yes

☐ No

Meningitis / encephalitis ☐ Yes ☐ No

If yes, indicate:

First organism

Second organism

Third organism

Specify other organism

If meningitis / encephalitis was present, was it a prominent feature of ID?

☐ Yes

☐ No

Pneumonia ☐ Yes ☐ No

If yes, indicate:

First organism

Second organism

Third organism

Specify other organism

If pneumonia was present, was it a prominent feature of ID?

☐ Yes

☐ No

# Immune Function Form

[Study Name/ID pre-filled]

Site Name:
Subject ID:

Severe or protracted diarrhea ☐ Yes ☐ No

If yes, indicate:

First organism

Second organism

Third organism

Specify other organism

If diarrhea was present, was it a prominent feature of ID?

☐ Yes

☐ No

Systemic infection ☐ Yes ☐ No

If yes, indicate:

First organism

Second organism

Third organism

Specify other organism

If systemic infection was present, was it a prominent feature of ID?

☐ Yes

☐ No

Other infection ☐ Yes ☐ No

If yes, indicate:

First organism

Second organism

Third organism

Specify other organism

Specify other infection site:

If other infe ction was present, was it a prominent feature of ID?

☐ Yes

☐ No

# Immune Function Form

[Study Name/ID pre-filled]

Site Name:
Subject ID:

# Immune Function CRF Module Instructions

## General Instructions

Assessments are to be completed using the same follow-up form

- PRE INFUSION (include data up to start of preparative regimen)
- POST_INFUSION_YEAR_2
- POST_INFUSION_YEAR_5
- POST_INFUSION_YEAR_10
- POST_INFUSION_YEAR_15

## Specific Instructions

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

# Stem Cell Product Infusional Toxicity

[Study Name/ID pre-filled] Site Name:

Subject ID:

## 1. PRODUCT ADMINISTRATION

Date of Administration: __ __ / __ __ / __ __ __ __

Protocol Primary Treatment Indication (select one only)

☐ Sickle Cell Disease (Genotype _____)

Subject gender:

☐ Male

☐ Female

Subject date of birth:

__ __ / __ __ / __ __ __ __

CIBMTR Recipient ID#

(If registered) _____

Volume available for administration (mL): _____

Actual volume administered (mL): _____

Cell concentration: _____ - _____ 10 ☐

per ☐ kg

☐ $m^2$

_____ (24 hr clock)

_____ (24 hr clock)

Was product administration delayed or stopped prematurely? ☐ No ☐ Yes

If Yes, explain: _____

Administered by (Print name and Title): _____

Route of product administration: (check route of administration)

☐ Intravenous

☐ Bone Marrow

Device system used for delivering product:

☐ Catheter

☐ Other, specify _____

Product administration frequency:

☐ One-time administration

☐ Multiple administrations

Current product administration is number: _____ of _____

Date of first product administration: _____

# Stem Cell Product Infusional Toxicity

[Study Name/ID pre-filled] Site Name:

Subject ID:

Did the recipient provide written consent for data submission for the purpose of research studies?
☐ No
☐ Yes

Will outcome data be collected for this administration?
☐ No
☐ Yes

## 2. REACTION(S) POST PRODUCT ADMINISTRATION

| **Did the subject experience any post product administration reactions?** | ☐ **No** ☐ **Yes** ***(If YES, check all that apply)*** |
|---|---|

| **Reaction** | **Reaction Occurred (Check if Yes)** | **Reaction Time Post Product Administration (Hours)** | **Severity** | **Resolved** |
|---|---|---|---|---|
| ☐ Chills | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Fever | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Rigors | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Dyspnea | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Bradycardia | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Tachycardia | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Hypertension | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| **Reaction** | **Reaction Occurred (Check if Yes)** | **Reaction Time Post Product Administration (Hours)** | **Severity** | **Resolved** |
| ☐ Hypotension | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Hemoglobinuria | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Hemoglobinemia | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Urticaria | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Rash | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Pain | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Nausea | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Vomiting | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| ☐ Other, specify: | ☐ | ☐ 0-1 ☐ >1-24 ☐ >24-48 | ☐ Mild ☐ Moderate ☐ Severe | ☐ No ☐ Yes ☐ Unknown |
| Other reaction specified: | | | | |
| List medication(s)/treatment for reaction or symptoms: | | | | |

# Stem Cell Product Infusional Toxicity

[Study Name/ID pre-filled]

Site Name:

Subject ID:

## General Instructions

This form should be used for genetically modified cells

## Specific Instructions

Bulleted List/Text

# Hematopoietic Cellular Transplant (HCT) Infusion

[Study Name/ID pre-filled]

Site Name:

Subject ID:

*Sequence number:*

*Date Received:*

*Center Number:*

*Recipient ID:*

Date of HCT for which this form is being completed:

HCT Type (check only one):

☐ Autologous (back up infusion) ☐ Gene therapy (vector) product ☐ Gene editing product

Product Type (check only one):

