Instructions for Plasma Cell Disorders (PCD) Post-HCT Data (Form 2116 – Revision 3)

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Plasma Cell Disorders (PCD) Post-HCT Data Form.

E-mail comments regarding the content of the CIBMTR Forms Instruction Manual to: CIBMTRFormsManualComments@nmdp.org. Comments will be considered for future manual updates and revisions. For questions that require an immediate response, please contact your transplant center's CIBMTR CRC.

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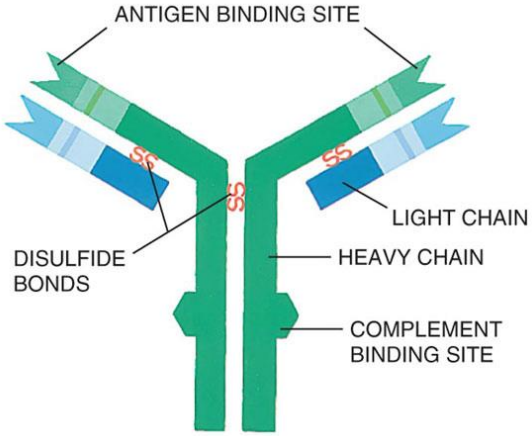
Plasma Cell Disorders (PCD) Post-HCT Data

The blood is composed of platelets, red blood cells, and several kinds of white blood cells. One kind of white blood cells, the plasma cells (also called plasma B cells, plasmocytes, or effector B cells) produce proteins called antibodies or immunoglobulins (Igs) that are part of our defense system against foreign substances (called antigens). Antibodies are produced in response to such things as viruses, bacteria, and other infectious agents.

Multiple myeloma is a cancer that leads to the proliferation of malignant plasma cells (myeloma cells). Myeloma cells usually proliferate in the bone marrow. When myeloma cells grow into isolated masses in other sites, these masses are

called plasmacytomas. Health problems caused by multiple myeloma can affect the bones, immune system, kidneys, and red blood cell count.
The immunoglobulins (antibodies) produced by healthy plasma cells are composed of pairs of heavy chains and light chains (see Graphic 1 below). Healthy plasma cells create many different kinds of immunoglobulins that are classified by their heavy chain type into five categories (IgG, IgA, IgM, IgD, or IgE). The light chain types are designated kappa (κ) or lambda (λ). The whole Ig molecule is then labeled IgG kappa, IgG lambda, IgA kappa, IgA lambda, etc. These protein levels can be measured in blood serum and/or urine.

Graphic 1: Structure of an Immunoglobulin (Antibody)



Secretory Multiple Myeloma:
Healthy plasma cells make immunoglobulins (antibodies) of all types. With the proliferation of malignant plasma cells, the level of one immunoglobulin type increases in the blood and/or urine. This abnormal immunoglobulin type is called the monoclonal immunoglobulin, monoclonal protein (M-protein/M-spike/M-component), or paraprotein. In most cases, the normal immunoglobulins are reciprocally depressed. Patients with this condition are said to have *secretory myeloma*.

Some myeloma patients make only an excess of the light chain portion of the immunoglobulin molecule (i.e., only monoclonal kappa or lambda light chains). The light chain is also called Bence Jones protein. In most patients whose myeloma cells only make light chains, this paraprotein may not be detectable in the blood, but only in the urine. These patients are said to have *light chain only disease*. Ninety-seven percent of patients diagnosed with multiple myeloma have a detectable paraprotein in the blood serum and/or urine.

Table 1. Distribution of Monoclonal Proteins in Secretory Multiple Myeloma

Monoclonal Proteins at Diagnosis	Percent
Source of monoclonal proteins	
Serum monoclonal proteins	80%
Urine monoclonal proteins	75%
Type of monoclonal proteins	
IgG	50-54%
IgA	20%
Monoclonal light chain (light chain only disease)	20%
IgD	2%

Kyle RA, et al. Review of 1027 patients with newly diagnosed multiple myeloma. *Mayo Clin Proc*. 2003;78(1):21-33.

International Myeloma Working Group. Criteria for the classification of monoclonal gammopathies, multiple myeloma and related disorders: a report of the International Myeloma Working Group. *Br J Haem*. 2003;121(5):749-757.

Nonsecretory Multiple Myeloma:

In some myeloma patients, the malignant plasma cells do not produce an excess of the heavy chain or light chain portion of the immunoglobulin molecule; therefore, a paraprotein is not detectable in the serum or urine. These patients are said to have *nonsecretory myeloma* (i.e., the absence of a paraprotein on immunofixation). Immunofixation detects the specific immunoglobulins after separating the proteins into bands on an electrophoresis gel. Nonsecretory myeloma accounts for 3% of myeloma cases.

Table 2. Epidemiology of Multiple Myeloma in the United States

Cases diagnosed per year	~21,700
US Prevalence (2009)	~71,213
Median Age at Diagnosis	69 yrs
Sex	Higher incidence in men
Race	Higher incidence in African Americans
5-year survival rate	40%

National Cancer Institute. Surveillance Epidemiology and End Results (SEER) Stat Fact Sheets: Myeloma. Acessed at: http:/seer.cancer.gov/statfacts/html/mulmy.html. Accessibility verified on August 8, 2013

Amyloidosis:

Amyloidosis is a disease in which abnormally folded proteins build up in different tissues of the body. In the most common amyloidosis, AL amyloidosis, the abnormally folded protein is the light chain component of an immunoglobulin. These light chains may build up in a variety of tissues, but the most common sites of build-up are the heart, kidneys, liver, and nerves. According to the Amyloidosis Foundation, AL Amyloidosis is a relatively rare disorder, with 1200-3200 new cases reported each year in the United States. The disease mostly impacts men over 40.[1]

[1]Amyloidosis Foundation. Amyloidosis - Primary AL.
Accessed at: http:/www.amyloidosis.org/TreatmentInformation/primaryAL.html.
Accessibility verified on August 8, 2013.

The Plasma Cell Disorder Post-HCT Data Form is one of the Comprehensive Report Forms. This form captures plasma cell disorder post-HCT data such as: disease assessment at the time of best response, hematologic and organ parameters at the time of best response, post-HCT therapy, disease status at the time of evaluation for this reporting period, and current status of amyloidosis for this reporting period.

This form must be completed for all recipients whose primary disease reported on Form 2400, question 357, is "Multiple myeloma/plasma cell disorder (PCD) (170)" The Post-HCT Plasma Cell Disorder form must be completed in conjunction with each Post-HCT follow-up form (Forms 2100, 2200, and 2300). This form is designed to capture specific data occurring within the timeframe of each reporting period (i.e., between day 0 and day 100 for Form 2100; between day 100 and the six-month date of contact for six-month follow-up for Form 2200; and between the date of contact for the six-month follow-up and the date of contact for the one-year follow-up for Form 2200, etc.).

Key Fields

Accuracy of the Key Fields is essential for ensuring that:

- Data are being reported for the correct recipient.
- Outcomes data accurately reflects appropriate transplant type and product for each transplant center.
- Data are being shared with the correct donor center, cord blood bank, cooperative registry, or other agency.

