2030: SCD Pre-Infusion

SCD Pre-Infusion Data

The Sickle Cell Disease (SCD) Pre-Infusion Data Form (Form 2030) is one of the Comprehensive Report Forms. This form captures SCD-specific pre-infusion data such as: disease classification at diagnosis, transfusion status prior to the start of the preparative regimen, organ assessments prior to the start of the preparative regimen, and the indication for transplant.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on the Pre-TED Disease Classification Form (Form 2402) as **Sickle Cell Disease (SCD)**.

Links to Sections of the Form

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

Date	Manual Section	Add/ Remove/ Modify	Description

10/25/2024	2030 SCD Pre-Infusion	Add	Version 2 of the 2030: Sickle Cell Disease (SCD) Pre-Infusion section of the Forms Instructions Manual released. Version 2 corresponds to revision 4 of the Form 2030.

Last modified: Jan 27, 2025

Q1: Subsequent Infusion

Question 1: Is this the report of a second or subsequent infusion?

Report **No** and go to *Was sickle cell disease diagnosed at birth?* in any of the following scenarios:

- This is the first infusion reported to the CIBMTR; or
- This is a second or subsequent infusion for a different disease (i.e., the patient was previously transplanted for a disease other than Sickle Cell Disease); or
- This is a second or subsequent infusion for the same disease subtype and this baseline disease insert was not completed for the previous transplant (i.e., the patient was on the TED track for the prior infusion, prior infusion was autologous with no consent, etc.).

Report **Yes** and go to *Were any red blood cell (RBC) transfusions administered?* if this is a subsequent infusion for the same disease ***and*** the baseline SCD disease insert was completed previously.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q2 – 5: Sickle Cell Diagnosis

Findings Prior to Infusion
When reporting data on the Sickle Cell Disease (SCD) Pre-Infusion Data Form (Form 2030 – Revision 4), report all findings at any time prior to the start of the preparative regimen, unless otherwise specified. If no preparative regimen was given, report all findings at any time prior to infusion (day 0).

Question 2: Was sickle cell disease diagnosed at birth? (i.e., newborn screening)

The most common method of diagnosis for Sickle Cell Disease (SCD) is a blood screen which looks for the defective hemoglobin molecule in the circulating blood. In the United States, this blood test is available as part of routine newborn screening. Infants are often diagnosed at birth or *in utero*.

Report **Yes** if the recipient was diagnosed with Sickle Cell Disease (SCD) at birth (or *in utero*). If the recipient was not diagnosed as birth, report **No** and provide the date of diagnosis. If it is unknown whether the recipient was diagnosed at birth, report **Unknown**. This option should be used sparingly and only when no information exists regarding SCD screening as an infant.

Question 3: Date of diagnosis

Report the date of diagnosis of SCD. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside facility and no documentation of the laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared.

If the exact pathological diagnosis date is not known, use the process described in General Instructions, Guidelines for Completing Forms.

Questions 4 – 5: What is the recipient's sickle cell disease genotype?

Genetics play a critical role in the development of sickle cell disorders. Clinical symptoms vary depending on which gene variants are inherited. Accurate identification of the recipient's sickle genotype may help guide clinical management of symptoms.

Specify the recipient's sickle cell disease genotype. If the recipient exhibits a sickle cell genotype that is not listed, select **Other genotype** and specify the sickle cell genotype in question 5.

See *Table 1. Sickle Cell Genotypes* below for a description and common characteristics of each genetic variant.

Table 1. Sickle Cell Genotypes

Genotype	Description

Hb SC	One sickle gene is inherited from one parent and one abnormal hemoglobin-producing “C” gene is inherited from the other parent. Typically characterized by mild symptoms but increased likelihood of proliferative sickle retinopathy has been observed.
Hb SD	One sickle gene is inherited from one parent and one abnormal hemoglobin-producing “D” gene is inherited from the other parent. The severity of symptoms varies for recipients with this genotype.
Hb SO Arab	A rare, compound, heterozygous hemoglobinopathy characterized by inheritance of one sickle gene from one parent and one abnormal hemoglobin-producing “O” gene inherited from the other parent. Severity is similar to those of homozygous SCD.
Hb SS	Most common type of sickle cell disease and is often called homozygous sickle cell anemia. One sickle gene is inherited from each parent. Often characterized by higher prevalence of hemolysis and lower hemoglobin values compared to Hb SC or beta+ thalassemia. Incidence of leg ulcers and episodes of priapism are increased. Regarded as a severe form of SCD.
Hb S beta^0 thalassemia	A more severe form of Sickle Cell Disease (SCD) characterized by crescent-shaped red blood cells (RBC) (e.g., sickle cells) that break down prematurely as well as populations of smaller RBCs, simultaneously.
Hb S beta[+] thalassemia	A mild form of Sickle Cell Disease (SCD) characterized by crescent-shaped red blood cells (RBC) (e.g., sickle cells) that break down prematurely as well as populations of smaller RBCs, simultaneously.
Hb S delta beta^0 thalassemia	A rare, homozygous hemoglobinopathy characterized by decreased production of the delta- and beta-globin chains. There is a compensatory increase in the production and expression of Hb F in affected individuals.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q6 – 16: Transfusion Therapy

Question 6: Were any red blood cell (RBC) transfusions administered?

Red blood cell (RBC) transfusions are often given as supportive care to lower hemoglobin S for recipients diagnosed with Sickle Cell Disease (SCD). If the recipient received any RBC transfusions between diagnosis and the start of the preparative regimen / infusion, select **Yes**. If the recipient did not receive any RBC transfusions or no information is available to determine if the recipient received RBC transfusions, report **No**.

Question 7: Number of RBC transfusion events within the last 12 months

Transfusions may be referred to as “simple” or “exchange” transfusions. A simple transfusion refers to a direct infusion of a blood product. An exchange transfusion refers to the slow removal and replacement of the recipient’s blood with that of a healthy donor’s blood. A transfusion event consists of one or more RBC unit(s) given in a day.