☐ Bone marrow ☐ PBSC

**Pre-Collection Therapy**

1. Did the patient receive therapy, prior to any stem cell harvest, to enhance the product collection for this HCT?

   ☐ Yes ☐ No

2. Growth and mobilizing factor(s)

   ☐ Yes ☐ No

3. Plerixafor (Mozobil):

   ☐ Yes ☐ No

4. Other growth or mobilizing factor:

   ☐ Yes ☐ No

   a. Specify other growth or mobilizing factor:

5. Systemic reporting therapy (chemotherapy):

   ☐ Yes ☐ No

6. Other therapy:

   ☐ Yes ☐ No

   a. Specify other therapy:

# Hematopoietic Cellular Transplant (HCT) Infusion

[Study Name/ID pre-filled] Site Name:

Subject ID:

**Product Collection**

7. Date of first collection for this mobilization:
8. Was there more than one collection required for this HCT?

   ☐ Yes ☐ No
9. Specify the number of subsequent days of collection in this episode:
10. Were anticoagulants added to the product during collection?

    ☐ Yes ☐ No

**Specify anticoagulant(s):**

11. Acid citrate dextrose (ACD)

    ☐ Yes ☐ No
12. Citrate phosphate dextrose (CPD)

    ☐ Yes ☐ No
13. Heparin

    ☐ Yes ☐ No
14. Other anticoagulant

    ☐ Yes ☐ No

    a. Specify other anticoagulant:
15. Were anticoagulants added to the product before freezing?

    ☐ Yes ☐ No

**Product Infusion (unmanipulated autologous product)**

16. Date of this product infusion: ____ -__ -__
17. Date Infusion started: _____ _
18. Time product infusion initiated (24-hourclock): _____ _

    ☐ Standard time ☐ Daylight savings time
19. Date infusion stopped: _____ _

# Hematopoietic Cellular Transplant (HCT) Infusion

[Study Name/ID pre-filled] Site Name:

Subject ID:

20. Time product infusion completed (24-hour clock): ___ ___

    ☐ Standard time ☐ Daylight savings time

21. Total volume of product plus additives intended for infusion: ____mL

22. Specify the route of product infusion

    ☐ Intravenous ☐ Other route of infusion

# CRF Name Instructions

[Study Name/ID pre-filled]

Site Name:

Subject ID:

**General Instructions**

This HCT form should only be used for autologous back up.

**Specific Instructions**

Bulleted List/Text

# Cellular Therapy Follow-Up

*[Study Name/ID pre-filled]* Site Name:

Clinicaltrials.gov Identifier Subject ID:

Event Date

Visit ☐ 100 day ☐ 6 months ☐ 1 year ☐ 2 years ☐ > 2 years, Specify:_

1. Name of product (for recent cell therapy infusion)_____
2. Was there evidence to initial recovery?

   ☐ Yes (ANC ≥ 500/mcL ($mm^3$) achived and sustained for 3 lab values)

   Date ANC ≥ 500/ mcL ($mm^3$) (first of 3 lab values)

   ☐ No (ANC ≥ 500/ mcL ($mm^3$) was not achieved)

   ☐ Not applicable (ANC never dropped below 500/ mcL ($mm^3$) at any time after the start of lymphodepleting therapy / no lymphodepleting therapy given)

   ☐ Previously reported (recipient's initial recovery was recorded on a previous report)

   you are asking for date _____
3. Was an initial platelet count ≥ 50 x $10^9$/L achieved (without antecedent platelet transfusion/s in the last 7 days)?

   ☐ Yes

   Date Platelets ≥ 50 x $10^9$/L (without platelet transfusions in the last 7 days)

   ☐ No

   ☐ Not applicable – Platelet count never dropped below 50 x 10^9/L at any time after the start of lymphodepleting therapy / no lymphodepleting therapy given

   ☐ Previously reported - ≥ 50 x $10^9$/L was achieved and reported previously
4. Date of most recent hemoglobin (see Lab form) MM/DD/YYYY
5. Hemoglobin

   ☐ Known ☐ Unknown

   Value

   Unit ☐ g/dL ☐g/L ☐ mmol/L

   Were RBC's transfused <= 30 days before date of test? ☐ Yes ☐ No

6. **Did a new malignancy, myeloproliferative, or lymphoprliferative disease/disorder occur (include clonal cytogenetic abnormalities, and post-transplant lyphoproliferative disorders) in this reporting period**

   ☐ Yes. Specify type _____ Date detected_____

   ☐ No

7. **Was tests performed to detect persistence of the genetically modified cellular product since the date of last report?**

   ☐ Yes ☐ No

# Cellular Therapy Follow-Up

*[Study Name/ID pre-filled]* Site Name:

Clinicaltrials.gov Identifier Subject ID:

8. Was persistence evaluated by molecular assay? (e,g, PCR)

   ☐ Yes ☐ No

   Date Sample collected_____

   Specify the cell source_____

   ☐ Bone marrow ☐ Peripheral blood ☐ Tumor ☐ Other source

   Specify other cell source_____

Vector Copy Number per cell_____ ☐ Not applicable

Percentage Gene Edited Cells_____ ☐ Not applicable

**Were the infused gene-modified cells detected? E.g. F cells.**

☐ Yes ☐ No

9. Was persistence evaluated by flow cytometry testing? (for specific type of hemoglobin expression, e.g. HbF, HbA, etc)

   ☐ Yes ☐ No

10. Name the specific type of hemoglobin assayed by flow cytometry?_____

    Date sample collected_____

    Specify the cell source_____

    ☐ Bone marrow ☐ Peripheral blood ☐ Tumor ☐ Other source

    Specify other cell source_____

    Specify percentage detected_____

11. Was Hemoglobin Electrophoresis or equivalent performed to detect hemoglobin subtypes? (e.g. HbA, HbF, etc)

    ☐ Yes ☐ No ☐ Not applicable

    Hb A%

    Hb F %

    Hb S %

12. Was persistence evaluated by other method?

    ☐ Yes ☐ No

    Specify other method_____

    Date sample collected_____

    Specify the cell source_____

    ☐ Bone marrow ☐ Peripheral blood ☐ Tumor ☐ Other source

# Cellular Therapy Follow-Up

*[Study Name/ID pre-filled]* Site Name:

Clinicaltrials.gov Identifier Subject ID:

Specify other cell source

Were the infused cells detected?

☐ Yes ☐ No

Specify quantity or percentage_____

**Other Toxicities**

Date of onset

13. Did other toxicity resolve?

☐ Yes ☐ No

Date resolved

Specify if the recipient has developed any of the following since the data of last report:

14. Has the recipient developed any grade 3 organ toxicity in this reporting period?

☐ Yes ☐ No ☐ Unknown

Grade 3 Toxicities:

15. Specify organ

☐ Cardiovascular
☐ Gastrointenstinal
☐ Kidneys
☐ Liver
☐ Lungs
☐ Musculoskeletal
☐ Nervous asystems
☐ Other

Specify the toxicity

Date of onset

16. Did the grade 3 toxicity resolve?

☐ Yes ☐ No

Date resolved

17. Has the recipient developed any grade 4 organ toxicity during this reporting period?

☐ Yes ☐ No ☐ Unknown

18. Specify organ

☐ Cardiovascular

# Cellular Therapy Follow-Up

*[Study Name/ID pre-filled]* Site Name:

Clinicaltrials.gov Identifier Subject ID:

- ☐ Gastrointenstinal
- ☐ Kidneys
- ☐ Liver
- ☐ Lungs
- ☐ Musculoskeletal
- ☐ Nervous asystems
- ☐ Other

Specify the toxicity

Date of onset

19. Did the grade 4 toxicity resolve?

☐ Yes ☐ No

Date resolved

**20. Did the recipient develop a clinically significant infection in this reporting period?**

☐ Yes ☐ No

Report each infection organism, site and date of diagnosis on Infection CRF

**21. Was the recipient pregnant at any time in this reporting period (Female only)**

☐ Yes ☐ No ☐ Unknown ☐ Previously reported

22. Was the recipients female partner pregnant at any time in this reporting period? (Male only)

☐ Yes ☐ No ☐ Unknown ☐ Previously reported

# Cellular Therapy Follow-Up CRF Module Instructions

**General Instructions**

This adapted from CIBMTR Form.

**Specific Instructions**

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

# Toxicity Form

*[Study Name/ID pre-filled]*

Site Name:

Subject ID:

1. Record date of evaluation: *(ddMMMyyyy)*

*Record the highest grade of toxicity diagnosed since the previous evaluation. If this is the first evaluation, record the highest toxicity diagnosed since Day 0. The toxicity grades are based on the NCI CTCAE Version 5.0. Grading should be completed based on the entire definition, as some definitions in this form may be truncated.*

**General Disorders**

2. Fever:
- 0-Grades 0-2
- 3-Grade 3 - >40.0 degrees C (>104.0 degrees F) for <=24 hrs
- 4-Grade 4 - >40.0 degrees C (>104.0 degrees F) for > 24 hrs
- 5-Grade 5 - Death

3. Fatigue:
- 0-Grades 0-2
- 3-Grade 3 - Fatigue not relieved by rest; limiting self care ADL

**Immune System Disorders:**

4. Allergic reaction
- 0-Grades 0-2
- 3-Grade 3 - Bronchospasm; hospitalization indicated; intravenous intervention indicated
- 4-Grade 4 - Life-threatening consequences; urgent intervention indicated
- 5-Grade 5 - Death

5. Anaphylaxis:
- 0-Grades 0-2
- 3-Grade 3 - Symptomatic bronchospasm; parenteral intervention indicated; edema/angioedema; hypotension
- 4-Grade 4 - Life-threatening consequences; urgent intervention indicated
- 5-Grade 5 - Death

**GI Disorders**

6. Mucositis:
- 0-Grades 0-2
- 3-Grade 3 - Severe symptoms; limiting self care ADL or interfering with oral intake; hospitalization
- 4-Grade 4 - Life-threatening consequences; urgent intervention indicated
- 5-Grade 5 - Death

a. Which location(s) did the mucositis occur?