The Key Fields precede the form body and are automatically populated in the FormsNet3^{SM} application based on information provided on the CRID Assignment Form 2804. If errors are noted in the key fields, correct Form 2804 and then review it for accuracy. After Form 2804 has been corrected, verify data has been updated on all completed forms. If the data has not been updated automatically, centers will need to reprocess the completed forms to correct the key field data. If errors are noted in key fields for second or subsequent transplants, contact your CRC to make any necessary corrections to the transplant or product type. Transplant and product type will not be automatically populated on product or donor specific forms (Forms 2004, 2005, and 2006) and will need to be manually reported.

Disease Specificity

Question 1: Was the recipient transplanted for or do they have a history of amyloidosis?

This form is designed to best capture data related to the recipient's specific plasma cell disorder. Select "yes" to indicate that the recipient was transplanted

for or has a history of amyloidosis and continue with question 2. Questions appropriate for amyloidosis will became active if completing the form electronically. Select “no” to indicate that the recipient was not transplanted for and does not have a history of amyloidosis and continue with question 3. When completing the form electronically, selecting no will prevent questions specific to amyloidosis from becoming active and only questions relating to non-amyloidosis plasma cell disorders will be shown.

Question 2: Did the recipient have features of multiple myeloma?
If the recipient had multiple myeloma in addition to amyloidosis, select “yes” & continue with question 3. If the recipient did not have multiple myeloma in addition to amyloidosis, select “no” and continue with question 6.

Disease Assessment at the Time of Best Response to HCT

Best response is based on response to the HCT and does NOT include response to therapy given for disease relapse or progression post-HCT.

- If the HCT was planned as part of initial therapy for a recipient with no disease progression or relapse at any time prior to HCT, determine the best response by comparing to the disease assessment at time of original diagnosis.
- If the HCT was performed later in the disease course for a patient who has not received any chemotherapy within 6 months of HCT or has untreated relapse or progression, determine the best response to HCT by comparing the disease status immediately prior to the start of the preparative regimen.
- If the patient had a disease progression or relapse of disease at any time prior to HCT, and was treated to reduce the myeloma burden prior to the start of the preparative regimen, determine the best response to HCT by comparing to the disease evaluation at the time of relapse or progression. In other words, the baseline is reset to the time of relapse or progression.

This comparison is meant to capture the best disease status in response to HCT that occurred in the reporting interval, even if a subsequent disease relapse or progression occurred during the same reporting interval. If a recipient already achieved their best response in a previous interval, confirm the best response and check the box to indicate “date previously reported.” This option is only applicable on report forms for the six-month reporting interval and beyond.

Question 3: Compared to the disease status prior to the preparative regimen, what was the best response to HCT since the date of last report? (Include response to any therapy given for post-HCT maintenance or consolidation, but exclude any therapy given for relapsed, persistent, or progressive disease):

The intent of this question is to determine the best overall response to HCT, which could include any response to planned therapy post-HCT, or to therapy given for maintenance or prophylaxis. (DO NOT include any response to treatment given for relapsed or progressive disease.) This is assessed in each reporting period. When evaluating the best response, determine the disease status within the reporting period and compare it to all previous post-HCT reporting periods. If the response in the current reporting period is the best response to date, report the disease status established within this reporting period. If a better response was established in a previous reporting period, report the previously established disease status. See question 4 to indicate that this disease status was previously reported.

NOTE:

Currently there is an issue on Form 2116 regarding the number of plasma cells required for CR. CR requires less than (but **not** equal to) 5% plasma cells in the bone marrow.

Table 3. Disease Status

Best Response	Definition
Stringent Complete Remission (sCR)	Follows criteria for CR as defined below, **plus all of the following**: • Normal free light chain ratio • Absence of clonal cells in the bone marrow by immunohistochemistry or immunofluorescence (confirmation with repeat bone marrow biopsy not needed). (Presence and/or absence of clonal cells is based upon the κ/λ ratio. An abnormal κ/λ ratio by immunohistochemistry and/or immunofluorescence requires a minimum of 100 plasma cells for analysis. An abnormal ratio reflecting the presence of an abnormal clone is κ/λ of > 4:1 or < 1:2.) sCR requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy sCR requirements.

Table 3. Disease Status *(cont.)*

Best Response	Definition
Complete Remission (CR)	A treatment response where **all** of the following criteria are met: • Negative immunofixation on serum and urine samples • Disappearance of any soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) **NOTE: CR Requirements** For recipients with light chain only myeloma, **all** of the following criteria must be met: • Normal serum free light chain ratio • Negative immunofixation on urine samples • Disappearance of any soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) For recipients with non-secretory myeloma, **all** of the following criteria must be met: • Disappearance of all soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) CR requires two consecutive assessments (by the same method) made at any time before the institution of any new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy CR requirements.
Near Complete Remission (nCR)	A treatment where **all** of the following criteria met: • Serum and urine M-protein detectable by immunoelectrophoresis (immunofixation, IFE) but not on electrophoresis (SPEP and UPEP) • ≤ 5% plasma cells in bone marrow. nCR requires two consecutive assessments (by the same method) made at any time prior to the start of a new therapy and no known evidence of progressive or new bone lesions if radiographic studies were performed; radiographic studies are not required to satisfy nCR requirements.

Table 3. Disease Status *(cont.)*

Best Response	Definition
Very Good Partial Response (VGPR)	**One or more** of the following must be present: • Serum and urine M-protein detectable by immunofixation but not on electrophoresis • ≥ 90% reduction in serum M-protein and urine M-protein level < 100 mg/24 hours. If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis): • Serum M-protein ≥ 1 g/dL • Urine M-protein ≥ 200 mg/24 hours; then a ≥ 90% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria. VGPR requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy VGPR requirements.
Partial Response (PR)	**Both** of the following must be present: • ≥ 50% reduction in serum M-protein • Reduction in 24-hour urinary M-protein by ≥ 90% or to < 200 mg/24 hours. If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria): • Serum M-protein ≥ 1 g/dL • Urine M-protein ≥ 200 mg/24 hours; then a ≥ 50% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria (provided the serum free light chain assay shows involved level > 10 mg/dL and the serum free light chain is abnormal). If serum and urine M-protein *and* serum-free light assay are not measurable, a ≥ 50% reduction in bone marrow plasma cells is required in place of M-protein, provided the baseline bone marrow plasma cell percentage was ≥ 30%. In addition to the above listed criteria, a ≥ 50% reduction in the size of soft tissue plasmacytomas is also required, if present at baseline. PR requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy PR requirements.

Table 3. Disease Status *(cont.)*

Best Response	Definition
Stable Disease (SD)	Does not meet the criteria for CR, VGPR, PR, or PD. SD requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy SD requirements.
Progressive Disease (PD)	Requires **one or more** of the following: Increase of ≥ 25% from the lowest response value achieved in: • Serum M-component with an absolute increase ≥ 0.5 g/dL (for progressive disease; serum M-component increases of ≥ 1 g/dL are sufficient if the starting M-component is ≥ 5 g/dL); **and/or** • Urine M-component with an absolute increase ≥ 200 mg/24 hours; **and/or** • For recipients without measurable serum and urine M-protein levels, the difference between involved and uninvolved free light chain levels with an absolute increase > 10 mg/dL; **and/or** • Bone marrow plasma cell percentage with absolute percentage ≥ 10%; **and/or** • Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas; **and/or** • Development of hypercalcemia (corrected serum calcium > 11.5 mg/dL or 2.65 mmol) that can be attributed solely to the plasma cell proliferative disorder. PD requires two consecutive assessments (by the same method) made at any time before classification as disease progression and/or the start of a new therapy.
Relapse from CR (untreated)	Requires **one or more** of the following: • Reappearance of serum or urine M-protein by immunofixation or electrophoresis; **and/or** • Development of ≥ 5% plasma cells in the bone marrow; **and/or** • Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia). Relapse requires two consecutive assessments (by the same method) made at any time before classification as relapse and/or the start of a new therapy.

