4100: Cellular Therapy Essential Data Follow-Up

This form must be completed for all recipients of cellular therapy (non-HCT), including post-HCT “DCI/DLI” infusions. For recipients of hematopoietic cellular transplants, complete the appropriate HCT follow-up form.

The Post-Cellular Therapy Essential Data (Post-CTED) follow-up form focuses on key follow-up information, including the survival status of the recipient, causes of death if the recipient died in the period since the last report, additional cellular infusions performed for the same indication, response to the cellular therapy, relapse, current hematologic findings, development of second or new malignancies, persistence of the cellular product depending on the product, development and severity of toxicities (e.g. cytokine release syndrome, neurotoxicity) and fertility information.

The Post-CTED form must be completed at the following time points: 100 days, six months, and annually post-cellular therapy. The follow-up reporting schedule is determined by the product, being genetically modified or not. The structure of the Post-CTED is such that each form should fit on a timeline with distinct start and stop dates that do not overlap any other forms, except in the case where an HCT is also received.

In scenarios where both HCT and cellular therapy forms are being completed, completion of this form should be based on the time period after cellular therapy infusion date (i.e. 100 days after the cellular therapy infusion date). Duplicate questions between HCT and cellular therapy forms may be disabled on the Post-CTED.

Links to sections of form:

Sections of the Forms Instruction Manual are frequently updated. In addition to documenting the changes within each manual section, the most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

Date	Manual Section	Add/ Remove/ Modify	Description
6/ 22/ 18	4100 Cellular Therapy Essential Data Follow-Up	Modify	Added (in red below) further instruction on reporting symptoms in a reporting period: If “yes” is reported for a symptom, report the date of diagnosis (YYYY-MM-DD) of each symptom and indicate if the symptom was explained entirely by non-CRS causes (e.g. infection, therapy). If a symptom occurs multiple times within the same reporting period (e.g. fever), report the first occurrence.
3/8/ 18	4100: Cellular Therapy Essential Data Follow-Up	Add	Added **GVHD** note box at the beginning of the GVHD section.
1/ 30/ 18	4100: Cellular Therapy Essential Data Follow-Up	Modify	Version 3 of the 4100: Cell Therapy Essential Data Follow-Up section of the Forms Instructions Manual released. Version 3 corresponds to revision 3 of the Form 4100.

Q1-6: Survival

Question 1: Date of actual contact with the recipient to determine medical status for this follow-up report:

Enter the date of actual contact with recipient to evaluate medical status for this follow up report. For cases where both cellular therapy and HCT forms are being completed, the contact date on the F4100 should be in relation to the cellular therapy event date.

In general, the date of contact should be reported closest to designated time period of the form (e.g. Day+100, 6 months, or annual follow-up visit). Report the date of actual contact with the recipient to evaluate medical status for the reporting period. Preferred evaluations include those from the cellular therapy physician, referring physician, or other physician currently assuming responsibility for the recipient's care. In the absence of contact with a physician, other types of contact may include a documented phone call with the recipient, a laboratory evaluation, or any other documented recipient interaction on the date reported. If there was no contact on the exact time point, choose the date of contact closest to the actual time point.

Below, the guidelines show an ideal approximate range for reporting each post-cellular therapy time point:

Form	Time Point	Approximate Range
F4100	100 days	+/- 15 days
F4100	6 months	+/- 30 days
F4100	Yearly	+/- 30 days

Recipients are not always seen within the approximate ranges and some discretion is required when determining the date of contact to report. In that case, report the date closest to the date of contact within reason. The examples below assume that efforts were undertaken to retrieve outside medical records from the primary care provider, but source documentation was not available.

Example 1. *The 100 day date of contact doesn't fall within the ideal approximate range.*
The recipient had an infusion on 1/1/13 and is seen regularly until 3/1/13. After that, the recipient was referred home and not seen again until 7/1/13 for a restaging exam and 7/5/13 for a meeting to discuss the results.

What to report:
100 Day Date of Contact: 3/1/13 (Since there was no contact closer to the ideal date of 4/11/13, this date is

acceptable)
6 Month Date of Contact: 7/5/13 (note the latest disease assessment would likely be reported as 7/1/13)

Example 2. *The 100 day date of contact doesn't fall within the ideal approximate range and the recipient wasn't seen again until 1 year post-HCT.*
The recipient had an infusion on 1/1/12 and is seen regularly until 3/1/12. After that, the recipient was referred home and not seen again until 1/1/13 for a restaging exam and 1/4/13 for a meeting to discuss the results.

What to report:
100 Day Date of Contact: 3/1/13 (Since there was no contact closer to the ideal date of 4/11/13, this date is acceptable)
6 Month Form: Indicate the recipient is lost to follow-up in FormsNet3^{SM}
1 Year Date of Contact: 1/4/13 (note the latest disease assessment would likely be reported as 1/1/13)

Additional information:

A date of contact should never be used multiple times for the same recipient's forms.
*For example, 6/1/13 should not be reported for both the 6 month and 1 year. Instead, determine the best possible date of contact for each reporting period; if there is not a suitable date of contact for a reporting period, this may indicate that the recipient was lost to follow-up.

If the recipient has a disease evaluation just after the ideal date of contact, capturing that data on the form may be beneficial.

- For example, if the recipient's 90 day restaging exam was delayed until day 115 and the physician had contact with the recipient on day 117, the restaging exams can be reported as the latest disease assessment and day 117 would be the ideal date of contact, even though it is just slightly after the ideal approximate range for the date of contact.

Date of Contact & Subsequent Infusion
The date of contact reported depends on the regulatory requirements of the product and whether follow-up is required.

Example 3. *The recipient receives a subsequent HCT or cellular therapy.*
The recipient had a cellular therapy on 1/1/14 and was seen regularly through the first 100 days. During the 6 month reporting period, the recipient goes on to receive an HCT or subsequent cellular therapy.

What to report

Regulatory requirements specify 15 years of follow-up data be collected on genetically modified cellular therapy products: The date of contact reported should be appropriate to the time frame of the form being completed (e.g. 6 months)

Cellular therapy products where regulatory requirements do not specify follow-up reporting: The date of contact reported will be the date prior to the start of the preparative regimen for the subsequent infusion (in cases where no prep is given, it is the day prior to the infusion).

Date of Contact & Death

In the case of recipient death, the date of death should be reported as the date of contact regardless of the time until the ideal date of contact. The date of death should be reported no matter where the death took place (inpatient at the transplant facility, at an outside hospital, in a hospice setting, or within the recipient's home).

Example 4. *The recipient has died before their six month reporting period.*

The recipient had an infusion on 1/1/13 and was seen regularly through the first 100 days. They had restaging exams on 4/4/13 and were seen on 4/8/13, and then died on 5/13/13 in the hospital emergency room.

What to report:

100 Day Date of Contact: 4/8/13 (note the latest disease assessment would likely be reported as 4/4/13); 6 Month Date of Contact: 5/13/13 (though the death does not occur within the ideal approximate range for 6 months)

Example 5. *The recipient has died after their six month time point.*

The recipient had an infusion on 1/1/13 and was seen regularly through the first 100 days. The recipient had restaging exams on 4/22/13 and was seen on 4/23/13. Based on findings in the restaging exam, the recipient was admitted for additional treatment. The disease was found to be refractory on a 6/25/13 restaging exam, and the recipient was discharged to hospice on 7/8/13. The hospital was notified via telephone that the recipient died on 7/16/13.

What to report:

100 Day Date of Contact: 4/23/13 (note the latest disease assessment would likely be reported as 4/22/ 13)
6 Month Date of Contact: 7/16/13 (note the latest disease assessment would likely be reported as 6/25/ 13)

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Survival status
For scenarios where both HCT and CT forms will be submitted at the same time, there are duplicate questions across the F2100 and F4100. To reduce the reporting burden, duplicated questions on the Cellular Therapy forms are disabled. This includes Survival Status reported on F4100.

Question 2: Specify the recipient's survival status at the date of last contact:

Indicate the clinical status of the recipient on the date of actual contact for follow-up evaluation.

If the recipient is alive, answers to subsequent questions should reflect the recipient's clinical status from the date of the last report. Continue with question 7.

If the recipient has died, answers to subsequent questions should reflect the recipient's clinical status between the date of the last report and immediately prior to death. Continue with question 3.

Question 3-4: Primary cause of death:

Cause of death is considered the main disease, complication, or injury that leads to death. Do not report the mode of death (e.g., cardiopulmonary arrest). Only one primary cause of death may be specified; select an option from the dropdown list. If the cause of death is reported as "other infection", "other pulmonary syndrome", "multiple organ failure", "other organ failure", "other hemorrhage", "other vascular" or "other cause", specify the other cause in question 4.

Form 2900 Recipient Death form is not required for cellular therapy recipients.

Question 5-6: Contributing cause of death: (check all that apply)

Report any additional causes of death by selecting all that are applicable. All contributing causes of death are important for analysis of cellular therapy outcomes. If the contributing cause of death is reported as "other infection", "other pulmonary syndrome", "multiple organ failure", "other organ failure", "other hemorrhage", "other vascular" or "other cause", specify the other cause in question 6.