| | | |
|---|---|---|
| Oral:. | ☐ 0-No | ☐ 1-Yes |
| Esophagus: | ☐ 0-No | ☐ 1-Yes |
| Intestinal: | ☐ 0-No | ☐ 1-Yes |
| Anal: | ☐ 0-No | ☐ 1-Yes |
| Other: | ☐ 0-No | ☐ 1-Yes |

Specify other organ location:

7. Nausea:
- 0-Grades 0-2
- 3-Grade 3 - Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated

# Toxicity Form

*[Study Name/ID pre-filled]*

Site Name:

Subject ID:

*8.* Vomiting:

0-Grades 0-2
3-Grade 3 - Tube feeding, TPN, or hospitalization indicated
4-Grade 4 - Life-threatening consequences
5-Grade 5 - Death

*9.* Diarrhea:

0-Grades 0-2
3-Grade 3 - Increase of >=7 stools per day over baseline; hospital indicated; severe ostomy output
4-Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

*10.* Pancreatitis:

0-Grades 0-2
3-Grade 3 - Severe pain; vomiting; medical intervention indicated (e.g., analgesia, nutritional supp)
4-Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

**Renal Disorders**

*11.* Cystitis noninfective:

0-Grades 0-2
3-Grade 3 - Gross hematuria; transfusion, IV medications, or hospitalization indicated
4-Grade 4 - Life-threatening consequences; urgent invasive intervention indicated
5-Grade 5 - Death

*12.* Acute kidney injury:

0-Grades 0-2
3- Grade 3 - Hospitalization indicated
4- Grade 4 - Life-threatening consequences; dialysis indicated
5-Grade 5 - Death

*13.* Chronic kidney disease:

0-Grades 0-2
3- Grade 3 - eGFR or CrCl 29 - 15 ml/min/1.73 m2
4- Grade 4 - eGFR or CrCl <15 ml/min/1.73 m2; dialysis or renal transplant indicated
5-Grade 5 - Death

*14.* Did the patient receive dialysis? ☐ 0-No ☐ 1-Yes

*a.* If yes, were laboratory values corrected? ☐ 0-No ☐ 1-Yes

**Hemorrhagic Disorders**

*15.* Hemorrhage:

0-Grades 0-2
3-Grade 3 - Transfusion indicated; invasive intervention indicated; hospitalization
4-Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

*a.* Which organ system was the hemorrhage associated with?

1- CNS
2- Gastrointestinal
3-Genitourinary
4- Pulmonary, Upper Respiratory
5- Other

Specify other organ system:

**Cardiac Disorders**

*16.* Hypotension:

0-Grades 0-2
3- Grade 3 - Medical intervention indicated; hospitalization indicated
4- Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

# Toxicity Form

*[Study Name/ID pre-filled]*

Site Name:

Subject ID:

*17.* Hypertension:

0-Grades 0-2
3-Grade 3 - Systolic BP >=160 mm Hg or diastolic BP >=100 mm Hg; medical intervention indicated
4-Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

*18.* Cardiac arrhythmia:

0-Grades 0-2
3-Grade 3 - Urgent intervention indicated; device (e.g. pacemaker); ablation
4-Grade 4 - Life-threatening consequences; hemodynamic compromise
5-Grade 5 - Death

Specify arrhythmia:

*19.* Myocardial infarction:

0-Grades 0-2
3-Grade 3 - Severe symptoms; ECG changes consistent with infarction
4-Grade 4 - Life-threatening consequences; hemodynamically unstable
5-Grade 5 - Death

*20.* Left ventricular systolic dysfunction:

0-Grades 0-2
3- Grade 3 - Symptomatic due to drop in ejection fraction responsive to intervention
4- Grade 4 - Refractory or poorly controlled heart failure; intervention or heart transplant indicated
5-Grade 5 - Death

*21.* Pericardial effusion:

0-Grades 0-2
3- Grade 3 - Effusion with physiologic consequences
4- Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

*22.* Restrictive cardiomyopathy:

0-Grades 0-2
3-Grade 3 - Symptomatic heart failure or other cardiac symptoms, responsive to intervention
4-Grade 4 - Refractory heart failure or other poorly controlled cardiac symptoms
5-Grade 5 - Death

*23.* Pericarditis:

0-Grades 0-2
3-Grade 3 - Pericarditis with physiologic consequences (e.g., pericardial constriction)
4-Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

**Nervous System Disorders**

*24.* Somnolence:

0-Grades 0-2
3- Grade 3 - Obtundation or stupor
4- Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

*25.* Seizure:

0-Grades 0-2
3-Grade 3 - New onset seizures partial or generalized; multiple seizures despite medical intervention
4-Grade 4 - Life-threatening consequences; prolonged repetitive seizures
5-Grade 5 - Death

*26.* Neuropathy:

0-Grades 0-2
3- Grade 3 - Severe symptoms; limiting self care ADL
4- Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

Specify neuropathy type:

1- Motor
2- Sensory
3- Both motor and sensory

# Toxicity Form

*[Study Name/ID pre-filled]*

Site Name:

Subject ID:

27. Reversible posterior leukoencephalopathy syndrome (RPLS/PRES):

0-Grades 0-2
3-Grade 3 - Severe symptoms; limiting self care ADL; hospitalization
4-Grade 4 - Life-threatening consequences
5-Grade 5 - Death