At any response level, if some but not all criteria met, the best response should be downgraded to next lower level of response.

> **Example**: A myeloma patient is transplanted in PR. In the 100-day reporting period all the CR criteria (3% plasma cells in the bone marrow, SPEP/UPEP negative) are met with the exception of a positive immunofixation on serum and urine (two disease assessments were performed in the reporting period indicating a positive immunofixation); in this case nCR should be reported as the best response to transplant.

The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may **NOT** be used to confirm CR (e.g., < 5% plasma cells in the bone marrow).

NOTE:

Only report the best response to HCT from all reporting periods.

Example 1. A recipient with myeloma goes to transplant having established a PR prior to transplant, achieves a VGPR during the first 100 days, and then progresses during the six-month reporting period. The best response to transplant should be reported as "VGPR" on all subsequent forms. See below:

Reporting Period	Disease Status	Q1. Best Response	Q5. Date assessed
Pre-transplant	PR	---	---
100-Days Post-HCT	VGPR	VGPR	[date of 1st confirmatory labs]
6-Months Post-HCT	Progression	VGPR	Previously reported
1-Year Post-HCT	PR	VGPR	Previously reported

Example 2. A recipient with myeloma goes to transplant having established a CR prior to transplant, maintains the response after transplant, and then relapses within the six-month reporting period. The best response to transplant would be reported as "CR" for all subsequent reporting periods. See below:

Reporting Period	Disease Status	Q1. Best Response	Q5. Date assessed
Pre-transplant	CR	---	---
100-Days Post-HCT	CR	CR	*[date of labs that first confirmed a continued CR]*
6-Months Post-HCT	Relapsed	CR	Previously reported
1-Year Post-HCT	VGPR	CR	Previously reported

Example 3. A recipient with myeloma goes to transplant having established a PR prior to transplant and maintains the response throughout the 100-day reporting period. During the six-month reporting period, the recipient progresses and begins unplanned therapy to treat the worsening disease. During the one-year reporting period, the recipient achieves VGPR. The best response to transplant occurred during the 100-day reporting period because response to unplanned therapy is not captured using this set of questions. See below:

Reporting Period	Disease Status	Q1. Best Response	Q5. Date assessed
Pre-transplant	PR	---	---
100-Days Post-HCT	PR	PR	*[date of labs that first confirmed a continued PR]*
6-Months Post-HCT	Progression	PR	Previously reported
1-Year Post-HCT	VGPR	PR	Previously reported

Example 4. A recipient with myeloma goes into transplant having established VGPR prior to transplant and maintains the response throughout the 100-day reporting period. During the six-month reporting period, the recipient achieves a CR and is placed on maintenance therapy. During the one-year reporting period the recipient maintains the CR. The best response to transplant occurred in the six-month reporting period. See below:

Reporting Period	Disease Status	Q1. Best Response	Q5. Date assessed
Pre-transplant	VGPR	---	---
100-Days Post-HCT	VGPR	VGPR	*[date of labs that first confirmed a continued VGPR*]
6-Months Post-HCT	CR	CR	*[date of labs that first confirmed CR]*
1-Year Post-HCT	CR	CR	Previously reported

Include response to any post-HCT treatment planned as of Day 0. If post-transplant therapy is given as prophylaxis or maintenance for recipients in CR, or as preemptive therapy for recipients with minimal residual disease, consider this "planned therapy" even if this was not documented prior to the transplant. Bisphosphonate therapy (e.g., Zometa) should not be considered when making this determination. ***Do not include any treatment administered as a result of relapse or progression.***

Question 4: Was the date of best response previously reported?
Indicate if the best response was reported on a previous *post-HCT* plasma cell disorder form (Form 2116). If "yes," continue with question 35. If "no," continue with question 5.

If the best response is the same as the pre-transplant disease status, select "no," report the date of the first assessment that confirmed the ongoing disease status post-HCT in question 5.

Question 5: Date assessed:
Enter the date the best response first began. In other words, report the date of the first assessment, ***not*** the date of the second confirmatory assessment. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathologic examination.

NOTE:

Questions are often raised about how to report the best response and the date it first began when there is not a second assessment within the same reporting period. One way to approach this is if you have a second assessment that confirms the best disease response from the next reporting period available at the time the form is being completed, you can report the best disease response and the date the response first began. If you don't have a second assessment to confirm the new disease status response at the time a form is being completed, you must report the disease response that was previously confirmed.

Example 1: A recipient with myeloma goes into transplant having established a PR prior to transplant. During the 100-day reporting period, the recipient achieves a VGPR. However, the second disease assessment to confirm the VGPR was not performed until one month later (which is in the next reporting period). Those results are available at the time the Day 100 disease form is being completed. The best response to transplant would be reported as "VGPR" with the date it first began in the 100-day reporting period. The recipient maintains the VGPR in the six-month reporting period. The best response to transplant would be reported as "VGPR" with the date as "previously reported" in the six-month reporting period.

Example 2: A recipient with myeloma goes into transplant having established a PR prior to transplant. During the 100-day reporting period, the recipient achieves a VGPR. However a second disease assessment to confirm the VGPR response is not available when the form is being completed. The best response to transplant would be reported as "PR" with the date continuing disease response was confirmed.

Example 3: A recipient with myeloma goes into transplant having established a PR prior to transplant. During the 100-day reporting period, the recipient achieves a VGPR. However a second disease assessment to confirm the VGPR response is not available when the form is being completed. The best response to transplant would be reported as "PR" with the date continuing disease response was confirmed in the 100-day reporting period. When completing the six-month form, a second disease assessment to confirm a VGPR response is available. The best response to transplant would be reported as "VGPR." However, since the VGPR first began during the Day 100 reporting period, an error correction needs to be completed to update the disease status and date first achieved on the Day 100 report.

NOTE:

- Under normal circumstances, a ***marrow aspirate*** is used to obtain the differential cell count, review morphology of the cells, and perform cytogenetic studies, flow cytometry, etc. A ***biopsy*** is obtained to evaluate the overall cellularity of the marrow. In the case of myeloma, the marrow plasma cells tend to be a patchy infiltrate rather than a diffuse infiltrate as in the case of acute leukemia. Therefore, it is possible that the plasma cell numbers may vary between the aspirate and the biopsy.
- The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may NOT be used as source documentation when reporting the data for questions 6-9.
- If the bone marrow pathology report states a range for plasma cells, enter the average of the range rounded to the nearest whole number (e.g., if 0-5%, enter 3%).
- If the report states > 90% plasma cells, enter 91% on the form.
- If the report states a marrow packed with plasma cells or sheets of plasma cells, report 99% on the form.
- If the report states < 5% plasma cells, enter 4% on the form.