Q7-11: Subsequent Cellular Infusions

Subsequent Cellular Infusions
All additional cellular therapy infusions given for the same indication per protocol require a separate infusion form and should be reported on the Form 4003 for this course of cellular therapy. If a cellular therapy was administered for treatment of a different indication, or in response to disease progression / no response, a new Form 4000 (Pre-CTED) must be completed.

Question 7: Has the recipient started a new course of cellular therapy (unplanned) since the date of the last report?

If the recipient started a new course of cellular therapy (unplanned) that is different than the course reported on the form 4000, answer “yes” and continue with question 8.

In cases where the course of cellular therapy is being given post-HCT and HCT follow-up forms are also being completed, and where the cellular therapy course overlaps two HCT reporting periods, the new course only needs to be reported once on the HCT follow-up forms.

Example 1. The new course of cellular therapy consisted of multiple infusions that happened at the end of the 6 month HCT reporting period into the beginning of the 1 year HCT reporting period. The new course of cellular therapy should be reported only on the 6 month HCT form.

If the recipient has not received a new course of cellular therapy (unplanned) since the date of last report, continue with question 10.

Question 8: Specify the reason for which cellular therapy was given:

If additional infusions were given for the same indication per protocol, do not report those here. Please update form 4003 for the applicable product with the correct number of infusions given per protocol. Each infusion requires a separate form 4006.

If the reason for the new course of cellular therapy was failure to respond or in response to disease assessment, or for a new indication, report the event date in question 9.

Question 9: Date of cellular therapy:

Report the date (YYYY-MM-DD) of the new course of cellular therapy (unplanned). If the new course of cellular therapy includes multiple infusions, the date of the first infusion should be reported here. This will require completion of a new form 4000.

> **Subsequent HCT**
> For scenarios where both HCT and CT forms will be submitted at the same time, there are duplicate questions across the F2100 and F4100. To reduce the reporting burden, duplicated questions on the Cell Therapy forms are disabled. This includes a subsequent HCT reported on F4100.

Question 10 & 11: Did the recipient receive an HCT since the date of last report?

If the recipient received an HCT since the date of the last report, report the date (YYYY-MM-DD) of HCT in question 11 and also complete CIBMTR HCT form 2400.

If the recipient did not receive an HCT since the date of the last report, continue with question 12.

Q12-14: Best Response to Cellular Therapy

This section may not fit perfectly to all possible indications for cellular therapy. Please select the response that would most apply to the indication being treated.

Question 12: What was the best response to the cellular therapy?

This section collects the data known as “best response to cellular therapy”. This section applies to both malignant and non-malignant diseases and disorders. If the recipient received a prior HCT, do not report the response to the HCT, a separate evaluation after the cellular therapy is required.

For malignant diseases, appropriate responses would be:

- complete response
- partial response
- no response
- disease progression
- unknown

For recipients with continued complete response (CCR) (those in CR at the time of infusion), please report CR for best response.

For non-malignant disorders, appropriate responses would be:

- normalization of organ function
- partial normalization of organ function
- no response
- worsening of organ function
- unknown

If the indication is infection, the appropriate responses would be:

- complete response
- partial response
- no response
- unknown

Table 1. Examples of Best Response to Cellular Therapy

Indication	Partial Response	Complete Response
Promote stem cell engraftment	-Neutrophil engraftment without platelet engraftment -Platelet engraftment without neutrophil engraftment	Engraftment occurs
Suboptimal donor chimerism (post-HCT)	Increase in chimerism but not 100% donor	100% donor chimerism
Immune Reconstitution (post-HCT)	N/A	CD3 >200/mm3
GVHD prophylaxis (with HCT)	N/A	N/A
GVHD treatment (post-HCT)	-Improvement but not resolution of symptoms -Remains on immune suppression	-Resolution of symptoms -Able to wean immune suppression
Prevent disease relapse	N/A	N/A
Relapsed, persistent or progressive disease (post-HCT)	Improvement in disease burden, but with persistent disease	No evidence of disease
Infection treatment	Decrease in infectious load without resolution	Undetectable infection
Infection prophylaxis	N/A	N/A
B-cell lymphoproliferative disorder (PTLD, EBV lymphoma)	Improvement in disease burden, but with persistent disease	No evidence of disease
Autoimmune Disease	Improvement in organ function but with residual organ dysfunction	Normalization of organ function
Cardiovascular Disease Musculoskeletal Disorder Neurologic Disease Ocular Disease Pulmonary Disease	Improvement in organ function but with residual organ dysfunction	Normalization of organ function
Solid Tumor	Improvement in disease burden, but with persistent disease	No evidence of disease
Malignant Hematologic Disorder	Improvement in disease burden, but with persistent disease	Hematologic Remission or MRD negative
Non-Malignant Disorder	Persistent Disease	Resolution of Disease Process

If the recipient relapses/progresses and receives therapy for the disease relapse/progression, the response to that additional therapy should not be reported in this section. The best response prior to the relapse/ progression should be reported.

Question 13-14: Was the date of best response previously reported?

If the date of best response was previously reported, select “yes” and continue with question 14. **This option is not available on the 100 day report.**

If the date of best response has not been reported, select “no” and report the date (YYYY-MM-DD) in question 14.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Q15-16: Disease Relapse or Progression

Questions 15-16
This section is applicable to malignant disease only.

Question 15-16: Was a disease relapse or progression detected since the date of last report?

Disease relapse or progression can be documented by a variety of methods including molecular, flow cytometry, cytogenetic/fluorescent in situ hybridization (FISH), radiographic or hematological/clinical. Answer “yes” if disease relapse or progression was documented by any one of the methods and report the date (YYYY-MM-DD) of the relapse or progression detected since the date of the last report in question 16.

If a disease relapse or progression was not documented, answer “no” and continue to question 17.

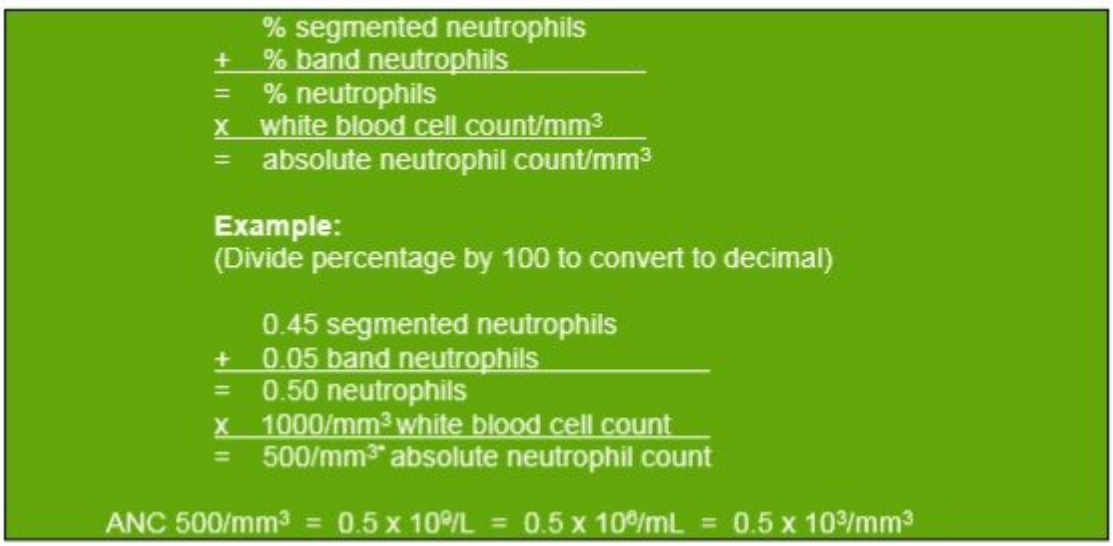
Q17-20: Peripheral Blood Count Recovery

> ! Questions 17-20 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.

Question 17: Was there evidence of initial recovery?

Absolute neutrophil recovery (ANC) recovery is defined as an ANC of ≥ 500/mm3 (or ≥ 0.5 × 109/L) for three consecutive laboratory values obtained on different days. Date of ANC recovery is the date of the first of three consecutive laboratory values where the ANC is ≥ 500/mm3. At some institutions, the laboratory reports display the ANC value once there are sufficient white blood cells to perform a differential count. At other institutions, the laboratory reports do not display the ANC, and it must be calculated from the white blood cell count (WBC) and the percent of segmented and band neutrophils (if the differential was performed on a machine, the percent neutrophils will include both segmented and band neutrophils). If the laboratory report displays an automated ANC value of exactly 500/mm3, the actual ANC value should be calculated from the manual differential if available. The calculated value from the manual differential will determine ANC recovery. If your institution's laboratory reports do not display the ANC value, use the following calculation to determine the ANC:

Example 1: Calculating Absolute Neutrophil Count (ANC)



Traditionally, the definition of ANC recovery required selecting the first date of three consecutive days in which the recipient's ANC was ≥ 0.5×109/L (500/mm3). For various reasons it may not be possible to obtain

daily laboratory values. Under those circumstances, report ANC recovery based upon three consecutive laboratory values (drawn more than a day apart) as long as the ANC remains ≥ 0.5×109/L (500/mm3).