**Blood and Lymphatic Disorders**

28. Thrombotic thrombocytopenic purpura / Thrombotic microangiopathy:

0-Grades 0-2
3- Grade 3 - Laboratory findings with clinical consequences (e.g., renal insufficiency, petechiae)
4- Grade 4 - Life-threatening consequences, (e.g. CNS hemorrhage or thrombosis/embolism; renal failure)
5-Grade 5 - Death

29. Splenomegaly Grades (as defined by CTCAE)

**Vascular Disorders**

30. Capillary leak syndrome:

0-Grades 0-2
3- Grade 3 - Severe symptoms; intervention indicated
4- Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

31. Thromboembolic event:

0-Grades 0-2
3- Grade 3 - Urgent medical intervention indicated (e.g., pulmonary embolism)
4- Grade 4 - Life-threatening consequences; hemodynamic or neurologic instability
5-Grade 5 - Death

**Musculoskeletal and Connective Tissue Disorders**

32. Avascular necrosis:*( AVASN)*

0-Grades 0-2
3-Grade 3 - Severe symptoms; limiting self care ADL; elective operative intervention indicated
4-Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

33. Osteoporosis:*( OSTEO)*

0-Grades 0-2
3-Grade 3 - Loss of height >=2 cm; hospitalization indicated; limiting self care ADL

**Respiratory, Thoracic and Mediastinal Disorders**

34. Hypoxia:*( HYPOX)*

0-Grades 0-2
3-Grade 3 - Decreased oxygen saturation at rest (e.g., pulse oximeter <88% or PaO2 <=55 mm Hg)
4-Grade 4 - Life-threatening airway compromise; urgent intervention indicated
5-Grade 5 - Death

35. Dyspnea:*( DYSPN)*

0-Grades 0-2
3- Grade 3 - Shortness of breath at rest; limiting self care ADL
4- Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

36. Pleural Effusion:*( PLEFF)*

0-Grades 0-2
3-Grade 3 - Symptomatic with respiratory distress and hypoxia; operative indication incl. chest tube
4-Grade 4 - Life-threatening respiratory or hemodynamic compromise; urgent intervention indicated
5-Grade 5 - Death

**Metabolism and Nutrition Disorders**

# Toxicity Form

*[Study Name/ID pre-filled]*

Site Name:

Subject ID:

37. Hyperglycemia:*( HYPGL)*

0-Grades 0-2
3- Grade 3 - Insulin therapy initiated; hospitalization indicated
4- Grade 4 - Life-threatening consequences; urgent intervention indicated
5-Grade 5 - Death

**Hepatic Disorders**

38. Hepatitis:*( HEPAT)* ☐ 0-No ☐ 1-Yes

39. Liver failure:*( LIVFL)* ☐ 0-No ☐ 1-Yes

40. ALT:*( ALT)*

0-Grades 0-2
3-Grade 3 - >5.0 - 20.0 x ULN
4-Grade 4 - >20.0 x ULN

41. AST:*( AST)*

0-Grades 0-2
3-Grade 3 - >5.0 - 20.0 x ULN
4-Grade 4 - >20.0 x ULN

42. Bilirubin:*( BILIR)*

0-Grades 0-2
3-Grade 3 - >3.0 - 10.0 x ULN
4-Grade 4 - >10.0 x ULN

43. Alkaline Phosphatase: *( ALKPH)*

0-Grades 0-2
3-Grade 3 - >5.0 - 20.0 x ULN
4-Grade 4 - >20.0 x ULN

**Indicate all clinical signs/symptoms of abnormal liver functioning:**

44. Jaundice:*( JAUND)* ☐ 0-No ☐ 1-Yes

45. Hepatomegaly:*( HEMLY)* ☐ 0-No ☐ 1-Yes

46. Right upper quadrant pain: *( RUQUA)* ☐ 0-No ☐ 1-Yes

47. Weight gain (>5%) from baseline:*( WGTGN)* ☐ 0-No ☐ 1-Yes

**Indicate the etiology of the abnormal liver function:**

# Toxicity Form

*[Study Name/ID pre-filled]*

Site Name:

Subject ID:

| | Etiology | Biopsy Results | Doppler Ultrasound Results |
|---|---|---|---|
| 49. VOD: | *VODET)* 0-No 1-Yes | *VODBY)* 1-Positive 2-Negative 3-Equivocal 4-Not done | *( VODDP)* 1-Confirmed 2-Not confirmed 3-Not done |
| 50. GVHD: | *GVHET)* 0-No 1-Yes | *GVHBY)* 1-Positive 2-Negative 3-Equivocal 4-Not done | *( GVHDP)* 1-Confirmed 2-Not confirmed 3-Not done |
| 51. Infection: | *INFET)* 0-No 1-Yes | *INFBY)* 1-Positive 2-Negative 3-Equivocal 4-Not done | *( INFDP)* 1-Confirmed 2-Not confirmed 3-Not done |
| 52. Other: | *OTHET)* 0-No 1-Yes | *OTHBY)* 1-Positive 2-Negative 3-Equivocal 4-Not done | *( OTHDP)* 1-Confirmed 2-Not confirmed 3-Not done |
| 53. Unknown: | *UNKET)* 0-No 1-Yes | *UNKBY)* 1-Positive 2-Negative 3-Equivocal 4-Not done | *( UNKDP)* 1-Confirmed 2-Not confirmed 3-Not done |