Questions 6-7: Plasma cells in bone marrow aspirate:
Indicate whether the percentage of plasma cells in the bone marrow **aspirate** was “known” or “unknown” at the time of best response to transplant. If “known,” report the percentage of plasma cells in the bone marrow aspirate documented on the pathology report in question 7. If “unknown,” continue with question 8.

Questions 8-9: Plasma cells in bone marrow biopsy:
Indicate whether the percentage of plasma cells in the bone marrow **biopsy** was “known” or “unknown” at the time of best response to transplant. If “known,” report the percentage of plasma cells in the bone marrow biopsy documented on the pathology report in question 9. If “unknown,” continue with question 10.

Questions 10-11: Serum monoclonal protein (M-spike): (only from electrophoresis)
Monoclonal gammopathy is defined as the increased production of one type of immunoglobulin by a single clone of cells. The abnormal protein produced is called paraprotein or M-protein. Indicate whether the serum monoclonal immunoglobulin was “known” or “unknown” at the time of best response to transplant. If “known,” report the value and unit of measure documented on the laboratory report in question 11. If “unknown” or “not applicable,” continue with question 12.
“Not applicable” is appropriate for recipients with non-secretory myeloma.

Questions 12: Serum immunofixation:
Serum immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the blood. If "known" at the time of best response to transplant, continue with question 13. If "unknown" or "not applicable," continue with question 16.

"Not applicable" is appropriate for recipients with non-secretory myeloma.

Question 13: Specify monoclonal immunoglobulin result:
If monoclonal immunoglobulin is "present," continue with question 14. If "absent," continue with question 16.

Question 14: Original monoclonal bands:
Indicate "yes" if the original monoclonal band was present or "no" if it was not present.

Question 15: New monoclonal (or oligoclonal) bands:
Indicate "yes" if a new monoclonal (or oligoclonal) band was present or "no" if it was not present.

Questions 16-17: Total urinary protein excretion:
Indicate whether the amount of urinary protein was "known" or "unknown" at the time of best response to transplant. The value reported here should be based on a 24-hour urine collection. If "known," report the laboratory value in question 17. If "unknown," continue with question 18.

NOTE: Urinary Monoclonal Protein
Questions 18-19 are intended to capture the 24-hour urine monoclonal protein results, not the 24-hour protein excretion (questions 16-17 capture the total protein secretion/24 hours). The results will be reported as XX g or XX g/dL. If the value is reported in XX g/dL, it can be multiplied by the volume of the urine to determine the 24-hour urine monoclonal protein.

For example:
(total in g/dL of monoclonal protein) x (total urine volume) = urinary M-protein/24 hours
(0.145 g/dL of monoclonal protein) x (1500 mL total urine) = 2.175 g/24 hours.

Do not report immunofixation results here.

Questions 18-19: Urinary monoclonal protein (M-spike):
Indicate whether the amount of urinary monoclonal protein was "known" or "unknown" at the time of best response to transplant. The value reported here should be based on a 24-hour urine collection. If "known," report the laboratory value in question 19. If "unknown" or "not applicable," continue with question 20.

"Not applicable" is appropriate for recipients with non-secretory myeloma.

Question 20: Urinary immunofixation:
Urine immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the urine. Indicate if the results of urinary immunofixation were "known" or "unknown" at the time of best response to transplant. If "known," continue with question 21. If "unknown" or "not applicable," continue with question 24.

"Not applicable" is appropriate for recipients with non-secretory myeloma.

Question 21: Specify monoclonal immunoglobulin result:
If monoclonal immunoglobulin was "present," continue with question 22. If "absent," continue with question 24.

Question 22: Original monoclonal bands:
Indicate "yes" if the original monoclonal band was present or "no" if it was not present.

Question 23: New monoclonal (or oligoclonal) bands:
Indicate "yes" if a new monoclonal (or oligoclonal) band was present or "no" if it was not present.

Questions 24-25: Serum free light chains – *κ* (kappa)
Indicate whether the serum *κ* (kappa) free light chain level was "known" or "unknown" at the time of best response to transplant. This value should reflect the quantity of serum **free** light chains, not a quantification of total light chains. If "known," report the value and unit of measure documented on the laboratory report in question 25 and continue with question 26. If "unknown" or "not applicable," continue with question 27.

Question 26: Upper limit of normal for *κ* free light chain:
Indicate the upper limit of normal for *κ* (kappa) free light chains value and the unit of measure used at your institution.

Questions 27-28: Serum free light chain – *λ* (lambda)
Indicate whether the serum *λ* (lambda) free light chain level was "known" or "unknown" at the time of best response to transplant. This value should reflect the quantity of serum **free** light chains, not a quantification of total light chains. If "known," report the value and unit of measure documented on the laboratory report in question 28 and continue with question 29. If "unknown" or "not applicable," continue with question 30.

Question 29: Upper limit of normal for *λ* free light chain:
Indicate the upper limit of normal for *λ* (lambda) free light chains value and the unit of measure used at your institution.

Question 30: Was the disease status assessed by cytogenetic testing (conventional or FISH)?
Cytogenetic assessment involves testing blood or bone marrow for the presence of a known cytogenetic abnormality that reflects the recipient's disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

If a cytogenetic assessment was performed to assess disease status at the time of best response to transplant, select "yes" and continue with question 31.

If a cytogenetic assessment was not performed, check "no" and continue with question 35.

Question 31: Was the disease status assessed via FISH?
FISH, fluorescence *in situ* hybridization, is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA commonly found in plasma cell disorders. These probes are mixed with cells from the recipient's blood. A fluorescent "tag" is then used to visualize the binding of the probe to the diseased cells.

Indicate if FISH studies were obtained at the time of best response to transplant. If FISH studies were obtained, select "yes" and continue with question 32.

If no FISH studies were obtained or it is unknown if FISH studies were performed, select "no" and continue with question 33.

Question 32: Date assessed:
Enter the date of FISH assessment at the time of best response. Report the date the sample was collected for the laboratory.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Question 33: Was the disease status assessed via conventional cytogenetics?
Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient's disease. Cytogenetics may also be referred to as karyotyping or g-banding.

Indicate if cytogenetic studies were obtained at the time of best response to transplant. If cytogenetic studies were obtained, select "yes" and continue with question 34.

If no cytogenetic studies were obtained or it is unknown if chromosome studies were performed, select “no” and continue with question 35.

Question 34: Date assessed:
Enter the date of conventional cytogenetic assessment at the time of best response. Report the date the sample was collected for the laboratory.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Hematologic and Organ Parameters at the Time of Best Response (for Amyloid Patients only)

Complete questions 35-60 for amyloid patients only. If diagnosis was other than amyloidosis or there is no history of it, continue with question 61.

The response time for amyloidosis tends to occur well after transplant, so the “best response” to transplant may not occur within the first 100 days. The intent of this question is to determine the best overall response to HCT, which could include any response to planned therapy post-HCT, or to therapy given for maintenance or prophylaxis. DO NOT include any response to treatment given for relapsed or progressive disease. This is assessed in each reporting period. When evaluating the best response, determine the disease status within the reporting period and compare it to all previous post-HCT reporting periods. If the response in the current reporting period is the best response to date, report the disease status established within this reporting period. If a better response was established in a previous reporting period, report the previously established disease status.