Indicate the total number of RBC transfusion events the recipient received within 12 months prior to the start of the preparative regimen / infusion to prevent sickle-related vaso-occlusive events.

- **Example**: The progress notes state a recipient was transfused with one RBC unit for each month, for six months. The number of transfusions increased, and the recipient receives two RBC units on the same day, each month, for the following six months prior to the start of the preparative regimen. The total number of RBC transfusion events within the last 12 months would be reported as “12.”

Question 8: Date of last transfusion administered

Report the date of the *most recent* RBC transfusion administered prior to the start of the preparative regimen / infusion.
If the last administration date is partially known (i.e., the recipient received their last RBC transfusion in mid-July 2019), use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Question 9: Was a transfusion administered to PREVENT sickle cell related events? (includes simple or exchange transfusions)

Transfusions administered routinely to offset the effects of sickle cell-related events are often called “chronic transfusions” within progress notes. In the context of reporting, “chronic transfusions” are defined as eight or more transfusion events per year, for at least a year, or a lifetime cumulation of ≥ 20 transfusion events between diagnosis and referral for transplant.

If any of the red blood cell transfusions were administered to prevent sickle cell related events, report **Yes**.

Report **No** in the following scenarios:

- If the recipient did not receive transfusions to prevent sickle cell related events.
- There is no information available to determine if the recipient received transfusions to prevent sickle cell-related events.
- If the recipient is receiving transfusion therapy for reasons other than to prevent sickle cell-related events.

Questions 10 – 11: Date transfusion started

Indicate if the date transfusion(s) administered to prevent sickle cell related events began is **Known** or **Unknown**. If **Known**, enter the date when the first transfusion began. If transfusions were given over multiple days, report the first date of administration where the intent of transfusion was to offset or prevent the effects of sickle cell-related events. The reported start date should align with the recipient's sickle cell-related event for which the transfusion was administered and may not be the same transfusion event reported in *Date of last transfusion administered*. If the reported transfusion start date is an estimated date, also select **Date estimated**.

If the therapy start date is not known, report **Unknown** and go to *Date therapy stopped*.

If the start date is partially known (i.e., the recipient started treatment in mid-July 2019), use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Questions 12 – 13: Date therapy stopped

Indicate if the transfusion therapy stop date is **Known** or **Unknown**. If the therapy stop date is **Known**, enter the date when the transfusion(s) to prevent sickle cell related events stopped. If the reported transfusion start date is an estimated date, also select **Date estimated**.

Report **Unknown** if the stop date is not known.

If the recipient is still receiving transfusions to prevent sickle cell related events at the start of the preparative regimen / infusion, report **Not applicable**.

If the stop date is partially known (i.e., the recipient stopped treatment in mid-September 2019), use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Question 14: Are the RBC units used for transfusion of an extended phenotype match (D, C, c, E, e, K)? (includes partial extended phenotype matches)

Extended phenotype testing may be performed on RBC units prior to transfusion to ensure donor and recipient matches are confirmed beyond the standard ABO compatibility matching to decrease the risk of alloimmunization. This information is typically found within the blood bank section of the medical record.

Report **Yes** if the RBC unit(s) used for transfusion are of an extended phenotype match (particularly D, C, c, E, e, or K). If the RBC unit(s) used for transfusion were not matched for extended phenotype D, C, c, E, e, or K or it is unknown if matched, report **No**.

Questions 15 – 16: Are RBC alloantibodies present?

The presence of RBC alloantibodies may cause serologic incompatibility and make the selection of RBC units for future transfusions difficult. RBC alloantibodies are typically present once alloimmunization has occurred.

If RBC alloantibodies are present prior to the start of the preparative regimen / infusion, report **Yes** and specify the number of alloantibodies identified. If testing for RBC alloantibodies were performed multiple times prior to the start of the preparative regimen / infusion, report the most recent assessment.

If RBC alloantibodies were not present prior to the start of the preparative regimen / infusion, report **No**.

Report **Unknown** if testing was not performed or it is not known if alloantibodies were present.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q17 – 19: Therapy for Iron Overload

Question 17: Was iron chelation therapy received at any time?

Iron chelation therapy is used to prevent or reduce iron overload. Examples include Deferoxamine (Desferal) and Deferasirox (Jadenu, Exjade).

Select **Yes** if iron chelation therapy was performed at any time prior to the start of the start of the preparative regimen / infusion. If iron chelation therapy was not given or it is unknown whether iron chelation therapy was given, select **No** or **Unknown**.

Questions 18 – 19: Specify therapy (check all that apply)

Specify the iron chelation therapy(ies) administered to reduce iron overload. Select all that apply. If the administered agent is not listed, select **Other** and specify the agent.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q20 – 24: Pulmonary Assessments

Questions 20 – 21: Were pulmonary function tests (PFT) performed? (If PFT tests were conducted we ask that you attach the most recent report)

Indicate if pulmonary function tests (PFTs) were performed prior to the start of the preparative regimen / infusion. If pulmonary function tests were performed, report **Yes** and specify if the PFT report is attached. If multiple PFTs were performed, attach the most recent report. Attaching PFT reports will prevent future requests to submit additional data for research studies.

If pulmonary function tests were not performed between diagnosis and the start of the preparative regimen / infusion, select **No**.

For instructions on how to attach documents in FormsNet3[SM], refer to the Training Guide.

Question 22: For children unable to perform a PFT, was oxygen saturation on room air > 95%?

Indicate if oxygen saturation on room air was > 95%. If oxygen saturation is > 95%, report **Yes**. If the oxygen saturation on room air was ≤ 95%, report **No**. If oxygen saturation was assessed multiple times, report the most recent assessment.

If oxygen saturation was not assessed, report **Not done**. This question is only applicable for children ≤ 5 years of age.