Tracking the date of ANC recovery may not always be straightforward. In some cases the ANC may fluctuate for a period of time before the recipient fully recovers. In other cases the ANC may remain above ≥ 500/mm3 for several days immediately post-HCT and then fall below ≥ 500/mm3. Do not begin counting ANC values of ≥ 500/mm3 towards recovery until the ANC has dropped to the lowest level (nadir) post-infusion. See the following example for more information regarding tracking the date of ANC recovery.

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

Example 2: Tracking ANC Recovery

Infusion Date = May 6
Contact Date = August 15

Date	WBC	%Neutrophils	ANC	
May 7	900	0.6	540	
May 8	850	0.59	502	
May 9	720	0.7	504	
May 10	300	0.45	135	
May 11	15	No differential	—	
May 12	30	No differential	—	
May 13	50	No differential	—	
May 14	250	0.4	100	
May 15	800	0.7	560	*Date of initial recovery: ANC ≥ 500/mm^3 (report this date in question 18)*
May 16	1050	0.8	840	
May 17	1000	0.7	700	
May 18	1800	0.6	1080	
May 19	2000	0.55	1100	
May 20	2500	0.53	1325	
May 21-August 14	—	—	—	ANC ≥ 500/mm^3 for timeframe
August 15 (contact date)	2250	0.43	968	

Question 18: Date ANC >500/mm3 (first of 3 lab values):

Enter the **first** date of the three consecutive laboratory values obtained on different days where the ANC was ≥ 500/mm3 (or ≥ 0.5 × 109/L). For an example of tracking ANC, see Example 2 above.
For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Question 19: Was an initial platelet count > 20 × 109/L achieved?

The following questions refer to initial platelet recovery following the cellular therapy infusion for which this form is being completed. All dates should reflect **no platelet transfusions administered for seven consecutive days**. Report the date of the first of three consecutive laboratory (≥ 20 × 109/L) obtained on different days, as shown in Example 1 below. Note that platelet recovery may take place well after the recipient has returned to the referring physician for care. It is essential that information and laboratory values be obtained from the referring physician.

Transfusions temporarily increase platelet counts. When the data is later used for analysis, it is important to be able to distinguish between a recipient whose own body was creating the platelets and a recipient who required transfusions to support the counts.

The following example illustrates the procedure to follow for reporting platelet recovery.

Example 1. Reporting Platelet Recovery

	Transfusion ↓										
Day	0	1	2	3	4	5	6	7	8	9	10
Platelet Count	10,000	35,000	30,000	25,000	10,000	15,000	19,000	23,000	25,000	40,000	50,000
Date	1/1/2008	1/2/2008	1/3/2008	1/4/2008	1/5/2008	1/6/2008	1/7/2008	1/8/2008	1/9/2008	1/10/2008	1/11/2008
								↑ 1st of 3			

Report 1/8/08 as date platelet count ≥ 20 x 10^9/L

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

Indicate whether or not there was evidence of initial platelet recovery following this cellular therapy infusion.

Check only **one** response:

- If “yes,” continue with question 20.
- If “no,” continue with question 21.
- Check “not applicable,” if the recipient’s platelets never dropped below 20 × 109/L at any time post-cellular therapy infusion and a platelet transfusion was never required. If the recipient’s platelet count drops below 20 × 109/L and/or the recipient received a platelet transfusion even once, do not use this option. This option is only applicable in the 100 day reporting period. Continue with question 21.
- Check “previously reported” if this is the 6 month or annual follow-up, and initial platelet recovery has already been reported on a previous form. Continue with question 21.

Question 20: Date platelets > 20 × 109/L:

Enter the first date of three consecutive laboratory values obtained on different days where the platelet count was ≥ 20 × 109/L. Ensure that no platelet transfusions were administered for seven days immediately preceding this date. Include day seven, as shown in Example 1 above, when determining the recovery date. If three laboratory values were not obtained on consecutive days, but a sequential rise of ≥ 20 × 109/L is demonstrated, follow the examples below when determining an estimated date.

Reporting Scenarios:
A. The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is 22 × 109/L on January 2, 24 × 109/L on January 3, and 28 × 109/L on January 4. The recipient does not come into the clinic for evaluation until one month later. The recipient has not received any more platelet transfusions and the platelet count is well above 20 × 109/L. Report January 8 (day seven post-platelet transfusion) for the date of platelet recovery.
B. The recipient is being seen in the outpatient clinic and receives a platelet transfusion on January 1. The platelet count is ≥ 20 × 109/L on January 2, January 3, and January 4. The recipient is then discharged back to their primary care physician. The transplant center receives a follow-up note from the primary care physician that states “recipient recovered their platelets in January of 2011.” Report an estimated date of recovery using the guidelines available in General Instructions, General Guidelines for Completing Forms.

Q21-35: Current Hematologic Findings

! Questions 21-35 can only be completed on the 100 day, 6 month, 1 year, and 2 year follow-up forms. These questions will be skipped for all subsequent reporting periods.

Questions 21-35: Provide the most recent laboratory values recorded

These questions are intended to determine the hematological status of the recipient after the infusion. Testing may be performed multiple times within the reporting period; however, report only the most recent (closest to the contact date) laboratory values.

Report the laboratory value and unit (if applicable) for each hematologic finding. If a value is not known, select “unknown” and continue with the next laboratory value.

For hematocrit, check the box if red blood cells were transfused within 30 days prior to the testing.

For platelets, check the box if platelets were transfused within seven days prior to the testing.

Q36: New Malignancy, Lymphoproliferative or Myeloproliferative Disease / Disorder

New Malignancies
Report new malignancies that are different than the disease / disorder for which cellular therapy was performed. Do not include relapse, progression or transformation of the same disease subtype. New malignancy related questions will now be asked on the Subsequent Neoplasm Form 3500. The form will come due when question 36 is answered as 'yes'.

Question 36: Did a new malignancy, myelodysplastic, myeloproliferative, or lymphoproliferative disease / disorder occur that is different from the disease / disorder for which the cellular therapy was performed? (Include clonal cytogenetic abnormalities, and post-transplant lymphoproliferative disorders):

Indicate whether a new or second primary malignancy, including lymphoproliferative disorder, or myeloproliferative disorder, has developed. Do not report recurrence, progression, or transformation of the recipient's primary disease (disease for which the cellular therapy was performed) or relapse of a prior malignancy.

New malignancies, lymphoproliferative disorders, and myeloproliferative disorders include but are not limited to:

- Skin cancers (basal, squamous, melanoma)
- New leukemia
- New myelodysplasia
- Solid tumors
- PTLD (post-transplant lymphoproliferative disorder) report as lymphoma or lymphoproliferative disease

The following should not be reported as new malignancy:

- Recurrence of primary disease (report as relapse or disease progression)
- Relapse of malignancy from recipient's pre-cellular therapy medical history
- Breast cancer found in other (i.e., opposite) breast (report as relapse)
- Post-cellular therapy cytogenetic abnormalities associated with the pre-cellular therapy diagnosis (report as relapse)

If a new malignancy is reported, please complete the Subsequent Neoplasms Form 3500 to answer questions specific to the new malignancy. The option of ‘Previously reported’ is reserved for recipients participating in certain studies only. If there is a question regarding use of this option, please contact your CIBMTR CRC.

Q37-58: Persistence of Cells

! This section pertains to the evaluation of persistence of a cellular product in the recipient. It only applies to genetically-modified cellular products.

Question 37: Were tests performed to detect persistence of the cellular product since the date of last report?

Methods such as PCR assays, flow cytometry (immunophenotyping) or immunohistochemistry can be used to detect persistence of the cellular product in the recipient.

If tests were performed to detect persistence of the cellular product since the date of the last report, select “yes” and continue with question 38.

If tests were not performed to detect persistence of the cellular product since the date of the last report, select “no” and continue with question 59.

Question 38: Was persistence evaluated by molecular assay (PCR)?

Molecular assessment involves testing blood, bone marrow, tumor or other source for the presence of known molecular markers. Molecular assessments are the most sensitive test and involve amplifying regions of cellular DNA by polymerase chain reaction (PCR), typically using RNA to generate complementary DNA through reverse transcription (RT-PCR). The amplified DNA fragments are compared to a control, providing a method of quantifying log increase of genetic mutation transcripts. Each log increase is a 10-fold increase of gene transcript compared to control.

Indicate whether molecular assay testing was performed to detect the persistence of the genetically-modified cellular product within the reporting period. If “yes”, continue with question 39. If “no”, continue with question 43.

Question 39: Date Sample collected:

Report the date (YYYY-MM-DD) the sample was collected for molecular assay. If multiple tests were performed in the reporting period and

- all tests were negative: report the first negative test result
- there were positive and negative results: report the date of the last positive test.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 40-41: Specify the cell source:

Select bone marrow, peripheral blood, tumor, or other source as the cell source of the sample collected for evaluation by molecular assay. If the source is “other”, specify in question 41.

Question 42: Were the infused cells detected?

Select “yes” if the infused cells were detected by molecular assay. Select no” if the infused cells were not detected by molecular assay.

Question 43: Was persistence evaluated by flow cytometry testing (immunophenotyping)?

Flow cytometry is a technique that can be performed on blood, bone marrow, or tissue preparations where cell surface markers can be quantified on cellular material. The nature of flow cytometry is to detect cells based on a specific probe. To report flow cytometry results, the test must have been performed to specifically detect the genetically-modified cellular product.