Question 35: Specify the recipient’s best hematologic response to the HCT:
Indicate the recipient’s best hematologic response to HCT to date.

Table 4. Hematologic Response

Disease Response	Description
Complete response (CR)	Requires **all** of the following: • Serum and urine negative for monoclonal proteins by immunofixation • Normal free light chain ratio • Plasma cells in marrow < 5%

Table 4. Hematologic Response *(cont.)*

Disease Response	Description
Partial response (PR)	Requires **any** of the following: • ≥ 50% reduction in current serum monoclonal protein levels > 0.5 g/dL • ≥ 50% reduction in current urine light chain levels > 100 mg/day with a visible peak • ≥ 50% reduction in current free light chain levels > 10mg/dL
No response (NR)/stable disease (SD)	Does not meet the criteria for CR, PR, or progressive disease.
Progressive disease (PD)	Requires **any** of the following: • If progressing from CR, any detectable monoclonal protein or abnormal free light chain ratio (light chain must double) • If progressive from PR or SD, ≥ 50% increase in the serum M protein to > 0.5 g/dL, or ≥ 50% increase in urine M protein to > 200mg/day with visible peak present. • Free light chain increase of ≥ 50% to > 10 mg/dL (100 mg/L)

If best response is CR, PR, NR, SD, or progressive disease, continue with question 36.

If the recipient's hematologic status was not assessed during the reporting period, select "not assessed" and continue with question 38. "Not applicable" should rarely, if ever, be chosen.

Questions 36-37: Date assessed:
Indicate if the date the best hematologic response to transplant was assessed is "known," "unknown," or "previously reported." If the hematologic response is known, report the date in question 37. If the date is unknown, select "unknown" and continue with question 38. If the best response to transplant was already reported in a previous reporting period, select "previously reported" and continue with question 38.

Question 38: Specify the recipient's best cardiac response to the HCT:
Indicate the recipient's best cardiac response to HCT to date.

Table 5. Cardiac Response

Disease Response	Description
Cardiac response	Requires **any** of the following: • ≥ 2 mm decrease in mean intraventricular septal wall thickness by echocardiogram • ≥ 20% increase in left ventricular ejection fraction • ≥ 2 grade decrease in New York Heart Association functional class without an increase in diuretic use and no increase in wall thickness • Reduction (≥ 30% and ≥ 300ng/L) of NT-proBNP in patients whom the eGFR is ≥ 45 ml/minute/1.73m^2
No response/stable disease	Does not meet the criteria for cardiac response or progressive disease
Progressive disease	Requires **any** of the following: • ≥ 2 mm increase from baseline in the intraventricular wall thickness by echocardiogram • ≥ 10% decrease in the left ventricular ejection fraction. • ≥ 1 grade increase in New York Heart Association functional class

If the recipient's cardiac status was not assessed during the reporting period, select "not assessed." If the recipient never had evidence of cardiac involvement in their disease, select "not applicable."

Table 6. New York Heart Association Function Classification

Class	Description
Class I	Able to perform ordinary activities without symptoms; no limitation of physical activity
Class II	Ordinary physical activity produces symptoms; slight limitation of physical activity
Class III	Less-than-ordinary physical activity produces symptoms; moderate limitation of physical activity
Class IV	Symptoms present even at rest; severe limitation of physical activity.

Questions 39-40: Date assessed:
Indicate if the date the best cardiac response to transplant was assessed is "known," "unknown," or "previously reported." If the cardiac response is known, report the date in question 40. If the date is unknown, select "unknown" and

continue with question 41. If the best response to transplant was already reported in a previous reporting period, select "previously reported" and continue with question 41.

Question 41: Was there clinical improvement in GI involvement in response to the HCT (decrease in diarrhea)?
Indicate if there was clinical improvement of GI involvement to date. Judgment is required by a clinician to determine if there is evidence of improvement. If "yes" or "no," continue with question 42. If "unknown," continue with question 44.

Questions 42-43: Date assessed:
Indicate if the date the GI involvement was assessed is "known," "unknown," or "previously reported." If the date the GI response was assessed is known, report the date in question 43. If the date is unknown, select "unknown" and continue with question 44. If the best response to transplant was already reported in a previous reporting period, select "previously reported" and continue with question 44.

Question 44: Specify the recipient's best hepatic response to the HCT:
Indicate the recipient's best hepatic response to HCT to date.

Table 7. Hepatic Response

Disease Response	Description
Hepatic response	Requires **all** of the following: • ≥ 2 cm decrease in liver span if hepatomegaly present (liver > 15 cm) • ≥ 50% decrease and/or normalization of serum alkaline phosphatase (ALP) level
No response/stable disease	Does not meet the criteria for hepatic response or progressive disease
Progressive disease	Requires the following: • ≥ 50% increase in the serum alkaline phosphatase (ALP) level

If the recipient's hepatic status was not assessed during the reporting period, select "not assessed." If the recipient never had evidence of hepatic involvement in their disease, select "not applicable."

Questions 45-46: Date assessed:
Indicate if the date the best hepatic response to transplant was assessed is "known," "unknown," or "previously reported." If the hepatic response is known, report the date in question 46. If the date is unknown, select "unknown" and continue with question 47. If the best response to transplant was already

reported in a previous reporting period, select “previously reported” and continue with question 47.

Question 47: Specify the best response of the autonomic neuropathy to the HCT:
Indicate the recipient’s best autonomic neuropathy response to HCT to date.

Table 8. Autonomic Neuropathy Response

Disease Response	Description
Autonomic neuropathy response	Resolution of symptomatic orthostatic hypotension
No response/stable disease	Does not meet the criteria for autonomic neuropathy response or progressive disease
Progressive disease	Worsening of symptomatic orthostatic hypotension

If the recipient’s autonomic neuropathy was not assessed during the reporting period, select “not assessed.” If the recipient never had evidence of disease related autonomic neuropathy, select “not applicable.”

Questions 48-49: Date assessed:
Indicate if the date the best autonomic neuropathy response to transplant was assessed is “known,” “unknown,” or “previously reported.” If the autonomic neuropathy response is known, report the date in question 49. If the date is unknown, select “unknown” and continue with question 50. If the best response to transplant was already reported in a previous reporting period, select “previously reported” and continue with question 50.

Question 50: Specify the best response of peripheral neuropathy to the HCT:
Indicate the recipient’s best peripheral neuropathy response to HCT to date.

Table 9. Peripheral Neuropathy Response

Disease Response	Description
Peripheral neuropathy response	Requires **any** of the following: • Resolution of abnormal physical findings • Resolution or improvement of abnormal electromyography (EMG) and/or Nerve Conduction Velocity (NCV) findings
No response/stable disease	Does not meet the criteria for peripheral neuropathy response or progressive disease
Progressive disease	Requires **any** of the following: • Worsening of physical findings • Worsening of EMG and/or NCV findings

If the recipient's peripheral neuropathy was not assessed during the reporting period, select "not assessed." If the recipient never had evidence of disease-related peripheral neuropathy, select "not applicable."

