**All Core (required for all studies in genetic therapy for sickle cell disease) elements have asterisk (\*).**

1. **PRE\_INFUSION\_BASELINE\_FEMALE

This form captures data up until transplant (“Baseline”)[[1]](#footnote-2)**
2. PATIENT AGE AT INFUSION: \_\_\_\_\_\_\_\_
3. PUBERTY STAGE[[2]](#footnote-3) AT INFUSION: \_\_\_\_\_\_
4. Height (cm): \_\_\_\_\_\_\_\_\_\_\_
5. Weight (kg)[[3]](#footnote-4):\_\_\_\_\_\_\_\_\_\_\_
6. 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? [ ]  Yes [ ]  No [ ]  Unknown

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**

## Short Stature/Growth Hormone Deficiency

Have you ever been diagnosed with short stature?

1. [ ]  Yes [ ]  No [ ]  Unknown

\*Have you ever been diagnosed with growth hormone deficiency?[ ]  Yes [ ]  No [ ]  Unknown

\*If Yes, did you receive growth hormone? [ ]  Yes [ ]  No [ ]  Unknown

## Other Endo

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

[ ]  Yes [ ]  No [ ]  Unknown

* 1. 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:

1. If yes, age at menarche:
2. If yes, regular/irregular periods:
3. If no, why don’t you get regular menses
4. Menstrual suppressing contraception?
5. History of chemotherapy causing premature menopause
6. Anatomic, endocrinologic or genetic cause unrelated to sickle cell disease, explain \_\_\_\_\_\_\_\_
7. Fertility assessments[[4]](#footnote-5) performed: [ ]  Yes [ ]  No
8. If no, why not (check all that apply): [ ]  family / patient refused [ ]  inappropriate for age [ ]  not available at Center [ ]  costs associated with testing
9. Was testing performed in relation to a menstrual cycle? [ ]  Yes [ ]  No
10. Fertility Preservation: [ ]  Yes [ ]  No [ ]  Decline
11. If no, why (pt may decline to answer) \_\_\_
12. 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\_\_\_\_\_\_
13. If Yes, taking hydroxyurea at fertility preservation? Yes/No
14. If HU has been stopped, please indicate for how long?
15. If yes, what is banked: oocytes, ovarian tissue, embryos
16. If yes, storage cost for cryopreserved tissue/gametes (per year):
17. 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 [ ]  No
18. Yes, at our center
19. Yes, at a referral center (academic practice)
20. Yes, at a referral center (private practice)
21. No
22. 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: [ ]  Yes [ ]  No

[ ]  Luteinizing Hormone

 Day 3 – 5: [ ]  Yes [ ]  No

[ ]  Estradiol
 Day 3 – 5: [ ]  Yes [ ]  No

[ ]  Total antral follicle count

**Fertility Preservation Results**

1. Ovarian tissue preserved [ ]  Yes [ ]  No
2. If oocytes preserved [ ]  Yes [ ]  No If yes, how many? \_\_\_\_\_
3. If embryos preserved [ ]  Yes [ ]  No If yes, how many? \_\_\_\_\_

**Pre-BMT Reproduction History**

1. Contraception concurrent with infusion [ ]  Yes [ ]  No
2. If yes, name contraception: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Pregnancy + Outcomes**

1. Have you been an expectant father before? [ ]  Yes [ ]  No
2. If yes, complete form: PRE\_INFUSION\_PREGNANCY\_MALE

**Pre BMT-Menstrual History**

Regular [ ]  Yes [ ]  No

Menorrhagia [ ]  Yes [ ]  No

Associated with VOC [ ]  Yes [ ]  No

1. **PRE\_INFUSION\_BASELINE\_MALE**

**BONES (see above)**

 **ENDOCRINE (see above)**

**FERTILITY**

**To be Answered by Patient/Parent**

1. Semen analysis to assess fertility performed: [ ]  Yes [ ]  No
2. If no, why not (check all that apply): [ ]  family / patient refused [ ]  inappropriate for age not available at Center [ ]  costs associated with testing
3. Fertility Preservation: [ ]  Yes [ ] No [ ]  Decline
4. If no, why (pt may decline to answer) \_\_\_
5. If Yes, how paid for (check all that apply): [ ]  insurance [ ]  self-pay [ ]  grant/foundation support [ ]
6. research study about fertility preservation [ ]  paid for by gene therapy study
If insurance, copay\_\_\_\_\_\_
7. If yes, what is banked: sperm, embryos, testicular tissue
8. If yes, storage cost for cryopreserved tissue/gametes (per year):
9. 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 [ ]  No
10. Yes, at our center
11. Yes, at a referral center (academic practice)
12. Yes, at a referral center (private practice)
13. No

If yes, do the reproductive endocrinology/infertility specialists perform ovarian tissue cryopreservation?

1. If semen analysis performed, results:
2. Sperm concentration:
3. Sperm motility:
4. 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:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Was semen analysis performed more than once? [ ]  Yes [ ]  No

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?