Indicate whether flow cytometry testing was performed to detect the persistence of the genetically-modified cellular product within the reporting period. If “yes”, continue with question 44. If “no”, continue with question 48.

Question 44: Date sample collected:

Report the date (YYYY-MM-DD) the sample was collected for flow cytometry testing (immunophenotyping). If multiple tests were performed in the reporting period and

- all tests were negative: report the first negative test result
- there were positive and negative results: report the date of the last positive test

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 45-46: Specify the cell source:

Select bone marrow, peripheral blood, tumor, or other source as the cell source of the sample collected for evaluation by flow cytometry. If other, specify in question 46.

Question 47: Were the infused cells detected?

Select “yes” if the infused cells were detected by flow cytometry testing (immunophenotyping). Select “no” if the infused cells were not detected by flow cytometry testing (immunophenotyping).

Question 48: Was persistence evaluated by immunohistochemistry?

Immunohistochemistry is a process that uses antibodies to test for certain antigens (markers) in a sample. When the antibodies bind to the antigen in the tissue sample, the enzyme or dye is activated, and the antigen can then be seen under a microscope.

Indicate whether immunohistochemistry testing was performed to detect the persistence of the genetically-modified cellular product within the reporting period. If “yes”, continue with question 49. If “no”, continue with question 53.

Question 49: Date sample collected:

Report the date (YYYY-MM-DD) the sample was collected for immunohistochemistry studies. If multiple tests were performed in the reporting period and

- all tests were negative: report the first negative test result
- there were positive and negative results: report the date of the last positive test

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 50-51: Specify the cell source:

Select bone marrow, peripheral blood, tumor, or other source as the cell source of the sample collected for evaluation by immunohistochemistry testing. If other, specify in question 51.

Question 52: Were the infused cells detected?

Select “yes” if the infused cells were detected by immunohistochemistry testing. Select “no” if the infused cells were not detected by immunohistochemistry testing.

Question 53: Was persistence evaluated by other method?

If persistence of cells was tested by a method not listed above, select “yes” and continue with question 54. If “no”, continue with question 59.

Question 54: Specify other method:

Specify the other method used to evaluate persistence of cells.

Question 55: Date sample collected:

Report the date (YYYY-MM-DD) the sample was collected for the other method. If multiple tests were performed in the reporting period and

- all tests were negative: report the first negative test result
- there were positive and negative results: report the date of the last positive test

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 56-57: Specify the cell source:

Select bone marrow, peripheral blood, tumor, or other source as the cell source of the sample collected for evaluation by other method. If other, specify in question 57.

Question 58: Were the infused cells detected?

Select “yes” if the infused cells were detected by other method. Select “no” if the infused cells were not detected by other method.

Q59-78 Graft vs. Host Disease

Autologous Infusions
Questions 59-78 should be completed for allogeneic infusions only. If this was an autologous infusion, continue to question 79.

GVHD
For scenarios where both HCT and CT forms will be submitted at the same time, there are duplicate questions across the F2100 and F4100. To reduce the reporting burden, duplicated questions on the Cellular Therapy forms are disabled. This includes GVHD reported on F4100.

Graft versus Host Disease (GVHD) is an immunological phenomenon resulting from the reaction of donor immune cells against major or minor histocompatibility antigens of the recipient. GVHD is primarily caused by donor-derived T-cells. Very rarely, GVHD may occur due to autologous reactivity (autologous GVHD), third party transfusions, or with identical twin transplantation.

Factors influencing the severity of GVHD are related to three main categories: 1) donor or graft, 2) recipient, and 3) treatment. The most influential donor/graft factor is the degree of genetic disparity between the donor and the recipient (HLA match), but other risk factors include female donor to male recipient, donor parity, older donors, and T-cell dose. The occurrence of acute GVHD becomes a risk factor for the development of chronic GVHD. Recipient age and prior infections are also factors.

In the past, GVHD was classified as acute or chronic based on its time to diagnosis following transplant, and other clinical and histological (biopsy or post-mortem) features. Today, there has been increased recognition that acute and chronic GVHD are not dependent upon time since infusion, so determination of acute or chronic should rest on clinical and histologic features. However, organ staging and overall grade should only be calculated from the clinical picture, not histology. Acute GVHD usually begins between 10 and 40 days after HCT but can appear earlier or later. The organs most commonly affected by acute GVHD are the skin, gut, or liver. Other sites, such as the lung, may be involved.

Acute / Chronic GVHD
If acute GVHD is diagnosed prior to chronic GVHD, report the diagnosis information, maximum severity of any symptoms, and treatment administered up to the date of diagnosis of chronic GVHD in the acute GVHD section of the form (questions 59-70). Do not include

any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section.
Report any new or persistent acute GVHD symptoms occurring on or after the onset of chronic GVHD only in the chronic GVHD section. If chronic GVHD was diagnosed in a prior reporting period, report "no" for questions 59 and 61 in each subsequent reporting period. See reporting scenarios included in question 44.

Question 59: Did acute GVHD develop since the date of last report?

Questions 59 and 61 on the Cellular Therapy Essential Data Follow-Up Form are meant to capture whether the recipient had active symptoms of acute GVHD during the reporting period. If the recipient had active acute GVHD during the reporting period, either question 59 or question 61 must be answered "yes" unless there has been a prior / concurrent diagnosis of chronic GVHD (see note above question 59). There will not be a situation where "yes" is reported for both question 59 and question 61. If question 59 is answered yes and a diagnosis date has been reported in question 60, question 61 will be disabled in FormsNet3^{SM}. Centers should report "yes" for question 59 to indicate the recipient developed acute GVHD in the following scenarios:

- Acute GVHD is diagnosed for the first time during the reporting period.
- An acute GVHD flare is diagnosed during the current reporting period **and** all of the following conditions are met:
  - The recipient's prior acute GVHD symptoms did **not** persist from the prior reporting period into the beginning of the current reporting period.
  - The flare is diagnosed **after at least 30 days** without any active acute GVHD symptoms.
  - The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 59).

If the recipient does have active acute GVHD during the reporting period, but does not match either of the scenarios above, the center will likely need to report "no" for question 59 and "yes" for question 61. Question 61 is intended to capture acute GVHD which has continued from a prior reporting period. This includes any flares which do not meet the above conditions. The intent of classifying GVHD episodes as newly developed or persistent is to avoid having centers re-report diagnosis information which has been captured on a prior form. Refer to the Acute GVHD Diagnosis Scenarios below to see examples of how to answer questions 59 and 61.

Report "no" for questions 59 and 61 if the recipient had no active acute GVHD symptoms during the reporting period **OR** all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 59).

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

Acute GVHD Diagnosis Scenarios:

A. A recipient receives a cellular therapy infusion of an allogeneic product on 1/1/2015 and develops acute GVHD which is clinically diagnosed on 2/1/2015. At least one of their symptoms, attributed to acute

GVHD, persists beyond the 100 day date of contact which is 4/5/2015. Treatment continues and symptoms completely resolve on 5/1/2015. Immunosuppression is tapered until a flare of acute GVHD is diagnosed on 5/25/2015. Immunosuppression is given and symptoms quickly resolve with no active acute GVHD beginning 6/10/2015. The six month date of contact is 6/20/2015. Another flare of acute GVHD is clinically diagnosed on 8/15/2015.

100 Day Post-TED Form:
Question 59: Report “yes” to indicate a new clinical diagnosis of acute GVHD.
Question 60: Report the initial date of diagnosis (2/1/2015).
Question 61: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 60.
Questions 62-68: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).

Six Month Post-TED Form:
Question 59: Report “no” to indicate acute GVHD persists from a previous report. Note, the flare of acute GVHD was < 30 days from symptoms resolution so it doesn’t count as a new reportable episode.
Question 60: Leave blank. This question will be skipped whenever question 59 is answered “no.”
Question 61: Report “yes” to indicate GVHD persists from a previous report.
Questions 62-68: Leave blank. Answering “yes” for question 61 prevents the center from re-reporting diagnosis information already captured on the 100 day form.

One Year Post-Infusion Data Form:
Question 59: Report “yes” to indicate a flare of acute GVHD occurred at least 30 days after resolving during a prior reporting period.
Question 60: Report the diagnosis date of the flare occurring during the reporting period (8/15/2015).
Question 61: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 60.
Questions 62-69: Answer these questions based on the assessments performed at the time of diagnosis of the flare of acute GVHD (8/15/2015).

B. A recipient receives a cellular therapy infusion of an allogeneic product on 1/1/2015 and develops acute skin GVHD on 2/1/2015 and then chronic eye GVHD on 3/1/2015. Both acute and chronic symptoms resolve by the 100 day date of contact (4/5/2015). While tapering their immunosuppression, the recipient has a flare of their acute skin GVHD on 5/30/2015. Treatment continues and symptoms completely resolve by the six month date of contact (6/20/2015).

100 Day Post-Infusion Data Form:
Question 59: Report "yes" to indicate a new clinical diagnosis of acute GVHD.
Question 60: Report the initial date of diagnosis (2/1/2015).
Question 61: Leave blank. This question will be skipped whenever a diagnosis date has been entered in question 60.
Questions 62-68: Answer these questions based on the assessments performed at the time of diagnosis (2/1/2015).