Questions 51-52: Date assessed:
Indicate if the date the best peripheral neuropathy response to transplant was assessed is "known," "unknown," or "previously reported." If the peripheral neuropathy response is known, report the date in question 52. If the date is unknown, select "unknown" and continue with question 53. If the best response to transplant was already reported in a previous reporting period, select "previously reported" and continue with question 53.

Question 53: Specify the recipient's best renal response to the HCT:
Indicate the recipient's best renal response to HCT to date.

Table 10. Renal Response

Disease Response	Description
Renal response	• ≥ 50% decrease of at least 0.5 g/day (500mg/24hr) in 24-hour urine protein of > 0.5 g/day (500mg/24hr) pre-treatment • Creatinine clearance must not have worsened by ≥ 25% over baseline
No response/stable disease	Does not meet the criteria for renal response or progressive disease
Progressive disease	Requires **any** of the following: • ≥ 50% increase of at least 1 g/day (1000mg/24hr) for urine protein to > 1g/day (1000mg/24hr) • 25% worsening of serum creatinine or creatinine clearance

If the recipient's renal status was not assessed during the reporting period, select "not assessed." If the recipient never had evidence of renal involvement in their disease, select "not applicable."

Questions 54-55: Date assessed:
Indicate if the date the best renal response to transplant was assessed is "known," "unknown," or "previously reported." If the renal response is known, report the date in question 55. If the date is unknown, select "unknown" and continue with question 56. If the best response to transplant was already reported in a previous reporting period, select "previously reported" and continue with question 56.

Questions 56-57: Did any other system respond to the HCT?
Indicate if any other system was assessed for response to HCT. If the recipient had other site involvement reported in questions 179-185 of the Pre-HCT Plasma Cell Disorder form (Form 2016) and that site was assessed, the response to HCT must be reported here, even if there was no response.

Indicate the involved system/site in question 57.

Question 58: Specify best response to HCT for this system:
Indicate if the site's/system's best response to transplant was "response," "no response/stable disease," "progressive disease," or "not applicable."

Questions 59-60: Date assessed:
Indicate if the date the other site's/system's best response to transplant was assessed is "known," "unknown," or "previously reported." If the other site's/system's response is known, report the date in question 60. If the date is unknown, select "unknown" and continue with question 61. If the best response to transplant was already reported in a previous reporting period, select "previously reported" and continue with question 61.

Post-HCT Therapy

Question 61: Was therapy given since the date of last report for reasons other than relapse or progressive disease? (Include any maintenance and consolidation therapy.):
Indicate if the recipient received therapy post-transplant for any reason other than relapse or progressive disease since the date of last report. If "yes," continue with question 62. If "no" or "unknown," continue with question 100.

Recipients are generally transplanted under a specific protocol that defines the systemic therapy the recipient is intended to receive as a preparative regimen prior to the HCT; the infection and GVHD prophylaxis to be administered pre- and/or post-HCT; and any systemic therapy, radiation, and/or other treatments to be administered post-HCT as planned (or maintenance) therapy. Planned (maintenance or consolidation) therapy is given to help prolong a remission. This protocol may be either a research protocol or standard-of-care protocol and should be referred to when completing this section.

Additionally, if post-transplant therapy is given as prophylaxis or maintenance for recipients in CR, or as preemptive therapy for recipients with minimal residual disease, consider this "planned therapy" even if this was not documented prior to the transplant. However, bisphosphonate therapy (e.g., Zometa) should not be reported as a planned therapy since it is universally administered to myeloma patients.

Do not include any treatment administered as a result of relapse or progression.

For the purposes of this question, a line of therapy is one or more cycles of a defined treatment program given to a patient with no progression of disease in between. A new line of therapy may be started for reasons including drug toxicities, planned changes to medications, etc. If a drug dose was changed due to toxicity, do not report this as a new line of therapy; however, if a drug is stopped and a new one started due to toxicity, report this as a new line of therapy.

> **Example A:** A recipient with myeloma goes into transplant having established nCR prior to transplant and maintains the response throughout the 100-day reporting period. During the six-month reporting period, the recipient achieves a CR and is placed on maintenance lenalidomide therapy at 15 mg/day.
>
> **Example B:** A recipient with myeloma goes into transplant having established PR prior to transplant and achieves a VGPR in the 100-day reporting period. During the six-month reporting period, the recipient maintains the VGPR and is placed on maintenance lenalidomide therapy at 10 mg/day. During the one-year reporting period, the recipient progresses and unplanned treatment is initiated. Only the maintenance lenalidomide would be reported in questions 61-99.

Question 62: Systemic therapy
Systemic therapy may be injected into a vein or given orally, and is delivered to the whole body via the blood stream. If “yes,” continue with question 63. If “no,” continue with question 91.

Questions 63-64: Date therapy started:
Indicate if the date the therapy started was “known” or “unknown.” If known, enter the date the recipient began this line of therapy in question 64. If the start date was reported on a previous report, report the same date again when the start/stop dates overlap reporting periods. If “unknown,” continue with question 65.

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.

Questions 65-66: Date therapy stopped:
Indicate if the date the therapy stopped is “known” or “unknown.” If the stop date is known and the recipient is receiving therapy administered in cycles, report the date the recipient started the last cycle for this line of therapy in question 66. If “unknown,” continue with question 67.

If the recipient is receiving therapy administered on a daily basis (e.g., lenalidomide therapy at 10 mg/day) report the last date the recipient received the line of therapy.

If therapy won't be stopped until the next reporting period or later, question 65 should be left blank. Override the error with "UA," unable to answer.
If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Questions 67-68: Number of cycles:
Systemic therapy is usually administered in cycles with rest periods between the cycles. This enables cancer cells to be attacked at vulnerable times and provides healthy cells adequate time to recover from the damage. A cycle can last one or more days and may repeat weekly, bi-weekly, or monthly. A systemic therapy course may consist of multiple cycles.

Indicate if the number of cycles is "known" or "unknown." If known, report the number of cycles the recipient received during the line of therapy being reported in question 68. If the therapy is not given in cycles or the number of cycles is not known, select "unknown" and continue with question 69.

Questions 69-90: Specify systemic therapy
Treatments vary based on protocol and in most cases are administered in the outpatient setting. A treatment may consist of a single drug or a combination of drugs. Additionally, the drugs may be administered on one day, over consecutive days, or continuously. Indicate "yes" or "no" for each chemotherapy treatment drug administered for the line of therapy being reported. Do not leave any yes/no responses blank. If the recipient received a chemotherapy treatment that is not listed, check "yes" for "other systemic therapy" and specify the treatment in question 90. Report the generic name of the agent, not the brand name.

Question 91: Radiation therapy:
Radiation therapy uses high-energy radiation to kill cancer cells. For multiple myeloma, external beam radiation is used most frequently. In this method, a beam of radiation is delivered to a specific part of the body, such as a lytic lesion or plasmacytoma. Indicate if the recipient received radiation during this reporting period post-HCT. If "yes," continue with question 92. If "no," continue with question 96.

Questions 92-93: Date therapy started:
Indicate if the date the therapy started is "known" or "unknown." If known, enter the date the line of radiation therapy began in question 93.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms**.**

Questions 94-95: Date therapy stopped:
Indicate if the date the therapy started is "known" or "unknown." If known, enter the date the line of radiation therapy ended in question 95.
If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms**.**

Question 96: Best response to line of therapy:
Indicate the best response to the line of therapy.