Specify other etiology: *( OTHSP)*

62. Did any of the toxicities reported for this assessment period meet the criteria of an SAE? Y/N

63. If yes, specify any event(s) that met the criteria of an SAE: [Free text]



**Transfusion Reaction**

Did the patient receive a transfusion during the reporting period Yes No

Infusion related reaction
0 – Grades 0-2
3 – Prolonged;recurrence of symptoms following initial improvement;hospitalization indicated
4 – Life threatening consequences; urgent intervention indicated
5 – Death

Fever
0- Grade 0-2
3- >40.0 degrees C (>140.0 degrees F) for <= 24 hours
4- >40 degrees C (>104.0 degrees F) for > 24 hours
5- Death

Maculo-papular rash
0- Grade 0-2
3- Macules/papules covering >30% BSA with or without associated symptoms;limiting self-care ADL

Urticaria

# Toxicity Form

*[Study Name/ID pre-filled]*

Site Name:

Subject ID:

0- Grade 0-2
3- Urticaria lesions covering >30% BSA; IV intervention indicated

Allergy reaction
0- Grade 0-2
3- Prolonged;recurrence of symptoms following initial improvement; hospitalization indicated
4- Life-threatening consequences; urgent intervention indicated
5- Death

Broncospasm
0- Grade 0-2
3- Limiting self-care ADL; oxygen saturation decreased
4- Life-threatening respiratory or hemodynamic compromise; intubation or urgent intervention indicated
5- Death

Hypoxia
0- Grade 0-2
3- Decreased oxygen saturation at rest (e.g., pulse oximeter <88% or PaO2 <= 55mm Hg)
4- Life-threatening airway compromise;urgent intervention indicated
5- Death

Anaphylaxis
0- No event
3- Symptomatic bronchospasm; parenteral intervention indicated; allergy-related edema/angioedema
4- Life-threatening consequences ;urgent intervention indicated
5- Death

Hematuria
0- Grade 0-2
3- Gross hematuria; transfusion, IV med, hosp, endoscopic, radiologic/operative intervention indicated
4- Life-threatening; urgent radiologic or operative intervention indicated
5- Death

Hemolysis
0- Grade 0-2
3- Transfusion or medical intervention indicated (e.g., steroids)
4- Life-threatening; urgent radiologic or operative intervention indicated
5- Death

Infection
0- Grade 0-2
3- IV antiobiotic, antifungal, or antiviral indicated; radiologic, operative intervention indicated
4- Life-threatening consequences; urgent intervention indicated
5- Death

Iron overload
0- Grade 0-2
3- Severe symptoms; intervention indicated
4- Life-threatening; urgent radiologic or operative intervention indicated
5- Death

Did the patient develop allo-antibodies? Yes No

# Toxicity Form

*[Study Name/ID pre-filled]*

Site Name:

Subject ID:

**Hydroxyurea Reaction**

Did the patient receive Hydroxyurea during this reporting period? Yes No

Anemia
0- Grade 0-2
3- Hgb <8.0-6.5 g/dL; <4.9-4.0 mmol/L; <80-65g/L; transfusion indicated
4- Life-threatening consequences; urgent intervention indicated
5- Death

Neutropenia
0- Grade 0-2
3- <1000 – 500 mm^3; <1.0-0.5 x 10^9 L
4- <500/mm^3; <0.5 x 10^9 L

Nausea
0- Grade 0-2
3- Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated

Diarrhea
0- Grade 0-2
3- Increase of >= 7 stools per day; incontinence; severe increase in ostomy; limiting self care ADL
4- Life-threatening consequences; urgent intervention indicated
5- Death

Constipation
0- Grade 0-2
3- Obstipation with manual evacuation indicated; limiting self care ADL
4- Life-threatening consequences; urgent intervention indicated
5- Death

Does the patient have hyperpigmentation of the skin under the nails?
Yes No

Does the patient have thinning hair?
Yes No

Oligospemia (reduced sperm)
0- Grade 0-2
3- Sperm concentration <13 million/mL or motility <32%

**Serious Adverse Event Reporting (See SAE Form)**

Did any of the events above lead to an advanced care intervention or intensive care unit admission/transfer as outline in the AE reporting?