Questions 23 – 24: Was a 6-minute walk test performed?

A 6-minute walk test is used to assess total distance walked within 6 minutes to determine aerobic capacity and endurance. Indicate if a 6-minute walk test was performed at any time between diagnosis and the start of the preparative regimen / infusion. If **Yes**, report the total distance walked and specify the unit of measure.

If a 6-minute walk test was not performed or if the recipient is unable to walk or cannot perform the 6-minute walk test due to their current clinical status, report **No**.

If multiple walk tests were performed prior to the start of the preparative regimen / infusion, report the results of the most recent assessment.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q25 – 34: Cardiovascular Assessments

Figure 1: Echogcardiogram

M-MODE					
LV Diastolic Diameter	23.8 mm	37-56	Posterior wall	4.3 mm	8-12
LV Systolic Diameter	13.7 mm		LV_Mass	16.7 g	
LV Ejection Fraction Teich	76 %		Aortic Sinuses	10.6 mm	=<37
Interventricular septum	3.9 mm	8-12	LA Systolic Diameter	16.4 mm	=<40
DOPPLER					
AV Peak Velocity	114 cm/s		PV Peak Velocity	99.1 cm/s	
AV Peak Gradient	5.2 mmHg		PV Peak Gradient	3.9 mmHg	
LVOT Peak Velocity	108 cm/s				

LV: There is normal situs. Normal LV size and systolic function. The heart is displaced inferiorly but structurally normal. The ventricular septum appears intact and there is no shunting noted. The LVEDD normal range is 2.11 - 2.92 Z is -0.64. IVS normal range is 0.36 - 0.63 Z is -1.56. PW normal range is 0.35 - 0.58 Z is -0.60.

RV: Normal RV size and systolic function.

Atria: The atria are of normal size. The atrial septum appears intact and there is no shunting noted.

AV: The aortic valve is tricuspid and normal.

MV: Structurally normal mitral valve.

TV&PV: The tricuspid valve is normal. There is trace tricuspid regurgitation. The pulmonary valve is normal with normal doppler flow.

Aorta: Normal sized aortic sinuses and proximal ascending aorta. The arch, and descending aorta are normal. Th AoR normal range is 0.93 - 1.43 Z is -1.07

Peri: No pericardial effusion.

IVC: Normal

Questions 25 – 27: Was left ventricular ejection fraction (LVEF) or left ventricular shortening fraction reported?

The left ventricular ejection fraction (LVEF) is a percentage that represents the volume of blood pumped from the left ventricle into the aorta (also known as stroke volume) compared to the volume of blood in the ventricle just prior to the heart contraction (also known as end diastolic volume). The left ventricular shortening fraction is the percentage change in cavity dimensions of the left ventricle with systolic contraction. The LVEF and left ventricular shortening fraction are assessed via an echocardiogram. Refer to Figure 1 above for an example of an echocardiogram report.

Report **Yes** if either LVEF or left ventricular shortening fraction was assessed at any time prior to start of the preparative regimen / infusion and provide the percentage(s). If the LVEF and left ventricular shortening

fraction were assessed, report the results of both. If the LVEF or left ventricular shortening fraction were assessed multiple times prior to the start of the preparative regimen / infusion, report the most recent value(s).

Report **No** if the LVEF and left ventricular shortening fraction were not assessed.

Questions 28 – 29: Is there evidence of pulmonary hypertension?

Pulmonary hypertension (PH) refers to elevated pulmonary arterial pressure and is diagnosed either by an echocardiogram or right heart catheterization. PH can be due to a primary elevation of pressure in the pulmonary arterial system alone (pulmonary arterial hypertension), or secondary to elevations of pressure in the pulmonary venous and pulmonary capillary systems (pulmonary venous hypertension; post-capillary PH).

Indicate **Yes** if the recipient had evidence of PH at any time between diagnosis and the start of the preparative regimen and indicate which method was used to diagnose PH. Report **No** if the recipient did not have evidence of PH at any time between diagnosis and the start of the preparative regimen.

Question 30: Is a copy of the echocardiogram report attached?

Indicate whether the echocardiogram report is attached to this form. For instructions on how to attach documents in FormsNet3^{SM}, refer to the Training Guide.

Questions 31 – 32: Cardiac iron T2 imaging (found on MRI results)

Cardiac T2* mapping is a noninvasive MRI method that is used to identify myocardial iron accumulation in several iron storage diseases. If **Known**, report the unit of measure from the MRI results in m/sec.

Questions 33 – 34: Was brain natriuretic peptide (BNP) assessed?

Brain natriuretic peptide (BNP) is a hormone secreted by cardiac ventricle cells in response to increased ventricular blood volume. BNP is typically measured using various immunoassay techniques. Confirm with the attending physician on where to locate immunoassay results measuring BNP, if available.

Indicate if the BNP was assessed at any time between diagnosis and the start of the preparative regimen. If **Yes**, report the value as documented on the laboratory report (in pg / mL). If BNP was assessed multiple times, report the results of the most recent test. If BNP was not assessed or if no information is available to determine if BNP was tested, report **No** or **Unknown**, respectively.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q35 – 40: Renal Assessments

Questions 35 – 36: Urine albumin

Indicate whether urine albumin was measured prior to the start of the preparative regimen / infusion. If measured, select **Known** and report the laboratory value and unit of measure documented on the laboratory report. If urine albumin was assessed on multiple dates, report the most recent results. If urine albumin was not measured or if no information is available to determine if urine albumin was measured, report **Unknown**.

If the urine albumin is < 0.1 mg / L, report the urine albumin value as “0 mg / L.”

> **Glomerular Filtration Rate (GFR)**
> Glomerular filtration rate (GFR)_ is only enabled for adult recipients (> 18 years of age). _The GFR is collected for pediatric recipients (≤ 18 years of age) on the Pre-TED (2400) Form.