Six Month Post-Infusion Data Form:
Question 59: Report "no" to indicate acute GVHD did not develop during the reporting period.
Question 60: Leave blank. This question will be skipped whenever question 59 is answered "no."
Question 61: Report "no" to indicate acute GVHD did not persist from a previous report.

If chronic GVHD has been diagnosed in a prior reporting period, report "no" for questions 59 and 61. Any new or persistent acute GVHD symptoms occurring after the onset of chronic GVHD must be reported in the chronic GVHD section of the form. Do not include any signs, symptoms, or treatment occurring on or after the onset of chronic GVHD when completing the acute GVHD section. This instruction has been provided in the note above question 59.

Question 60: Date of acute GVHD diagnosis:

Report the date of clinical diagnosis of acute GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed a rash one week prior to the physician clinically diagnosing acute skin GVHD). If the clinical diagnosis is documented, but the diagnosis date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

If the recipient developed more than one episode of acute GVHD in the same reporting period, report the date of onset of the first episode of acute GVHD.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 61: Did acute GVHD persist since the date of last report?

Question 61 will only be enabled in FormsNet3^{SM} if the center has reported "no" for question 59 and, therefore, has not reported a date of diagnosis in question 60. If prompted to answer question 61, report "yes" if acute GVHD was diagnosed in a prior reporting period and any of the following conditions are met:

- The recipient's acute GVHD symptoms have been active since diagnosis and continue to be active during the current reporting period (i.e., no period of resolution or quiescence since diagnosis).
- The recipient's acute GVHD symptoms had resolved before the first day of the current reporting period, but a flare occurred within 30 days of symptom resolution / quiescence.
- The recipient was not diagnosed with chronic GVHD on or before the date of the flare (see note above question 59).

Report "no" for questions 59 and 61 if the recipient had no active acute GVHD symptoms during the reporting period or all acute GVHD signs / symptoms during the reporting period occurred after a diagnosis of chronic GVHD (see note above question 59).

Indicate "unknown" if there is no information about the recipient's GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

Question 62: Overall grade of acute GVHD at diagnosis:

Indicate the overall grade of acute GVHD at the time of diagnosis. The acute GVHD grading scale is based on clinical evidence (physician observation), not histology. Pathology reports sometimes list a histologic grade of GVHD. Do not report the histologic grade. GVHD scoring and grading is based on clinical severity, not histologic severity. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD. However, overall grading remains clinical and is based on the criteria published by Przepiorka et al., Bone Marrow Transplant 1995; 15(6):825-8, see the GVHD Grading and Staging table below.

If acute GVHD was present, but the grade at diagnosis was not documented and it cannot be determined from the grading and staging table, report "not applicable."

Examples may include:

- Only elevated liver function tests without increased bilirubin
- Any other organ involvement without skin, liver, or gut symptoms attributable to GVHD
- Lower intestinal tract involvement where the stage cannot be determined in select scenarios (see lower intestinal tract involvement description below)

Upper GI GVHD
If the recipient only has upper GI GVHD during the reporting period, report this as overall grade II. This may differ from prior instructions regarding how to report upper GI GVHD.

GVHD Grading and Staging

Stage	Skin	Liver	Gut
1	Rash on <25% of skin[1]	Bilirubin 2-3 mg/dl[2]	Diarrhea > 500 ml/day[3] or persistent nausea[4] *Pediatric*: 280-555 ml/m^2/day or 10-19.9 mL/kg/day
2	Rash on 25-50% of skin	Bilirubin 3-6 mg/dl	Diarrhea >1000 ml/day *Pediatric*: 556-833 ml/m^2/day or 20-30 mL/kg/day
3	Rash on >50% of skin	Bilirubin 6-15 mg/dl	Diarrhea >1500 ml/day *Pediatric*: >833 ml/m^2/day or > 30 mL/kg/day
4	Generalized erythroderma with bullous formation	Bilirubin >15 mg/dl	Severe abdominal pain with or without ileus
Grade[5]			
I	Stage 1-2	None	None
II	Stage 3	Stage 1	Stage 1
III	—	Stage 2-3	Stages 2-4
IV[6]	Stage 4	Stage 4	—

[1] Use “Rule of Nines” (Percent Body Surfaces table) or burn chart to determine extent of rash.

[2] Range given as total bilirubin. Downgrade one stage if an additional cause of elevated bilirubin has been documented.

[3] Volume of diarrhea applies to adults. For pediatric patients, the volume of diarrhea should be based on body surface area. Downgrade one stage if an additional cause of diarrhea has been documented.

[4] Persistent nausea with or without histologic evidence of GVHD in the stomach or duodenum.

[5] Criteria for grading given as minimum degree of organ involvement required to confer that grade.

[6] Grade IV may also include lesser organ involvement with an extreme decrease in performance status

Question 48-53: List the stage for each organ at diagnosis of acute GVHD:

Question 63-68: List the stage for each organ at diagnosis of acute GVHD:

Skin: Select the stage that reflects the body surface area involved with a maculopapular rash attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. See the Percent Body Surfaces table below to determine the percent of body surface area involved with a rash. Do not report ongoing rash not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

Percent Body Surfaces

Body Area	Percent	Total Percentage
Each Arm	9%	18%
Each Leg	18%	36%
Chest & Abdomen	18%	18%
Back	18%	18%
Head	9%	9%
Pubis	1%	1%

Lower intestinal tract (use mL/day for adult recipients and mL/m2/day for pediatric recipients): Select the stage that reflects the volume of diarrhea attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Use mL/day for adult recipients and mL/m2/day for pediatric recipients. Input and output records may be useful in determining the volume of diarrhea. Do not report ongoing diarrhea not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

If diarrhea is attributed to acute GVHD during the reporting period, but the volume of stool output is not documented, report “stage 0” for lower intestinal tract involvement. In this case, report “not applicable” for the overall grade unless stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status was also documented at the time point being reported (at diagnosis or maximum grade during the reporting period). Report an overall grade of IV if stage 4 acute skin GVHD, stage 4 acute liver GVHD, or an extreme decrease in performance status is documented at the time point being reported (see GVHD Staging and Grading Table). Report overall grade III if stage 2-3 liver involvement is documented at the time point being reported and there is no evidence of grade IV GVHD.

Upper intestinal tract: Select the stage that reflects the presence of persistent nausea or vomiting attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Do not report ongoing nausea or vomiting not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

Liver: Select the stage that reflects the bilirubin level attributed to acute GVHD at the time of acute GVHD diagnosis or flare in the reporting period. Do not report ongoing hyperbilirubinemia not attributed to acute GVHD at the time of acute GVHD diagnosis or flare.

For recipients who have a normal bilirubin level with elevated transaminase levels attributed to acute GVHD, report this in questions 67-68 “Other site(s) involved with acute GVHD”.

Other site(s) involved with acute GVHD: Indicate whether acute GVHD affected an organ other than skin, upper GI, lower GI, or liver manifesting with hyperbilirubinemia. This includes transaminitis attributed to acute GVHD. Report only other organ involvement at the time of acute GVHD diagnosis or flare in the reporting period. Do not report symptoms ongoing but not attributed to acute GVHD at the time of acute GVHD diagnosis or flare. Specify the other organ system involvement in question 68. If reporting transaminitis under “other site,” write in “transaminitis” rather than “liver” when specifying the site. This will prevent queries regarding incorrectly reporting liver GVHD (with bilirubin elevation) under “other site.”

Question 69: Maximum Overall Grade of Acute GVHD:

Indicate the overall maximum grade of acute GVHD since the date of the last report. Grading is based on clinical evidence (physician observation), not histology. Pathology reports sometimes list a histologic grade of GVHD. Do not report the histologic grade. GVHD scoring and grading is based on clinical severity, not histologic severity. Biopsy of affected organs allows for more precise diagnosis as to the presence or absence of GVHD. However, overall grading remains clinical and is based on the criteria published by *Przepiorka et al., Bone Marrow Transplant 1995; 15(6):825-8*; see the GVHD Grading and Staging table above.

If chronic GVHD was diagnosed during the reporting period, report the maximum severity of acute GVHD prior to the onset of chronic GVHD. See question 59 for further instructions. Acute GVHD grading scenario D below has been provided for further clarification.

Report the recipient’s maximum acute GVHD grade in the reporting period; this may differ from the grade at diagnosis or may be the same. If acute GVHD was present, but the maximum grade was not documented and it cannot be determined from the grading and staging table, report “not applicable.”

Examples may include:

- Only elevated liver function tests without increased bilirubin

- Any other organ involvement without skin, liver, or gut symptoms attributable to GVHD
- Lower intestinal tract involvement where the stage cannot be determined in select scenarios (see lower intestinal tract involvement description above)

> **Upper GI GVHD**
> If the recipient only has upper GI GVHD during the reporting period, report this as overall grade II. This may differ from prior instructions regarding how to report upper GI GVHD.

Acute GVHD Grading Scenarios:

A. A recipient developed stage 2 skin involvement and elevated liver function tests (LFTs) attributed to acute GVHD; however, there was no total bilirubin manifestation. In this case, overall maximum grade I acute GVHD should be reported since the staging / grading can be determined using the GVHD Grading and Staging table above.