Yes No

Specify Event:

# Serious Adverse Event Report Form

[Study Name/ID pre-filled]

Initials of Completer:
Date Form Completed: (mm/dd/yyyy)

**Subject Information:**
Site Name:
Subject ID:

1. Sex: ☐ Male ☐ Female
2. Age**:** (please provide)
3. Weight: (please provide) ☐ lbs or ☐ kgs
4. Height: (please provide) ☐ inches or ☐ cm

## Serious Adverse Event (SAE) Information:

5. Date of Onset: (m m/dd/yyyy)
6. Resolution Date: (m m/dd/yyyy) ☐ Not resolved
7. Adverse Events:
8. Describe event or problem:
9. Outcomes attributed to event (check all that apply):
   - ☐ Death on (m m/dd/yyyy)
   - ☐ Life-threatening event
   - ☐ In-patient hospitalization/prolongation of present hospitilization
   - ☐ Persistent or significant disability/incapacity
   - ☐ Required intervention to prevent permanent impairment/damage
   - ☐ Congenital anomaly/birth defect
   - ☐ Other, specify:
10. Record treatment for event or attach appropriate documentation:

**Table 1 Treatment for Event**

| Record treatment for event |
|---|
| Data to be filled in by site |

11. Record relevant tests or laboratory data, including dates or attach the appropriate documentation:

**Table 2 Relevant Tests or Laboratory Data**

| Record relevant tests or laboratory data |
|---|
| Data to be filled in by site |

# Serious Adverse Event Report Form

[Study Name/ID pre-filled]

Initials of Completer:
Date Form Completed: (mm/dd/yyyy)

12. Record concomitant medications or attach the appropriate Case Report Form (CRF) page(s):

**Table 3 Concomitant Medications**

| Record concomitant medications |
|---|
| Data to be filled in by site |

13. Record relevant history including pre-existing medical conditions or attach appropriate CRF page(s):

**Table 4 Relevant History**

| Record relevant History including pre-existing medical conditions |
|---|
| Data to be filled in by site |

## Study Intervention Information:

14. Name of study intervention:
15. Describe administration of study intervention (e.g. dose, frequency and route used for a drug):
16. Was study intervention discontinued due to the event?
    ☐ Yes ☐ No ☐ N/A
17. Was the seriousness of the event abated after discontinuation of the study intervention?
    ☐ Yes ☐ No ☐ N/A
18. Did event reappear after reintroduction of the study intervention?
    ☐ Yes ☐ No ☐ N/A
19. Was study blind broken?
    ☐ Yes ☐ No ☐ N/A

## Principal Investigator's Assessment

20. Principal Investigator's Opinion of what caused the event:
    ☐ Study intervention
    ☐ Concomitant medication, Specify:
    ☐ Concurrent disorder, Specify:
    ☐ Withdrawal of study intervention, Specify:
21. Was this type of event anticipated in the protocol and consent form?
    ☐ Yes ☐ No
22. Comments:

# Serious Adverse Event Report Form

[Study Name/ID pre-filled]

Initials of Completer:
Date Form Completed: (mm/dd/yyyy)

## Reporter Information

23. Principal Investigator's name and address: (please specify)
24. Reporter name and telephone number: (please specify)
25. Type of report:

☐ Initial report ☐ Follow-up report ☐ Final report

26. Date Report Completed: (m m/dd/yyyy)

## Sponsor's Assessment

27. Does this adverse event meet the definition to be a serious adverse event?[1]

☐ Yes ☐ No

28. Does this adverse event meet the definition to be an unexpected event?[2]

☐ Yes ☐ No

29. Based on the sponsor's assessment, is there at least a reasonable possibility that the adverse event was caused by use of the investigational agent or device?

☐ Yes ☐ No



[1]Serious: An adverse event is defined by the investigator or sponsor as "serious" because it is life-threatening, results in death, requires in-patient hospitalization, prolongs existing hospitalization, results in persistent or significant disability, or is a congenital anomaly/birth defect.

[2]Unexpected: An adverse event is categorized by the sponsor as "unexpected" because the adverse event has not been previously described in the Investigator's Brochure or has increased in frequency or severity compared to what is described by the Investigator's Brochure.

# Serious Adverse Event Report Form CRF Module Instructions

## General Instructions

ADVERSE EVENTS

Adverse events (AEs) document any unfavorable or untoward medical occurrence that is observed with use of a drug or medical device in a participant or subject enrolled in a study without regard for cause or relationship. Adverse events should be recorded using a standard medical terminology, such as the Medical Dictionary for Regulatory Activities (MedDRA) or Common Terminology Criteria for Adverse Events (CTCAE).

SERIOUS ADVERSE EVENT Definition

Serious Adverse Event (SAE) - Any untoward medical occurrence that:

- Results in death,
- Is life-threatening,
- Requires inpatient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability or incapacity, or
- Is a congenital anomaly or birth defect.

SAE REPORTING

The Serious Adverse Event (SAE) Report is used to provide detailed information about each SAE that occurs during the study. It contains the information MedWatch, the FDA Safety Information and Adverse Event Reporting Program, requires for reporting SAEs.

The study protocol should outline who should receive SAE Reports and in what time frame. Depending on the study, SAE Reports may have to be sent to the study coordinating center, Data Safety Monitoring Board (DSMB), the Institutional Review Board (IRB), and the NHLBI.

Important note: None of the data elements included on this CRF are considered Core (i.e., strongly recommended for all studies to collect). All of the data elements are supplemental and should be collected only if the research team considers them appropriate for their study.