Questions 37 – 38: Glomerular Filtration Rate (GFR)

The glomerular filtration rate (GFR) estimates how much blood passes through the glomeruli each minute and is used to check how well the kidneys are working. Indicate whether the GFR was measured prior to the start of the preparative regimen / infusion. If measured, select **Known** and report the laboratory value and unit of measure documented on the laboratory report. If testing was performed multiple times, report the most recent laboratory value obtained. If the GFR was not measured or if no information is available to determine if the GFR was assessed, report **Unknown**.

GFR may be reported to the CIBMTR as “actual” or “calculated.” If your center’s laboratory does not calculate the actual GFR value, use the Cockcroft-Gault equation (see equation below) to determine the calculated value.

Cockcroft-Gault Equation

GFR = ((140-age)x Wt)/(72 x Cr)

- GFR_cg = Glomerular Filtration Rate (Cockcroft) (mL / min)
- Age = Patient Age (years)
- Sex = Gender (Male)
  - If female, multiply result by 0.85
- Wt = Body Weight (kg)
- Cr = Creatinine (S, mg / dL)

If the laboratory report indicates the GFR as a range, report the average. Example, if the laboratory report indicates GFR is 80 – 120, report “100.”

For values expressed as g “> X,” report the value as “X+1.” Example, if the laboratory report indicates the

GFR is greater than 120, report “121.”

If the laboratory report indicates the GFR “< X,” report the value as “X-1.” Example, if f the GFR is reported as < 80, report “79.”

Questions 39 – 40: Cystatin-C (*if multiple, report the most recent tested*)

Cystatin-C is a protein in the blood that can be used to evaluate kidney function. If measured, select **Known** and report the laboratory value. If testing was performed multiple times, report the most recent laboratory value obtained. If the cystatin-C was not measured or if no information is available to determine if the cystatin-C was assessed, report **Unknown**.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q41 – 45: Splenic Assessments

Question 41: Was splenic function assessed?

Evaluation of splenic tissue may be necessary to determine the extent of the recipient's disease. Splenic assessments include the following:

- Complete RBC: Also called an erythrocyte count, this assessment is used to determine how many red blood cells are present. A test included in a CBC.
- Pitted RBC score: As red blood cells (RBC) age, membrane vacuoles ("pits") occur. Pitted RBCs may be listed on laboratory reports as a "PIT count."
- Splenic scan: Radionuclide spleen scans (liver-spleen scans) are nuclear scan utilizing a radioactive tracer substance that is administered intravenously. The tracer collects in large amounts and shows as bright spots on imaging results. One of the most common methods used is single photon emission computed tomography (SPECT / CT).

Indicate **Yes** if splenic function was assessed by a complete RBC, pitted RBC score, or splenic scan at any time between diagnosis and the start of the preparative regimen / infusion.

If splenic function was not assessed or no information is available to determine if splenic function was assessed at any time between diagnosis and the start of the preparative regimen / infusion, select **No** or **Unknown**, respectively. **Unknown** should be used sparingly.

Report **Not applicable** if the recipient had a prior splenectomy or was born without a spleen (congenital asplenia).

Questions 42 – 45: Select which splenic tests was completed

Indicate which splenic test (completed RBC, pitted RBC score, and/or splenic scan) was completed.

If the assessment was performed multiple times prior to the start of the preparative regimen / infusion, report the most recent results.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q46 – 50: Acute Chest Syndrome

Question 46: Has acute chest syndrome (ACS) occurred in the last two years?

Acute chest syndrome (ACS) is a term used to identify symptoms of chest pain, cough, fever, decreased oxygen (hypoxia), and lung infiltrates. Due to the sickling nature of red blood cells as a result of sickle cell disease, ACS may result in pulmonary infarction / emboli or viral / bacterial pneumonia. Diagnosis of ACS should be made based on clinical judgement.

Indicate if the recipient was clinically diagnosed with ACS in the last two years. If diagnosed, report **Yes**. If not clinically diagnosed or was diagnosed more than two years prior to the start of the preparative regimen / infusion, report **No**. If no information is available to determine if ACS was clinically diagnosed, report **Unknown** .

Questions 47 – 48: Total number of episodes within the last two years

Indicate if the total number of ACS episodes in the last two years is **Known** or **Unknown**. If **Known**, specify the number of episodes. If the number of ACS episodes are not known, select **Unknown**.

In this context, an “episode” is defined as having clinical symptoms requiring intervention (i.e., antibiotics, steroids, etc.) followed by resolution of symptoms and discontinuation of intervention. This should not be interpreted as the number of days the recipient was receiving treatment or had active symptoms. An episode may also be referred to as an “event.”

Question 49: Were red blood cell transfusions required for treatment of ACS in the last two years? (report any simple or exchanged transfusions prior to infusion)

Report **Yes** if RBC transfusion support was required to offset the clinical symptoms of ACS for any episode(s) within the last two years. This includes both simple and exchange transfusions. If RBC transfusions were not required in the last two years, report **No**. If no information is available to determine if RBC transfusion were required, report **Unknown**.

Question 50: Was intubation / mechanical ventilation required for treatment of ACS in the last two years?

A history of intubation and/or mechanical ventilation may impact the recipient’s pulmonary function post-infusion.

If the recipient was intubated and/or placed on mechanical ventilation due to ACS within the last two years, report **Yes**. If the recipient was not intubated and/or placed on mechanical ventilation within the last two years, report “No.” If no information is available to determine if the recipient was intubated and/or placed on mechanical ventilation, report **Unknown**.

Do not report **Yes** if the recipient uses a BIPAP or CPAP machine for sleep apnea.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q51 – 53: Pain

Question 51: Have vaso-occlusive pain episodes occurred that required hospitalization or treatment within the last 2 years? (*treatment that is in a hospital or clinic setting*)

Vaso-occlusive pain, sometimes called a pain crisis, is a common painful complication of sickle cell disease in adolescents and adults. Recurrent episodes may cause irreversible organ damage.