B. A recipient developed acute liver GVHD with elevated LFTs (i.e., transaminases) with no total bilirubin manifestation. The progress notes indicate stage 1 (grade II overall) acute GVHD of the liver. In this case, the clinical manifestations do not fit the criteria used in the GVHD Grading and Staging table above; “not applicable” would be the best option to report.

C. A recipient developed stage 2 skin involvement, which showed improvement in response to topical steroids. However, the recipient then developed hyperbilirubinemia attributed to stage 1 liver involvement; the skin involvement at that time was stage 1. In this case, grade II would be reported (assuming this was the extent of the recipient’s acute GVHD in the reporting period).

D. A recipient developed stage 2 skin involvement which resolved in response to topical steroids. Later in the reporting period, the recipient was diagnosed with mild chronic eye GVHD. Shortly thereafter, they were diagnosed with a stage 3 flare of acute skin GVHD. In this case, grade I would be reported. Do not consider any new or persistent acute GVHD symptoms occurring after the onset of chronic GVHD when completing the acute GVHD section of the form.

Question 70: Date maximum overall grade of acute GVHD

Report the date (YYYY-MM-DD) of maximum acute GVHD involvement, based on clinical grade. If the recipient had multiple instances in which their GVHD reached the same maximum grade, report the earliest date. If “not applicable” was reported for question 69, question 70 must be left blank.

Question 71: Did chronic GVHD develop since the date of last report?

Indicate whether a new clinical diagnosis of chronic GVHD was documented during the reporting period. If chronic GVHD was diagnosed during the reporting period, report “yes” and continue with question 72.

If the recipient had a flare of chronic GVHD occurring after at least a 30 day period of symptom quiescence, report “yes” and continue with question 72. Report “no” if symptoms resolve or become quiescent prior to the date of last report and then flare within 30 days. This should be reported as persistent chronic GVHD which is captured in question 73.

Report “no” if chronic GVHD was not clinically diagnosed – initially or as a flare – in the reporting period; this includes instances where chronic GVHD persists from a prior reporting period without flare in the current reporting period.

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

Question 72: Date of chronic GVHD diagnosis:

Report the date (YYYY-MM-DD) of clinical diagnosis of chronic GVHD. The clinical diagnosis date may not necessarily be the date the symptoms began (example: the recipient developed shortness of breath one month prior to the clinical diagnosis of pulmonary chronic GVHD). If the clinical diagnosis is documented, but the diagnosis date is unclear, obtain documentation from the primary physician confirming the clinical diagnosis date.

If the recipient developed more than one episode of chronic GVHD in the same reporting period, report the date of onset of the first episode of chronic GVHD.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 73: Did chronic GVHD persist since the date of last report?

Question 73 will only be enabled in FormsNet3SM if the center has reported “no” for question 71 and, therefore, has not reported a date of diagnosis in question 72. Indicate whether chronic GVHD was clinically diagnosed during a previous reporting period and persisted, with active symptoms, into the present reporting period. Do not report quiescent or inactive chronic GVHD, or a prior history of GVHD. If “yes,” continue with question 74; See question 71 for instructions on reporting a chronic GVHD flare.

If the recipient has no active symptoms during the reporting period, report “no” and continue with question 77.

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

Question 74: Maximum grade of Chronic GVHD (according to best clinical judgement):

Report the maximum chronic GVHD involvement, based on clinical grade, as documented by the recipient’s primary care provider. The intent of this question is to capture the maximum grade based on the best clinical judgment. If the maximum clinical grade is not documented, request documentation from the recipient’s primary care provider.

Indicate “unknown” if there is no information about the recipient’s GVHD status for the reporting period. This option should be used sparingly and only when no judgment can be made about the presence or absence of GVHD in the reporting period.

Question 75: Specify if chronic GVHD was limited or extensive:

The grading system for chronic GVHD is divided into two categories: limited and extensive. Definitions are based on Sullivan KM, Blood 1981; 57:267.

Report “limited” if chronic GVHD includes only localized skin involvement and/or liver dysfunction. Report “extensive” if any of the following symptoms are attributed to chronic GVHD:

- Generalized skin involvement and/or liver dysfunction
- Liver histology showing chronic aggressive hepatitis, bridging necrosis, or cirrhosis
- Involvement of the eye: Schirmer’s test with <5 mm wetting**, or
- Involvement of the salivary glands or oral mucosa, or
- Involvement of any other target organ

Note: Schimer’s test is required if eye involvement is the only symptom of chronic GVHD. If there are other symptoms of chronic GVHD such as lichen sclerosis of the mouth and skin involvement in addition to the eye symptoms, the Schirmer’s test is not required.

Question 76: Date of maximum grade of chronic GVHD:

Report the date (YYYY-MM-DD) of maximum chronic GVHD involvement, based on clinical grade. If the recipient had multiple instances in which their GVHD reached the same maximum grade, report the earliest date.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 77: Is the recipient still taking systemic steroids? (Do not report steroids for adrenal insufficiency, ≤10 mg/day for adults, <0.1 mg/kg/day for children)

Corticosteroids
Corticosteroids are captured differently depending on whether they are used topically or systemically. Use the following guidelines when determining how to report corticosteroids used to treat GVHD:
Topical Creams for Skin: Do not report topical ointments or creams used to treat skin GVHD including corticosteroid creams such as Triamcinolone or Hydrocortisone.
Other Topical Treatments: Certain corticosteroid treatments are inhaled or ingested, but are not absorbed and are therefore considered topical. Examples include beclomethasone and budesonide. Do not consider these medications when answering question 77
Systemic Treatments: Systemic administration of corticosteroids, including use of prednisone and dexamethasone, should be reported in question 77.

Indicate whether the recipient is still taking immunosuppressive agents to treat or prevent GVHD on the date of contact. Refer to the guidelines included in the question text if the recipient is taking low dose steroids or steroids for adrenal insufficiency.

Indicate “not applicable” in any of the following scenarios:

- The recipient has never received systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD.
- The recipient stopped taking systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) to treat or prevent GVHD in a previous reporting period and did not restart systemic steroids (> 10 mg / day for adults or ≥ 0.1 mg / kg / day for children) during the current reporting period.

Indicate “unknown” if there is no information to determine if the recipient is still taking systemic steroids. This option should be used sparingly and only when no judgment can be made about the recipient still receiving treatment for GVHD on the date of contact. If the recipient has died prior to the discontinuation of systemic steroids used to treat or prevent acute and / or chronic GVHD, select “yes.”

Question 78: Is the recipient still taking (non-steroid) immunosuppressive agents (including PUVA) for GVHD?

Indicate whether the recipient is still taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent acute and / or chronic GVHD on the date of contact. Descriptions of many immunosuppressive agents are included below.

If the recipient did not receive non-steroidal immunosuppressive agents to treat or prevent acute and / or chronic GVHD during the reporting period, report “not applicable.”

Indicate “not applicable” in any of the following scenarios:

- The recipient has never received non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD.
- The recipient stopped taking non-steroidal immunosuppressive agents (including PUVA) to treat or prevent GVHD in a previous reporting period and did not restart non-steroidal immunosuppressive agents (including PUVA) during the current reporting period.

Indicate “unknown” if there is no information to determine if the recipient is still taking non-steroidal immunosuppressive agents. This option should be used sparingly and only when no judgment can be made about the recipient still receiving treatment for GVHD in the reporting period.

Examples of Immunosuppresive Agents:

Aldesleukin (Proleukin): Increases production of several white blood cells including regulatory T-cells. This drug is also known as interleukin-2.

ALG (Anti-Lymphocyte Globulin), ALS (Anti-Lymphocyte Serum), ATG (Anti-Thymocyte Globulin) ATS (Anti-Thymocyte Serum): Serum or gamma globulin preparations containing polyclonal immunoglobulins directed against lymphocytes. These drugs are usually prepared from animals immunized against human lymphocytes. Also report the animal source. If “other” is selected, specify the source.

ATS (Anti-Thymocyte Serum): Serum or gamma globulin preparations containing polyclonal immunoglobulins directed against lymphocytes. These drugs are usually prepared from animals immunized against human lymphocytes. Also report the animal source. If “other” is selected, specify the source.

Azathioprine (Imuran): Azathioprine inhibits purine synthesis. Usually it is used at low doses in combination with other treatments.

Bortezomib (Velcade): A proteasome inhibitor.

Cyclosporine (CSA, Neoral, Sandimmune): Calcineurin inhibitor which decreases cytokine production by T-cells. Usually given for ≥ 3 months.

Cyclophosphamide (Cytoxan): Given in high doses near the date of infusion as single agent prophylaxis.

Extra-corporeal photopheresis (ECP): The recipient's blood is removed from the body, exposes to psoralen and ultraviolet light, and re-infused.
FK 506 (Tacrolimus, Prograf): Inhibits the production of interleukin-2 by T-cells.

FK 506 (Tacrolimus, Prograf): Inhibits the production of interleukin-2 by T-cells.

Hydroxychloroquine (Plaquenil): Hydroxychloroquine inhibits transcription of DNA to RNA and is commonly used as an anti-malarial drug.

Interleukin Inhibitor: Interleukin inhibitors suppress production of white blood cells and are grouped according to their target. Examples of IL-2 inhibitors include daclizumab (Zynbryta) and basiliximab (Simulect). Examples of IL-6 inhibitors include tocilizumab (Actemra) and siltuximab (Sylvant).