For more information on determining what baseline values to use to determine best response, see Appendix V.

Table 11. Best Response

Best Response	Definition
Stringent Complete Remission (sCR)	Follow criteria for CR as defined below, **plus all of the following**: • Normal free light chain ratio, • Absence of clonal cells in the bone marrow by immunohistochemistry or immunofluorescence (confirmation with repeat bone marrow biopsy not needed). (Presence and/or absence of clonal cells is based upon the κ/λ ratio. An abnormal κ/λ ratio by immunohistochemistry and/or immunofluorescence requires a minimum of 100 plasma cells for analysis. An abnormal ratio reflecting the presence of an abnormal clone is κ/λ of > 4:1 or < 1:2.) sCR requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy sCR requirements.

Table 11. Best Response *(cont.)*

Best Response	Definition
Complete Remission (CR)	A treatment response where **all** of the following criteria are met: • Negative immunofixation on serum and urine samples • Disappearance of any soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) **NOTE: CR Requirements** For recipients with light chain only myeloma, **all** of the following criteria must be met: • Normal serum free light chain ratio • Negative immunofixation on urine samples • Disappearance of any soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) For recipients with non-secretory myeloma, **all** of the following criteria must be met: • Disappearance of all soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) CR requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy CR requirements.
Near Complete Remission (nCR)	A treatment where **all** of the following criteria met: • Serum and urine M-protein detectable by immunoelectrophoresis (immunofixation, IFE) but not on electrophoresis (SPEP and UPEP) • ≤ 5% plasma cells in bone marrow. nCR requires two consecutive assessments (by the same method) made at any time prior to the start of a new therapy and no known evidence of progressive or new bone lesions if radiographic studies were performed; radiographic studies are not required to satisfy nCR requirements.

Table 11. Best Response *(cont.)*

Best Response	Definition
Very Good Partial Response (VGPR)	**One or more** of the following must be present: • Serum and urine M-protein detectable by immunofixation but not on electrophoresis • ≥ 90% reduction in serum M-protein and urine M-protein level < 100 mg/24 hours. If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis): • Serum M-protein ≥ 1 g/dL • Urine M-protein ≥ 200 mg/24 hours; then a ≥ 90% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria. VGPR requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy VGPR requirements.
Partial Response (PR)	**Both** of the following must be present: • ≥ 50% reduction in serum M-protein • Reduction in 24-hour urinary M-protein by ≥ 90% or to < 200 mg/24 hours. If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria): • Serum M-protein ≥ 1 g/dL • Urine M-protein ≥ 200 mg/24 hours then a ≥ 50% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria (provided the serum free light chain assay shows involved level > 10 mg/dL and the serum free light chain is abnormal). If serum and urine M-protein *and* serum-free light assay are not measurable, a ≥ 50% reduction in bone marrow plasma cells is required in place of M-protein, provided the baseline bone marrow plasma cell percentage was ≥ 30%. In addition to the above-listed criteria, a ≥ 50% reduction in the size of any soft tissue plasmacytomas that were present at baseline is also required. PR requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy PR requirements.

Table 11. Best Response *(cont.)*

Best Response	Definition
Stable Disease (SD)	Does not meet the criteria for CR, VGPR, PR, or PD. SD requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy SD requirements.
Progressive Disease (PD)	Requires **one or more** of the following: Increase of ≥ 25% from the lowest response value achieved in: • Serum M-component with an absolute increase ≥ 0.5 g/dL (for progressive disease, serum M-component increases of ≥ 1 g/dL are sufficient if the starting M-component is ≥ 5 g/dL); **and/or** • Urine M-component with an absolute increase ≥ 200 mg/24 hours; **and/or** • For recipients without measurable serum and urine M-protein levels, the difference between involved and uninvolved free light chain levels with an absolute increase > 10 mg/dL; **and/or** • Bone marrow plasma cell percentage with absolute percentage ≥ 10%; **and/or** • Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas; **and/or** • Development of hypercalcemia (corrected serum calcium > 11.5 mg/dL or 2.65 mmol) that can be attributed solely to the plasma cell proliferative disorder. PD requires two consecutive assessments (by the same method) made at any time before classification as disease progression, and/or the start of a new therapy.
Relapse from CR (untreated)	Requires **one or more** of the following: • Reappearance of serum or urine M-protein by immunofixation or electrophoresis; **and/or** • Development of ≥ 5% plasma cells in the bone marrow; **and/or** • Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia). Relapse requires two consecutive assessments (by the same method) made at any time before classification as relapse, and/or the start of a new therapy.

At any response level, if some but not all criteria met, the best response should be downgraded to next lower level of response.

The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may **NOT** be used to confirm CR (e.g., < 5% plasma cells in the bone marrow).

If the disease response following this line of therapy is unknown, select "unknown."

If the recipient had amyloidosis, but no evidence of myeloma, select "Not Applicable (Amyloidosis with no evidence of myeloma)."

Question 97: Date response established:
Any response requires two consecutive assessments (of the same labs, where applicable based on response criteria) made at any time before the start of a new therapy. Enter the date the best response to the line of therapy was established. In other words, report the date of the first assessment, not the date of the second confirmatory assessment. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathological evaluation.

Question 98: Did disease relapse/progress following this line of therapy?
Indicate "yes" if a relapse or progression occurred following the line of therapy being reported and continue with question 99. Documentation of relapse or progression requires two consecutive assessments (of the same labs, where applicable based on response criteria) made at any time before classification as relapse or progression, **and/or** the start of a new therapy. Indicate "no" if the recipient did not relapse or progress following this line of therapy and continue with question 100.

Table 12. Relapse or Progression

Response	Definition
Progressive Disease (PD)	Requires **one or more** of the following: Increase of ≥ 25% from the lowest response value achieved in: • Serum M-component with an absolute increase ≥ 0.5 g/dL (for progressive disease, serum M-component increases of ≥ 1 g/dL are sufficient if the starting M-component is ≥ 5 g/dL); **and/or** • Urine M-component with an absolute increase ≥ 200 mg/24 hours; **and/or** • For recipients without measurable serum and urine M-protein levels, the difference between involved and uninvolved free light chain levels with an absolute increase > 10 mg/dL; **and/or** • Bone marrow plasma cell percentage with absolute percentage ≥ 10%; **and/or** • Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas; **and/or** • Development of hypercalcemia (corrected serum calcium > 11.5 mg/dL or 2.65 mmol) that can be attributed solely to the plasma cell proliferative disorder. PD requires two consecutive assessments (by the same method) made at any time before classification as disease progression, and/or the start of a new therapy.
Relapse from CR (untreated)	Requires **one or more** of the following: • Reappearance of serum or urine M-protein by immunofixation or electrophoresis; **and/or** • Development of ≥ 5% plasma cells in the bone marrow; **and/or** • Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia). Relapse requires two consecutive assessments (by the same method) made at any time before classification as relapse, and/or the start of a new therapy.

Question 99: Date of relapse/progression:
Enter the date the relapse or progression was established following the line of therapy. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathological evaluation. However, if there was

not a second assessment (where applicable by response criteria) obtained prior to the start of new therapy, report the date the new therapy started as the date of relapse/progression. Continue with question 100.

Copy questions 62 -99 to report more than one line of therapy.