Report **Yes** if the recipient experienced vaso-occlusive pain requiring hospitalization or treatment (i.e., ER admission, day hospital, inpatient admission, etc.) within the last two years. If the recipient did not experience vaso-occlusive pain requiring hospitalization or treatment, or if no information is available to determine if the recipient required hospitalization for vaso-occlusive pain in the past two years, report **No** or **Unknown**.

Questions 52 – 53: Number of episodes in the last two years:

Indicate if the number of vaso-occlusive pain episodes the recipient experienced in the last two years is **Known** or **Unknown**. If **Known**, report the number of vaso occlusive pain episodes requiring hospitalization or treatment within the past two years. If the number of vaso-occlusive pain episodes requiring hospitalization or treatment is not known within the past two years, select **Unknown**.

In this context, an “episode” is defined as being admitted to a hospital setting (i.e., ER admission, day hospital, inpatient admission, etc.) followed by a discharge. This should not be interpreted as the number of days for which the recipient was hospitalized.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q54 – 56: Avascular Necrosis

Question 54: Has avascular necrosis occurred?

Avascular necrosis is the death of bone tissue due to a lack of adequate blood supply. It is sometimes called osteonecrosis. Avascular necrosis can lead to minute fractures in the bone followed by eventual collapse.

Report **Yes** if the recipient developed avascular necrosis at any time between diagnosis and the start of the preparative regimen / infusion. If avascular necrosis did not occur or no information is available to determine if avascular necrosis occurred at any time between diagnosis and the start of the preparative regimen / infusion, report **No** or **Unknown**.

Questions 55 – 56: Specify joint(s) affected (check all that apply)

Specify the joint affected by avascular necrosis. If more than one joint was affected, select all that apply. If avascular necrosis affected a joint that is not listed, report **Other** and specify the affected joint.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q57 – 65: Central Nervous System

Questions 57 – 59: Was transcranial doppler velocity assessed for this reported CNS event? (pediatric only)

Transcranial doppler and transcranial color doppler are types of ultrasonography that measure the velocity of blood flow through the brain's blood vessels by measuring the echoes of ultrasound waves moving transcranially.

Indicate if transcranial doppler velocity was assessed at the time of diagnosis for the reported CNS event. If **Yes**, report the date of the assessment and the transcranial doppler velocity value in cm / sec. If transcranial doppler velocity was not assessed or if no information is available to determine if transcranial doppler velocity was assessed at the time of diagnosis for the reported CNS event, report **No** or **Unknown**, respectively.

Question 60: Was there a sickle cell central nervous system (CNS) complication?

A CNS complication is the development of different neurologic signs and symptoms that occur in recipients with sickle cell disease. See *Specify type of CNS complication* for a list of CNS events.

Report **Yes** if the recipient experienced a CNS event at any time between diagnosis and the start of the preparative regimen / infusion. If a CNS event did not occur or no information is available to determine if a CNS event occurred, report **No** or **Unknown**, respectively.

> **Note: CNS Events – Reporting Multiple Events**
> For each CNS complication the recipient experienced in the reporting period, complete questions *Specify type of CNS complication*, *Year of onset*, and *Was an MRI / MRA of the brain performed for the diagnosis of this reported CNS complication?* for each complication in the reporting period by adding an additional instance in the FormsNet3^{SM} application.

Question 61: Specify type of CNS complication

Indicate the type of CNS event that occurred. If multiple events occurred, report each event as a separate instance, even if it is the same event experienced at different times.

- **Cerebral venous thrombosis**: A blood clot in the cerebral vein in the brain.
- **Hemorrhagic stroke**: Blood vessels break and bleeds in the brain.
- **Ischemic stroke**: The most common type of stroke. Occurs when a blood vessel in the brain is blocked or narrowed, causing reduced blood flow.
- **Moyamoya**: A rare condition where the carotid artery is blocked or narrowed which reduces the blood flow to the brain.
- **Overt stroke**: A focal neurological deficit lasting more than 24 hours. If the type of CNS event is not documented and only noted as a "stroke," select this option.
- **Seizure**: Uncontrolled electrical activity in the brain, which may produce a physical convulsion, minors

physical sings, thought disturbances or a combination of symptoms.
- **Silent stroke**: Asymptomatic stroke.
- **Transient ischemic stroke**: A temporary period of mild stroke symptoms that lasts only a few minutes and does not result in permanent damage. This is also known as transient ischemic attack or a ministroke.

Questions 62 – 63: Year of onset

Indicate if the year of onset of the CNS event reported is **Known** or **Unknown**. If **Known**, report the year of onset.

Questions 64 – 65: Was an MRI / MRA of the brain performed for the diagnosis of this reported CNS event?

Magnetic resonance imaging (MRI) is an imaging technique used to form pictures of the anatomy and the physiological processes of the body. Magnetic resonance angiography (MRA) is similar to MRI but is used to specifically examine blood vessels.

Indicate if an MRI or MRA was performed to diagnose the reported CNS event. If **Yes**, indicate if a copy of the *diagnostic* MRI / MRA report is attached. Only attach the MRI / MRA report performed “at diagnosis” of the CNS event – do not attach an MRI / MRA report performed at any other time-point. The diagnostic MRI / MRA report may not be the most recent scan performed prior to the start of the preparative regimen.

For instructions on how to attach documents in FormsNet3 ^{SM}, refer to the Training Guide.

If an MRI / MRA was not performed to diagnose the reported CNS event or if no information is available to determine if an MRI / MRA was performed at diagnosis of the CNS event, report **No** or **Unknown**, respectively.

Section Updates:

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Last modified: Oct 27, 2024

Q66 – 76: Other Symptoms

Priapism:
Questions regarding priapism are applicable to only biologically male recipients.