In vivo monoclonal antibody: Antibody preparations that are infused in the recipient following HSCT. Specify the antibody used as: anti CD25 (Zenapax, Daclizumab, AntiTAC), alemtuzumab (Campath), entanercept (Enbrel), infliximab (Remicade), and / or rituximab (Rituxan).

In vivo immunotoxin: Antibody preparations linked to a toxin that is infused in the recipient following HCT. Specify the immunotoxin.

Janus Kinase 2 Inhibitors: Suppress function of T-effector cells. Examples: ruxoloitinib (Jakafi, Jakavi) and tofacitinib (Xeljanz, Jakvinus).

Methotrexate (MTX) (Amethopterin): Inhibits the metabolism of folic acid. It is most often used with cyclosporine and is usually for a short duration of time.

Mycophenolate mofetil (MMF) (CellCept, Myfortic): Inhibits the de novo pathway used for lymphocyte proliferation and activation.

Pentostatin (Nipent): Inhibits adenosine deaminase, which blocks DNA (and some RNA) synthesis.

Sirolimus (Rapamycin, Rapamune): Inhibits the response to interleukin-2, blocking the activation of T-cells.

Tyrosine Kinase Inhibitor (TKI): Suppress function of tyrosine kinases thereby downregulating the function of many other cellular proteins / processes including fibrosis and inflammation. Examples: imatinib (Gleevec, Glivec), nilotinib (Tasigna), and dasatinib (Sprycel).

UV Therapy: UVA or UVB radiation administered to affected areas of the skin in order to suppress proliferation of cells responsible for GVHD.

PUVA (Psoralen and UVA): Psoralen is applied or taken orally to sensitize the skin, and then the skin is exposed to UVA radiation.

UVB: Broadband- or Narrowband-UVB radiation is applied to the affected areas of the skin.

Q79-174: Toxicities

Question 79: Did the recipient develop Cytokine Release Syndrome (CRS) since the date of last report?

Cytokine Release Syndrome (CRS) is defined by development of a constellation of signs and symptoms that are seen after the infusion of monoclonal antibodies or cellular therapy products. It results from the sometimes rapid release of several inflammatory cytokines as a consequence of immune response triggered by a drug (i.e. monoclonal antibody) or cellular product. This rapid cytokine release into the circulation results in fever, nausea, chills, hypotension, tachycardia, asthenia, headache, rash, sore throat, respiratory failure or death. This section attempts to collect different clinical and laboratory information to understand the severity of this event.

If the recipient developed CRS since the date of last report, select “yes” and continue with question 80. If the recipient did not develop CRS, continue with question 86.

Question 80: Date of diagnosis:

Report the date (YYYY-MM-DD) when the first symptom of CRS was documented by a physician or other health care provider in the progress note or chart.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 81: Was therapy given? (for CRS)

Indicate “yes” if the recipient received therapy for CRS and continue with question 82. Indicate “no” if no therapy was given for CRS and continue with question 84.

Question 82-83: Specify therapy given for CRS: (check all that apply)

Check all that apply from the list if given to treat the CRS. If “other therapy” is selected, specify the therapy in question 83.

Question 84-85: Did cytokine release syndrome resolve?

If the cytokine release syndrome resolved, select “yes” and report the date (YYYY-MM-DD) in question 85.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 86-87: Neurotoxicity:

Neurotoxicity is the development of different neurologic signs and symptoms reported after the infusion of genetically modified lymphocytes. This was initially thought to be part of CRS, but it was also observed in the absence of any other signs of CRS. Neurotoxicity also appears to be a spectrum of signs and symptoms that vary from fine tremors and word finding difficulties to seizure and loss of conscience. This section collects different neurologic signs that have been described after cellular therapy infusions.

Indicate “yes” if neurotoxicity occurred and continue with question 87. Indicate “no” if neurotoxicity did not occur or “unknown” if unsure whether neurotoxicity occurred and continue with question 92.

Report the date (YYYY-MM-DD) in question 87 when the first symptom of neurotoxicity was documented by a physician or other health care provider in the progress note or chart.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 88-89: Specify symptoms of neurotoxicity: (check all that apply)

Select all symptom(s) of neurotoxicity.

Altered mental status: It is a disruption in how the brain works that causes a change in behavior. This change can happen suddenly or over days and ranges from slight confusion to total disorientation and increased sleepiness to coma.
Aphasia: The loss of ability to understand or express speech, caused by brain damage.
Hemiparesis or other focal motor deficit: Paralysis of one side of the body.
Seizure(s): Uncontrolled electrical activity in the brain, which may produce a physical convulsion, minor physical signs, thought disturbances or a combination of symptoms.
Tremors: Tremor is caused by the rapid alternating contraction and relaxation of muscles (involuntary) and is a common symptom of diseases of the nervous system.
Visual hallucinations: The sensation of seeing objects that are not really there.
Other symptom: Specify in question 89.

Question 90-91: Did neurotoxicity resolve?

If the cellular therapy associated neurotoxicity resolved, select “yes” and report the date (YYYY-MM-DD) in question 91. Resolution means complete normalization of neurologic function. It is possible that patients might remain with residual neurologic dysfunction which would not qualify as complete resolution of this complication.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 92-93: Hemorrhagic stroke

Hemorrhagic stroke occurs when a weakened blood vessel ruptures. Two types of weakened blood vessels usually cause hemorrhagic stroke: aneurysms and arteriovenous malformations (AVMs).

Report the date (YYYY-MM-DD) in question 93 when the hemorrhagic stroke was documented by a physician or other health care provider in the progress note or chart.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 94-95: Hypogammaglobulinemia:

Hypogammaglobulinemia refers to low levels of circulating gammaglobulins, or immunoglobulins, in the blood and often determined by quantitative levels of immunoglobulins G (Ig G), A (IgA) and M (IgM); or most commonly IgG only. Levels lower than 600mg/dL of circulating IgG are considered to be hypogammaglobulinemia. Normal limits of IgG concentration in the blood vary with age. Children ages 4 to 10, levels lower than 500mg/dL are considered hypogammaglobulinemia. Children younger than 4 years, as levels of IgG can be much lower and still be within normal ranges for the age, the diagnosis of hypogammaglobulinemia needs to be confirmed with the treating physician.

Hypogammaglobulinemia is common after CAR-T infusions that target CD19+ cells, which produce immunoglobulins. The degree of hypogammaglobulinemia is associated with a higher risk of infection.

Report the date (YYYY-MM-DD) in question 95 when the hypogammaglobulinemia was documented by a physician or other health care provider in the progress note or chart.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 96-97: Did hypogammaglobulinemia resolve?

If the hypogammaglobulinemia resolved, select “yes” in question 96 and report the date (YYYY-MM-DD) in question 97 as documented by a physician or other health care provider in the progress note or chart.

Question 98-99: Did recipient require immunoglobulin replacement therapy?

Replacement therapy is given to prevent infections. If the recipient required immunoglobulin replacement therapy as a result of hypogammaglobulinemia, select “yes” in question 98, and indicate if the recipient is still requiring the therapy at the time of this report in question 99.

Question 100-102: Other toxicity:

If the recipient experienced a toxicity that does not fit in a category above, select “yes” in question 100 and specify the other toxicity in question 101.

Report the date (YYYY-MM-DD) in question 102 when the other toxicity was documented by a physician or other health care provider in the progress note or chart.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 103-159: Symptoms

> ✻ The intent is to capture all symptoms experienced by the recipient to determine the significance of each symptom in relation to the cellular therapy infusion.

Specify if the recipient has developed any of the following symptoms since the date of last report. Report all symptoms if experienced by the recipient, regardless of cause or explanation. These symptoms will be collected for all recipients whether CRS/neurotoxicity developed or not.

Fevers (>100.4 F or >38 C)
Rigors: A sudden feeling of cold with shivering accompanied by a rise in temperature, often with sweating, especially at the onset or height of a fever
Malaise/Fatigue: Malaise is a general feeling of discomfort, illness, or uneasiness whose exact cause is difficult to identify. Fatigue is extreme tiredness, typically resulting from mental or physical exertion or illness
Anorexia: A lack or loss of appetite for food
Myalgias/arthralgias: Myalgia is pain in a muscle or group of muscles and arthralgia is pain in a joint.
Nausea/vomiting: Nausea is a feeling of sickness with an inclination to vomit. Vomiting is the expelling of undigested food or other content through the mouth
Other constitutional symptom: Includes weight loss, hyperhidrosis, chronic pain, etc
Hypoxia requiring minimal supplemental oxygen (FiO2<40%): A lower than normal concentration of oxygen in arterial blood requiring supplemental oxygen of <40% FiO2
Hypoxia requiring more than minimal supplemental oxygen (FiO2>40%): A lower than normal

concentration of oxygen in arterial blood requiring supplemental oxygen of >40% FiO2
Hypotension requiring therapy: Abnormally low blood pressure requiring treatment with volume resuscitation or vasopressors such as norepinephrine or dopamine
Grade 4 organ toxicity: As defined by the CTCAE criteria, grade 4 toxicity represents life-threatening consequences and urgent intervention is indicated

If “yes” is reported for a symptom, report the date of diagnosis (YYYY-MM-DD) of each symptom and indicate if the symptom was explained entirely by non-CRS causes (e.g. infection, therapy). If a symptom occurs multiple times within the same reporting period (e.g. fever), report the first occurrence.
The intent is to capture all symptoms experienced by the recipient to determine the significance of each symptom in relation to the cellular therapy infusion.