* 1. Sperm concentration:
	2. Sperm motility:
	3. Sperm morphology:

**Fertility Preservation Results**

Sperm preserved [ ]  Yes [ ]  No

1. Taking hydroxyurea at time of first semen analysis? [ ]  Yes [ ]  No
2. If no, how long not taking hydroxyurea (months) [ ]  Yes [ ]  No
3. If yes, how long taking hydroxyurea: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Pre-BMT Reproduction History**Contraception concurrent with infusion [ ]  Yes [ ]  No

If yes, name contraception: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Pregnancy + Outcomes** Have you ever been pregnant? [ ]  Yes [ ]  No

If yes, complete form: PRE\_INFUSION\_PREGNANCY\_MALE

1. **POST\_INFUSION\_FOLLOW\_UP\_YEAR\_X\_FEMALE**Current age: \_\_\_\_\_\_\_

**Medications**
Which medications are you currently using.

HORMONES (LIST)

* 1. INSULINs (expand list) [ ]  Yes [ ]  No
	2. THYROID [ ]  Yes [ ]  No
	3. HORMONE REPLACEMENT [ ]  Yes [ ]  No
	4. CORTICOSTEROIDS [ ]  Yes [ ]  No
	5. VITAMIN D [ ]  Yes [ ]  No
	6. BISPHOSPHONATES [ ]  Yes [ ]  No
* CONTRACEPTION (circle all that apply)
	1. Combined oral contraception (estrogen & progesterone)
	2. Progesterone-only pill
	3. The patch
	4. The shot
	5. The implant
	6. The hormonal IUD
	7. 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]](#footnote-6)**Do you get menses (periods): Yes/No

If yes, are your periods regular or irregular periods:

If no, why don’t you get regular menses

1. Menstrual suppressing contraception?
2. History of chemotherapy causing premature menopause
3. Anatomic, endocrinologic or genetic cause unrelated to sickle cell disease, explain \_\_\_\_\_\_\_\_
4. Menopause

If menopause, how old were you when you stopped getting periods:

If menopause, did you see a doctor to receive hormones: [ ]  Yes [ ]  No
If menopause, did the hormones cause you to resume menstrual cycles: [ ]  Yes [ ]  No

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?

1. Yes, at our center
2. Yes, at a referral center (academic practice)
3. Yes, at a referral center (private practice)
4. No
5. If yes, do the reproductive endocrinology/infertility specialists perform ovarian tissue cryopreservation?

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**

If preserved oocytes / ovarian tissue, has it been retrieved: [ ]  Yes [ ]  No
If yes, has patient pursued pregnancy: [ ]  Yes [ ]  N

If yes, complete PREGNANCY FORM

\*Are you continuing to preserve your oocytes/ ovarian tissue /embryos [ ]  Yes [ ]  No

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? [ ]  Yes [ ]  No

\*If yes, complete POST\_INFUSION\_FOLLOW-UP\_YEAR\_X\_PREGNANCY\_FEMALE

1. **POST\_INFUSION\_FOLLOW\_UP\_YEAR\_X\_MALE**

Current age: \_\_\_\_\_

**Medications**
Which medications are you currently using.

* HORMONES (LIST Y/N)
	1. INSULINs (expand list)
	2. THYROID
	3. HORMONE REPLACEMENT (list)
	4. CORTICOSTEROIDS
	5. VITAMIN D
	6. 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:

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?

1. Yes, at our center
2. Yes, at a referral center (academic practice)
3. Yes, at a referral center (private practice)
4. No
5. If yes, do the reproductive endocrinology/infertility specialists perform ovarian tissue cryopreservation?

**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:

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

1. **PRE\_INFUSION\_PREGNANCY\_FEMALE

Pregnancy 1**

Maternal age at pregnancy:

Paternal age at pregnancy:
Pregnancy conception: “natural”, assisted reproductive technology, other \_\_\_\_

Outcome of pregnancy: termination, miscarriage, live birth, still birth

If live birth, weight at birth:

Maternal complications of pregnancy:

Fetal complications of pregnancy:

1. **PRE\_INFUSION\_PREGNANCY\_MALE**

**Pregnancy 1**
Maternal age at pregnancy:

Paternal age at pregnancy:
Pregnancy conception: “natural”, assisted reproductive technology, other \_\_\_\_

Outcome of pregnancy: termination, miscarriage, live birth, still birth

If live birth, weight at birth:

Maternal complications of pregnancy:

Fetal complications of pregnancy:

1. **POST\_INFUSION\_PREGNANCY\_FEMALE

Pregnancy 1**

Maternal age at pregnancy:

Paternal age at pregnancy:
Pregnancy conception: “natural”, assisted reproductive technology, 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:

1. **POST\_INFUSION\_PREGNANCY\_MALE**

**Pregnancy 1**
Maternal age at pregnancy:

Paternal age at pregnancy:
Pregnancy conception: “natural”, assisted reproductive technology, 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:

**INSTRUCTIONS**This document contains assessments related to **bone health**, **endocrine function**, **fertility**, and **pregnancy**
This module contains the following assessments:

1. PRE\_INFUSION BASELINE FORM\_1\_FEMALE
2. PRE\_INFUSION BASELINE FORM\_1\_MALE
3. PRE\_INFUSION PREGNANCY\_FEMALE
4. PRE\_INFUSION PREGNANCY\_MALE
5. POST-INFUSION FOLLOW-UP\_Year X\_FEMALE
6. POST-INFUSION FOLLOW-UP\_Year X\_MALE
7. POST\_INFUSION\_PREGNANCY\_FEMALE
8. POST\_INFUSION\_PREGNANCY\_MALE

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

1. PRE INFUSION (include data up to start of preparative regimen)
2. POST\_INFUSION\_YEAR\_2
3. POST\_INFUSION\_YEAR\_5
4. POST\_INFUSION\_YEAR\_10
5. 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.

1. Confirmation that preparative regimen details are captured elsewhere [↑](#footnote-ref-2)
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/ [↑](#footnote-ref-3)
3. Suggest REDCap fields for automatically generating percentiles for pediatric subjects [↑](#footnote-ref-4)
4. The fertility assessments need to describe to patient in detail [↑](#footnote-ref-5)
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. [↑](#footnote-ref-6)