REPORTING OF SAFETY REPORTS FOR STUDIES UNDER AN IND or IDE

For studies conducted under an Investigational New Drug (IND) or Investigational Device Exemption (IDE), the U.S. Food and Drug Administration describes guidelines for Sponsors to report events related to use of an investigational agent or medical device.

The Sponsor must assess the adverse event and prepare an IND Safety Report when the event meets all of the definitions to be categorized as (1) suspected (at least a reasonable possibility for causality), (2) serious and (3) unexpected.

Safety reporting requirements can be found on the U.S. Food and Drug Administration websitel: U.S. Food and Drug Administration Investigational New Drug Reporting Requirements.

## Specific Instructions

See Food and Drug Administration Serious Adverse Event Report Form Instructions for instructions on how to fill out the SAE Report.

# Liver and Spleen Assessment

[Study Name/ID pre-filled]

Site Name:

Subject ID:

Hepatic Assessments

1. Was a liver MRI conduction?

☐ Yes

☐ No

☐ Unknown

*If Yes, what was the liver iron content (LIC)?

☐ Known

☐ Unknown

*If Known, LIC: __ __ __ * __

☐ mg Fe/g liver dry weight

☐ g Fe/kg liver dry weigh

☐ umol Fe/g liver dry weight

2. Was a liver biopsy performed?

☐ Yes

☐ No

☐ Unknown

*If Yes, date of most recent liver biopsy: __ __ __ __ / __ __ / __ __

YYYY MM DD

Was there evidence of fibrosis?

☐ Yes

☐ No

*If Yes, identify type of fibrosis ☐ Bridging ☐ Periportal

Was there evidence of cirrhosis?

☐ Yes

☐ No

Is a copy of biopsy report attached?

☐ Yes

☐ No

## Liver and Spleen Assessment

[Study Name/ID pre-filled] Site Name:

Subject ID:

Splenic Assessments

1. Was splenic function assessed?

☐ Yes

☐ No

☐ Not applicable

☐ Unknown

*If Yes, date of most assessment: __ __ __ __ / __ __ / __ __

*If Yes, select which splenic test was completed

☐ Complete red blood cell count

Complete RBC: __ __ __ __ * __ __ x10 __ __ cells/uL

☐ Pitted RBC score

Pitted RBC score: __ __ * __ %

☐ Splenic scan

Splenic scan results:

☐ Normal (radionuclide uptake)

☐ Abnormal (no radionuclide uptake)

# Liver and Spleen Assessment CRF Module instructions

General Instructions

Specific Instructions

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

…..

# Death Form

[Study Name/ID pre-filled] Site Name:

Subject ID:

3. Date last known alive: |___|___|-|___|___|-|___|___|___|___| → **STOP, complete Follow-up Form up to this date**
   Month Day Year

4. Date of death: |___|___|-|___|___|-|___|___|___|___| → **CONTINUE and complete Follow-up Form up to this date**
   Month Day Year

5. Place of Death: ☐ Hospital ☐ Home ☐ Community ☐ Hospice ☐ Other, specify _____

6. Cause of Death on death certificate (add ICD-10-CM Codes Supplemental-Highly Recommended)
   Primary cause: _____
   Secondary cause(s): _____
   ☐ Death certificate Not Available

7. Other sources of Cause of Death (check **all** that apply)
   ☐ No Other Sources ☐ Family Member ☐ Medical Record ☐ Autopsy Report

| 7a. Cause of Death from other sources (identify in consultation with PI) | Primary/ Immediate Cause (check one) | Secondary/ Underlying or Comorbid Causes (check all that apply) |
|---|---|---|
| Acute Chest Syndrome | ☐ | ☐ |
| Respiratory Failure | ☐ | ☐ |
| Sudden Death | ☐ | ☐ |
| Infection | ☐ | ☐ |
| Stroke, Ischemic | ☐ | ☐ |
| Stroke, Hemorrhagic | ☐ | ☐ |
| Cardiac Arrest | ☐ | ☐ |
| Sickle Cell Disease Multiorgan Failure Syndrome | ☐ | ☐ |
| Kidney Failure | ☐ | ☐ |
| Liver Failure | ☐ | ☐ |
| Pulmonary Embolism | ☐ | ☐ |
| Trauma | ☐ | ☐ |
| Cancer (specify type, location): _____ | ☐ | ☐ |
| Other primary (specify): _____ | ☐ | ☐ |
| Other secondary (specify): _____ | ☐ | ☐ |

8. Is an autopsy report available? (copies of autopsy reports should be maintained locally) ☐ Yes ☐ No

# Death Form Module Instructions

[Study Name/ID pre-filled]

Site Name:

Subject ID:

## General Instructions

Important note: *None of the data elements included on this CRF Module are classified as Core. All data elements are classified as Supplemental (i.e., non Core) and should only be collected if the research team considers them appropriate for their study. Please see the Data Dictionary for element classifications.*

## Specific Instructions

*Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.*

**Cause(s) of Death -** Record the cause or causes of death using explanatory text and the associated ICD-10-CM code. Include the primary cause of death first followed by any secondary causes.

## Reference

Sickle Cell Implementation Consortium