Specify the maximum lab results since the date of last report

Question 160-162: Interleukin-6:

Interleukin-6 is a pro-inflammatory cytokine derived from macrophages and endothelial cells that increases synthesis and secretion of immunoglobulins by B lymphocytes.

Indicate if the lab value is “known” or “unknown” in question 161. If known, report the value in question 161 and the date (YYYY-MM-DD) the sample was collected in question 162.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 163-165: Interferon gamma IFN-γ:

Interferon gamma is a pro-inflammatory cytokine produced by macrophages and T-cells that is involved in the regulation of the immune system and activation of phagocytes.

Indicate if the lab value is “known” or “unknown” in question 163. If known, report the value in question 164 and the date (YYYY-MM-DD) the sample was collected in question 165.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 166-168: Soluble interleukin-2 receptor α (sIL2RA or soluble CD25):

Interleukin-2 receptor alpha or CD25 can shed from the surface of cells during inflammatory conditions. This test detects soluble or circulating sIL2RA.

Indicate if the lab value is “known” or “unknown” in question 166. If known, report the value in question 167 and the date (YYYY-MM-DD) the sample was collected in question 168.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 169-171: Total serum ferritin:

Ferritin is an acute phase reactant and is often found in high concentration in highly inflammatory conditions.

Indicate if the lab value is “known” or “unknown” in question 169. If known, report the value in question 170 and the date (YYYY-MM-DD) the sample was collected in question 171.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Question 172-174: C-reactive protein:

C-reactive protein (CRP) is a protein produced by the liver and found in the blood. CRP levels increase with tissue injury or trauma, infection or inflammation. CRP is also highly associated with IL-6 levels.

Indicate if the lab value is “known” or “unknown” in question 172. If known, report the value in question 173 and the date (YYYY-MM-DD) the sample was collected in question 174.

If the exact date is unknown, please view General Instructions, General Guidelines for Completing Forms for more information on reporting partial and unknown dates.

Q175-179: Infection

Infections occur frequently in recipients of cellular therapy or transplant. Questions 175-179 are intended to capture detailed information on *clinically significant* infections diagnosed during the reporting period. A single infection may be found on multiple cultures or at multiple sites. Infections may recur following resolution of symptoms and negative testing. Use the instructions provided in this section to determine when an infection should be considered clinically significant, and therefore reported, as well as when to report new and / or recurrent infections.

Question 175-179: Did the recipient develop a clinically significant infection since the date of the last report?

Indicate whether the recipient developed a clinically significant bacterial, viral, or fungal infection during the reporting period. For the purpose of this manual, the term “clinically significant” refers to any infection requiring treatment. Surveillance cultures in which normal flora is present and the recipient is asymptomatic do not need to be reported. If no clinically significant infections occurred during the reporting period, report “no” for question 175 and skip to question 180.

Do **not** report the following scenarios:

- Culture-negative neutropenic fever without clear source;
- Suspected (unconfirmed) viral or bacterial infections;
- Upper respiratory infections which are presumed viral, but no virus has been identified;
- Candida detected in oral or stool samples (includes oral thrush);
- Toenail fungus;
- Yeast infection in the groin, vagina, or under the breasts;
- Surveillance cultures in which normal flora is present and the recipient is asymptomatic;
- Infections persisting from a prior reporting period (including infections which have progressed to new sites since the last report); or
- Infections recurring within the time frames specified in the Definitions for Same Infection table below.

If an organism is identified by molecular report, laboratory report, or other physician documentation, the infection should be reported in questions 175-179. If no organism is identified, the center should use the following guidelines to determine whether to report an infection:

- If a fungal infection is suspected (per radiology assessments), but no organism is isolated during the reporting period, report the suspected infection in questions 175-179.

- If a bacterial or viral infection is suspected, but not confirmed, do **not** report an infection in questions 175-179.
- If no particular organism group is identified or suspected, do **not** report an infection in questions 175-179.

For each infection, report the organism, site, and date of diagnosis.

Definitions for Same Infection

Organism:
Select the identified or suspected organism as reported on the microbiology report, laboratory report, or other physician documentation. If the specific organism is not listed, use the code “777 – Other organism” and report the name of the organism in the space provided. If a fungal infection is suspected, but not identified, report using code “503 – Suspected fungal infection.” As noted above, only report infections which are *clinically significant*.

Reporting the following infections, will cause a Fungal Infection Post-HCT Data Form (Form 2146) to come due:

- 211 Aspergillus flavus
- 212 Aspergillus fumigatus
- 213 Aspergillus niger
- 210 Aspergillus, NOS
- 214 Aspergillus ustus
- 215 Aspergillus terreus
- 270 Blastomyces (dermatitidis)
- 201 Candida albicans
- 208 Candida non-albicans
- 222 Cryptococcus gattii
- 221 Cryptococcus neoformans
- 230 Fusarium (all species)
- 261 Histoplamsa (capsulatum)
- 240 Zygomycetes, NOS
- 241 Mucorales (all species)
- 242 Rhizopus (all species)
- 272 Scedosporium (all species)
- 503 Suspected fungal infection

Site:
Infections can occur virtually anywhere. In order to capture sufficient detail without excess burden, there is a list for the potential sites. An infection may occur in more than one site at the same or at different times.

- If the infection is identified at multiple sites with the same organism and within the recurrence interval to be considered the same infection (Definitions for Same Infection table), please report all sites the organism was identified.
- If the infection is identified at multiple sites with an organism already reported, but is outside of the recurrence interval to be considered the same infection, please report as a new infection.

Select the site(s) of the infection from the options provided on the form. Report all sites of infection which were confirmed by microbiology, laboratory report, or other physician documentation during the reporting period. This includes any new sites identified after the date of diagnosis as well as after treatment has been initiated.

For clarification, the following site definitions are provided:

Blood: includes blood or serum obtained from a central IV line, catheter tip, or from a direct needle stick (Peripheral draw). Blood should be the reported site for infections identified in the **bone marrow**.

Bone: an infection in the bone itself (Osteomyelitis)

CNS: includes CSF (cerebrospinal fluid) specimens as well as abscesses and/or inflammation noted on brain imaging (encephalitis, meningitis)

Eyes: includes infection in any part of the eye (i.e. retinitis)

Genital: includes vagina, penis, perineum, ovaries, scrotum, testes, uterus

GI tract, lower: includes jejunum, ileum, colon, rectum, and stool

GI tract, upper: includes mouth, dentition, esophagus, stomach, and duodenum

Joints: includes fibrous connective tissue and cartilage at any site of bone articulation, typically isolated to a single area (i.e., not a diffuse infection) such as the knee, elbow, or shoulder

Liver/Spleen: includes the gallbladder and biliary tract

Lung: also known as the lower respiratory tract

Skin, cellulitis: a spreading bacterial or viral infection of the skin and tissues beneath the skin

Skin, necrotizing fasciitis: a severe bacterial infection of the fascia, the tissues that line and separate muscles, that causes extensive tissue death including damage to skin and overlying tissues

Sinus and/or upper respiratory tract: all areas from the nose to the throat and sinuses, does not include lungs (report as “Lung”), mouth, or dental infections (report mouth and dental as “GI tract, upper).

Urinary tract, lower: includes urinary tract infections and cystitis (bladder inflammation)

Urinary tract, upper: includes the kidneys and ureters

Date of Diagnosis:
Report the date of diagnosis of the infection as the collection date for the positive microbiology culture or laboratory report. For suspected fungal infections, enter the date of a radiological test or the date treatment was started as the date of diagnosis. If multiple sites of infection are identified during the reporting period, report the collection date of the first positive microbiology culture or laboratory report.

For more information regarding reporting partial or unknown dates, see General Instructions, General Guidelines for Completing Forms.

Q180-183: Functional Status

Questions 180-183
This section focuses on fertility. This is an important section due to the possibility of some genetically-modified cells persisting and possibly circulating to the fetus.

Question 180: Was the recipient pregnant at any time in this reporting period? (Female Only)

Indicate “yes” if the female recipient was pregnant at any time during the reporting period and continue with question 182. Indicate “no” if the female recipient was not pregnant at any time during the reporting period.

Question 181: Was the recipient’s female partner pregnant at any time in this reporting period? (Male only)

Indicate “yes” if the male recipient’s female partner was pregnant at any time during the reporting period and continue with question 182. Indicate “no” if the male recipient’s female partner was not pregnant at any time during the reporting period.

Question 182: Was the recipient or recipient’s partner still pregnant at the date of last contact?

Indicate “yes” if the female recipient or recipient’s female partner were still pregnant at the date of last contact. Indicate “no” if the female recipient or recipient’s female partner was not pregnant at the date of last contact and continue with question 183.

Question 183: Specify the outcome of pregnancy:

Indicate if the pregnancy ended in a “live birth”, “intrauterine fetal death”, “spontaneous abortion”, “elected abortion” or if the outcome is “unknown”.