Question 66: Did one or more episodes of priapism occur? (to be answered for males only)

Priapism is defined as prolonged erection of the penis, usually without sexual arousal.

Report **Yes** if the recipient experienced one or more episodes of priapism (with or without treatment) at any time between diagnosis and the start of the preparative regimen. If the recipient did not experience priapism or no information is available to determine if the recipient experienced priapism, report **No** or **Unknown**, respectively.

Question 67: Was surgery performed at any time to correct blood flow?

If the recipient experienced an episode(s) of priapism, indicate if surgery was required at any time to correct the blood flow. Report **Yes** if surgery was performed at any between diagnosis and the start of the preparative regimen / infusion to correct blood flow. If surgery was not performed or if no information is available to determine if surgery was performed to correct blood flow as a result of priapism, report **No** or **Unknown**, respectively.

Question 68: Has sickle cell retinopathy developed?

Sickle cell retinopathy is an ocular manifestation of sickle cell disorders characterized by ocular damage due to trapping of sickle-shaped cells in the small blood vessels of the eye. Diagnosis of sickle cell retinopathy should be made by an ophthalmologist and is typically documented within the recipient's medical record.

Indicate **Yes** if the recipient developed sickle cell retinopathy at any time between diagnosis and the start of the preparative regimen / infusion. Report **No** if there is no evidence of sickle cell retinopathy. The **Unknown** option should be selected sparingly and only when no information is available to determine if sickle cell retinopathy was diagnosed.

Question 69: Have chronic leg ulcers developed?

Chronic leg ulcers are defined as a defect of the skin below the level of the knee persisting for more than six weeks with no tendency to heal after three or more months.

Indicate whether the recipient developed chronic leg ulcers at any time between diagnosis and the start of the preparative regimen / infusion. If chronic leg ulcers developed, report Yes. If chronic leg ulcers did not develop or if no information is available to determine if chronic leg ulcers developed, report **No** or **Unknown**, respectively.

Question 70: Is there a diagnosis of asthma or a reactive airway disease?

Asthma is a condition where the airways narrow, swell, and produce extra mucus which results in breathing difficulty, coughing, wheezing, and shortness of breath. Reactive airway disease (RAD) is a general term used to describe coughing, wheezing or shortness of breath when a specific diagnosis has not been made (i.e., asthma, chronic obstructive pulmonary disease, etc.).

Indicate if there was a diagnosis of asthma or a reactive airway disease prior to the start of the preparative regimen / infusion. If the recipient has a diagnosis of asthma or a reactive airway disease, report **Yes**. If the recipient was not diagnosed with or if no information is available to determine if there was a diagnosis of asthma or reactive airway disease, report **No** or **Unknown**, respectively.

Questions 71: Has a venous thrombosis embolism developed?

Venous thrombosis embolism, also called a venous thromboembolism, is a condition characterized by formation of blood clots in deep veins of the body. These clots typically manifest in the lower leg, thigh, or pelvis, but have been noted to occur in the arm.

Indicate if the recipient developed a venous thrombosis embolism prior to the start of the preparative regimen / infusion. If a venous thrombosis embolism developed, report **Yes**. If a venous thrombosis embolism did not develop or if no information is available to determine if a venous thrombosis embolism developed, select **No** or **Unknown**, respectively.

Question 72: Was it associated with an indwelling (central line) catheter?

There are several types of long term indwelling central line catheters used to access veins. Examples include Hickman, Broviac, PICC, etc. which carry a risk of developing a blood clot.

Indicate **Yes** or **No** if the venous thrombosis embolism was associated with the recipient's indwelling (central line) catheter.

Questions 73: Has a pulmonary embolism developed?

Pulmonary embolism is a medical condition where a blood clot is lodged in an artery of the lung, blocking blood flow to that area.

Indicate if the recipient developed a pulmonary embolism between diagnosis and the start of the preparative regimen / infusion. If a pulmonary embolism developed, report **Yes**. If a pulmonary embolism did not develop or if no information is available to determine if a pulmonary embolism developed, select **No** or **Unknown**, respectively.

Question 74: Was it associated with an indwelling catheter?

There are several types of long term indwelling central line catheters used to access veins. Examples include Hickman, Broviac, PICC, etc. which carry a risk of developing a blood clot.

Indicate **Yes** or **No** if the pulmonary embolism was associated with the recipient's indwelling (central line)

catheter.

Question 75: Number of splenic sequestration events

The diagnosis of a splenic sequestration crisis is usually clinical, using recipient history, physical exam, and accompanying lab values. This typically requires seeking medical care for urgent diagnosis and management. An event is defined as the documentation of this diagnosis after seeking medical care either in clinic, emergency department, or hospitalization

Question 76: Date of last event

Report the date of the last splenic sequestration event requiring hospitalization or treatment prior to infusion. This is typically documented within the progress notes.

Section Updates:

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Last modified: Oct 27, 2024

Q77 – 87: Existing Organ Impairments

Multiple Organ Impairments
For each organ impairment the recipient experienced in the reporting period, complete questions *Specify co-existing diseases or organ impairments any time prior to start of preparative regimen*, *Date of diagnosis*, *Method used to assess osteopathies*, *DEXA scan vertebral*, *DEXA scan hip*, *Quantitative CT vertebral* and *Quantitative CT vertebral* for each organ impairment in the reporting period by adding an additional instance in the FormsNet3^{SM} application.

Question 77: Specify co-existing diseases or organ impairments any time prior to start of preparative regimen

Indicate if the recipient developed any of the co-existing diseases or organ impairments listed below at any time prior to the start of the preparative regimen. Include any impairments that resolved prior to the preparative regimen and did not recur. Select all that apply.

- **Amenorrhea:** Absence of menstruation
- **Cardiomyopathy:** A disease of the heart muscle that makes it more difficult for the heart to pump blood to the rest of the body
- *Cholelithiasis: Presence of one or more gallstones in the gallbladder
- **Growth hormone deficiency / short stature:** A condition in which the body does not produce enough growth hormone / a reduced overall rate of growth.
- **Hypersplenism:** Overactive spleen. Diagnosis is typically based on a physician's exam (checking for splenomegaly), a CBC to assess the concentration of red and white blood cells, and / or an ultrasound, measuring the size of the spleen.
- **Hypogonadism / Gonadal dysfunction:** A condition where there is a hyperfunction of the gonads. It can manifest as precocious puberty and is caused by abnormally high levels of testosterone or estrogen, crucial hormones for sexual development.
- **Hypothyroidism requiring replacement therapy:** Decreased activity of the thyroid gland. Diagnosis of hypothyroidism includes high levels of thyroid-stimulating hormone (TSH). Symptoms of hypothyroidism include fatigue, depression, weakness, weight gain, musculoskeletal pain, decreased taste, hoarseness, and / or puffy face.
- **Osteonecrosis:** Flow to part of a bone is disrupted. This results in death of bone tissue, and the bone can eventually break down and the joint will collapse.
- **Osteopathies (porosis, penia):** Includes osteoporosis or osteopenia. Osteopathies should be reported if osteopenia or osteoporosis is documented within the medical record by the physician or based on the Z or T-score. Osteopenia is defined as a Z or T-score between -1.0 and -2.0 by a DEXA or quantitative CT scan. Osteoporosis is defined as a Z or T-score less than -2.0 by a DEXA or quantitative CT scan.
- **Pulmonary hypertension:** Refers to elevated pulmonary arterial pressure and is diagnosed either by an echocardiogram or right heart catheterization.
- **Retinal changes:** Changes include but are not limited to macular degeneration, floaters, diabetic eye

disease, retinal detachment, and retinitis pigmentosa.
- **Thrombosis:** Blood clot within the vein or artery.

If the recipient did not develop any of the co-existing diseases or organ impairments listed above at any time prior to the start of the preparative regimen, select **None** and continue with *Were disease modifying therapies given?*.

Question 78: Date of diagnosis

Report the diagnosis date of the co-existing disease or organ impairment. If the organ impairment occurred multiple time times prior to the start of the preparative regimen, report the co-existing disease or organ impairment once and the diagnosis date of the most recent occurrence. See the example below for additional information.

If the exact date is not known report an estimated date and check the **Date estimated** box. Refer to General Instructions, Guidelines for Completing Forms . for information about reporting estimated dates.

- **Example A:** A recipient developed a blood clot (thrombosis) on 1/15/2018 which resolved; however, the recipient developed another blood clot 8/20/2023. The recipient's transplant was on 12/1/2023. The diagnosis date of the thrombosis should be reported as 8/20/2023 as this is the date of the most recent episode.

Question 79: Method used to assess osteopathies (*report the most recent Z or T-score available. Z-scores are used in patients younger than or equal to 20 and T-scores in patients older than 20*) (check all that apply)

Specify the method used to assess osteopathies prior to the start of the preparative regimen. Select all that apply.

If the osteopathy was not assessed prior to the start of the preparative regimen or is not known if assessed, select **Unknown**.

Questions 80 – 81: DEXA scan vertebral

Indicate if the vertebral Z-score by DEXA is known. If **Known**, report the Z or T-score. Select Negative value if the Z or T-score is a negative (i.e., Z-score is -1.0).

If multiple DEXA scans were performed prior to the start of the preparative regimen, report the most recent vertebral Z or T-score.

Questions 82 – 83: DEXA scan hip

Indicate if the hip Z-score by DEXA is known. If **Known**, report the Z or T-score. Select **Negative value** if the Z or T-score is a negative (i.e., Z-score is -1.0).
If multiple DEXA scans were performed prior to the start of the preparative regimen , report the most recent hip Z or T-score

Questions 84 – 85: Quantitative CT vertebral

Indicate if the vertebral Z-score by quantitative CT is known. If **Known**, report the Z or T-score. Select **Negative value** if the Z or T-score is a negative (i.e., Z-score is -1.0).
If multiple quantitative CT scans were performed prior to the start of the preparative regimen, report the most recent vertebral Z or T-score.

Questions 86 – 87: Quantitative CT hip

Indicate if the hip Z-score by quantitative CT is known. If **Known**, report the Z or T-score. Select **Negative value** if the Z or T-score is a negative (i.e., Z-score is -1.0).
If multiple quantitative CT scans were performed prior to the start of the preparative regimen, report the most recent hip Z or T-score.

Section Updates:

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Last modified: Oct 27, 2024

Q88 – 94: Disease Modifying Therapies

Question 88: Were disease modifying therapies given? (*excludes blood transfusions*)

Indicate if the recipient received disease modifying therapies (see the question below for a list of common disease modifying therapies) at any time between diagnosis and the start of the preparative regimen / infusion; excluding blood transfusion(s). If the recipient received disease modifying therapies, report **Yes**. If the recipient did not receive disease modifying therapies or if no information is available to determine if the recipient received disease modifying therapies, select **No** or **Unknown**, respectively.

Disease Modifying Therapies
For each disease modifying therapy the recipient received in the reporting period, complete questions *Specify the disease modifying therapy*, *Date therapy started*, *Date therapy stopped* for each disease modifying therapy received in the reporting period by adding an additional instance in the FormsNet3^{SM} application.

Same Therapy Restarted
If the same therapy was started and stopped multiple times prior to the start of the preparative regimen, only one instance needs to be reported. In this case, report the therapy start date as the date when therapy first began.

Questions 89 – 90: Specify the disease modifying therapy

Select the disease modifying therapy administered as part of the line of therapy being reported. If the recipient received a therapy which is not listed, select "**Other**" and specify the treatment. Report the generic name of the agent, not the brand name.

- **Crizanlizumab (Adakveo)**: A monoclonal antibody given to reduce the frequency of vaso-occlusive crises.
- **Hydroxyurea**: A type of chemotherapy. Common brand names include Droxia and Hydrea.
- **L-Glutamine (Endari)**: An amino acid in the form of an oral powder given to reduce the complications of sickle cell disease.
- **Voxelotor (Oxbryta)**: An oral medication given to inhibit sickle hemoglobin polymerization.

Questions 91 – 92: Date therapy started

Indicate whether the therapy start date is **Known** or **Unknown**. If the therapy start date is **Known**, report the date the recipient began this line of therapy. If the start date is partially known (i.e., the recipient started treatment in mid- July 2010), use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

If the therapy start date is not known, report **Unknown**.

Questions 93 – 94: Date therapy stopped

Indicate if the stop date is **Known** or **Unknown**. If the therapy is being given in cycles (i.e., Crizanlizumab), report the date the recipient started the last cycle for this line of therapy. Otherwise, report the final administration date for the therapy being reported. If the stop date is partially known, use the process for reporting partial or unknown dates as described in the General Instructions, Guidelines for Completing Forms.

If the disease modifying therapy stop date is not known, select **Unknown**.

Report **Not applicable** if the recipient is still receiving therapy at the start of the preparative regimen / infusion.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q95 – 118: Other Laboratory Studies

Questions 95 – 96: Was hemoglobin electrophoresis performed?

Indicate if hemoglobin electrophoresis studies were performed prior to the start of the preparative regimen / infusion. If hemoglobin electrophoresis studies were performed, report **Yes** and provide the date of the most recent hemoglobin electrophoresis study performed prior to the start of the preparative regimen / infusion.

If hemoglobin electrophoresis studies were not performed or if no information is available to determine if hemoglobin electrophoresis studies were performed prior to the start of the preparative regimen or infusion, report **No** or **Unknown**, respectively.

If RBC transfusion(s) were given within four weeks of the hemoglobin electrophoresis, report **Not applicable**.

Questions 97 – 109: Specify the hemoglobin allele types based on the reported sample

Specify the hemoglobin allele types identified in the reported hemoglobin electrophoresis study (reported above in *Was hemoglobin electrophoresis performed?*). If the hemoglobin allele type was identified, report **Yes** and specify the percentage. If additional sickle related hemoglobin allele types are identified and not listed as options on the form, report **Yes** for *Other sickle related hemoglobin allele type*, specify the other hemoglobin allele type, and provide the percentage.

Report **No** if the specified hemoglobin allele type was not assessed.

Questions 110 – 112: Were reticulocyte counts tested?

Indicate if reticulocyte counts were assessed prior to the start of the preparative regimen / infusion. If reticulocyte counts were assessed, report **Yes**. Provide the reticulocyte cell count in cells / µL and specify date the sample was collected for examination. If the reticulocyte count was assessed multiple times prior to the start of the preparative regimen / infusion, report the value and date of the most recent assessment.

If reticulocyte counts were not measured or if no information is available to determine if reticulocyte counts were assessed, select **No** or **Unknown**, respectively.

If the sample collection date is partially known (i.e., the recipient's RBC counts were measured in mid-July 2019), use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Questions 113 – 115: Were soluble transferrin receptors (sTfR) tested?

Soluble transferrin receptors (sTfR) are proteins found in the blood and used as a measure of functional iron status. These levels are typically elevated in individuals with an iron deficiency (i.e., iron deficiency anemia). This assessment is a blood test and may be performed at the transplant center or by an outside facility.

Indicate if sTfR was tested prior to the start of the preparative regimen / infusion. If sTfR counts were assessed, report **Yes**, provide the sTfR value in mg / L, and specify the date the sample was collected for examination. If the sTfR was assessed multiple times prior to the start of the preparative regimen / infusion, report the value and date of the most recent assessment.

If the sTfR was not measured or if no information is available to determine if sTfR was assessed, select **No** or **Unknown**, respectively.

If the sample collection date is partially known (i.e., the recipient's RBC counts were measured in mid-July 2019), use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Questions 116 – 118: Was an erythropoietin (EPO) level obtained?

Erythropoietin (EPO) is a hormone predominantly produced in the kidneys which plays a critical role in the production of red blood cells.
Indicate if an EPO level was obtained prior to the start of the preparative regimen / infusion. If EPO levels were assessed, report **Yes**, specify the EPO level in IU / L, and report the date the sample was collected for examination. If the EPO was assessed multiple times prior to the start of the preparative regimen / infusion, report the value and date of the most recent assessment.

If EPO levels were not measured or if no information is available to determine if EPO levels were assessed, select **No** or **Unknown**, respectively.

If the sample collection date is partially known (i.e., the recipient's RBC counts were measured in mid-July 2019), use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Section Updates:

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Last modified: Oct 27, 2024

Q119 – 120: Reason for Infusion

Questions 119 – 120: What was the primary reason for infusion?

Specify the recipient's *primary* reason for the infusion. If the indication for transplant is not listed, report **Other** and specify the reason.

If there are multiple indications for which the recipient is receiving the infusion, confirm with the physician the primary reason; only one indication may be reported.

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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Last modified: Oct 27, 2024

Q121: Marrow Evaluation at Last Evaluation

Marrow Evaluation
Complete *Was a marrow aspirate and / or biopsy performed?* for gene therapy infusions only

Questions 121: Was a marrow aspirate and / or biopsy performed?

Indicate **Yes** or No if a marrow aspirate and or biopsy was performed in this reporting period. Additionally, complete the Laboratory Studies (3502) Form and Marrow Surveillance (3506) Form. The intent is to screen for and/or identify changes in the marrow such as dysplasia, MDS, or new hematologic malignancy

Report **Unknown** if not documented

Section Updates:

Question Number	Date of Change	Add/Remove/Modify	Description	Reasoning (If applicable)
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