NOTE:

It is possible that the relapse or progression would be reported twice if already reported in question 98. Question 98 is asking about relapse or progression following any planned/maintenance therapy. Question 100 is asking about relapse or progression at any time, regardless of whether therapy was given or not.

Question 100: Has the disease relapsed or progressed since the date of last report?

Indicate “yes” if a relapse or progression occurred during the reporting period and continue with question 101. Documentation of relapse or progression requires two consecutive assessments (of the same labs, where applicable based on response criteria) made at any time before classification as relapse or progression, **and/or** the start of a new therapy. Indicate “no” if the recipient did not relapse or progress during the reporting period and continue with question 102.

Table 13. Relapse or Progression

Response	Definition
Progressive Disease (PD)	Requires **one or more** of the following: Increase of ≥ 25% from the lowest response value achieved in: • Serum M-component with an absolute increase ≥ 0.5 g/dL (for progressive disease, serum M-component increases of ≥ 1 g/dL are sufficient if the starting M-component is ≥ 5 g/dL); **and/or** • Urine M-component with an absolute increase ≥ 200 mg/24 hours; **and/or** • For recipients without measurable serum and urine M-protein levels, the difference between involved and uninvolved free light chain levels with an absolute increase > 10 mg/dL; **and/or** • Bone marrow plasma cell percentage with absolute percentage ≥ 10%; **and/or** • Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas; **and/or** • Development of hypercalcemia (corrected serum calcium > 11.5 mg/dL or 2.65 mmol) that can be attributed solely to the plasma cell proliferative disorder. PD requires two consecutive assessments (by the same method) made at any time before classification as disease progression, and/or the start of a new therapy.
Relapse from CR (untreated)	Requires **one or more** of the following: • Reappearance of serum or urine M-protein by immunofixation or electrophoresis; **and/or** • Development of ≥ 5% plasma cells in the bone marrow; **and/or** • Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia). Relapse requires two consecutive assessments (by the same method) made at any time before classification as relapse, and/or the start of a new therapy.

Question 101: Specify the date of disease relapse or progression:
Enter the date the relapse or progression was established following the line of therapy. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathological evaluation. However, if there was

not a second assessment (where required) obtained prior to the start of new therapy, report the date the new therapy started as the date of relapse/progression. Continue with question 102.

Disease Status at the Time of Evaluation for this Reporting Period

NOTE:

Under normal circumstances, the marrow **aspirate** is used to obtain the differential cell count, review morphology of the cells, and to perform cytogenetic studies, flow cytometry, etc. The **biopsy** is obtained to evaluate the overall cellularity of the marrow. In the case of myeloma, the marrow plasma cells tend to be a patchy infiltrate rather than a diffuse infiltrate as in the case of acute leukemia. Therefore, it's possible that the plasma cell numbers may vary between the aspirate and biopsy.

The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may NOT be used as source documentation when reporting the data for questions 102-105.

If the bone marrow pathology report states a range for plasma cells, enter the average of the range rounded to the nearest whole number (e.g., if 0-5%, enter 3%).

If the report states > 90% plasma cells, enter 91% on the form.

If the report states a marrow packed with plasma cells or sheets of plasma cells, report 99% on the form.

If the report states < 5% plasma cells, enter 4% on the form.

Questions 102-103: Plasma cells in bone marrow aspirate:
Indicate if the percentage of plasma cells in the bone marrow **aspirate** was "known" or "unknown" at the time of evaluation for this reporting period. If "known," report the percentage of plasma cells in bone marrow **aspirate** documented on the pathology report in question 103. If "unknown," continue with question 104.

Questions 104-105: Plasma cells in bone marrow biopsy:
Indicate whether the percentage of plasma cells in the bone marrow **biopsy** was "known" or "unknown" at the time of evaluation for this reporting period. If "known," report the percentage of plasma cells in the bone marrow biopsy documented on the pathology report in question 105. If "unknown," continue with question 106.

Questions 106-107: Serum monoclonal protein (M-spike): (only from electrophoresis)
Monoclonal gammopathy is defined as the increased production of one type of immunoglobulin by a single clone of cells. The abnormal protein produced is called paraprotein or M-protein. Indicate whether the serum monoclonal immunoglobulin was "known" or "unknown" at the time of evaluation for this reporting period. If "known," report the value and unit of measure documented on the laboratory report in question 107. If "unknown" or "not applicable," continue with question 108.

"Not applicable" is appropriate for recipients with non-secretory myeloma.

Questions 108: Serum immunofixation:
Serum immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the blood. If "known" at the time of evaluation for this reporting period, continue with question 109. If "unknown" or "not applicable" continue with question 112.

"Not applicable" is appropriate for recipients with non-secretory myeloma.

Question 109: Specify monoclonal bands:
If monoclonal immunoglobulin was "present," continue with question 110. If "absent," continue with question 112.

Question 110: Original monoclonal bands:
Indicate "yes" if the original monoclonal band was present or "no" if it was not present.

Question 111: New monoclonal (or oligoclonal) bands:
Indicate "yes" if a new monoclonal band (or oligoclonal) was present or "no" if not present.

Questions 112-113: Total urinary protein excretion:
Indicate whether the amount of urinary protein was "known" or "unknown" at the time of evaluation for this reporting period. The value reported here should be based on a 24-hour urine collection. If "known," report the laboratory value in question 113. If "unknown" or "not applicable," continue with question 114.

NOTE: Urinary Monoclonal Protein
Questions 114-115 are intended to capture the 24-hour urine monoclonal protein results, not the 24-hour protein excretion (questions 112-113 capture the total protein secretion/24 hours). The results will be reported as XX g or XX g/dL. If the value is reported in XX g/dL, it can be multiplied by the volume of the urine to determine the 24-hour urine monoclonal protein.

For example:
(total in g/dL of monoclonal protein) x (total urine volume) = urinary M-protein/24 hours
(0.145 g/dL of monoclonal protein) x (1500 mL total urine) = 2.175 g/24 hours.
Do not report immunofixation results here.

Questions 114-115: Urinary monoclonal protein (M-spike):
Indicate whether the amount of urinary monoclonal protein was "known" or "unknown" at the time of evaluation for this reporting period. The value reported here should be based on a 24-hour urine collection. If "known," report the laboratory value in question 115 and continue with question 116. If "unknown" or "not applicable," continue with question 116.

"Not applicable" is appropriate for recipients with non-secretory myeloma.

Question 116: Urinary immunofixation:
Urine immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the urine. Indicate if the results of urinary immunofixation were "known" or "unknown" at the time of evaluation for the reporting period. If "known," continue with question 117. If "unknown" or "not applicable," continue with question 120.

"Not applicable" is appropriate for recipients with non-secretory myeloma.

Question 117: Specify monoclonal immunoglobulin result:
If monoclonal immunoglobulin was "present," continue with question 118. If "absent," continue with question 120.

Question 118: Original monoclonal bands:
Indicate "yes" if the original monoclonal band was present or "no" if it was not present.

Question 119: New monoclonal (or oligoclonal) bands:
Indicate "yes" if a new monoclonal (or oligoclonal) band was present or "no" if it was not present.

Questions 120-121: Serum free light chains – *κ* (kappa)
Indicate whether the serum *κ* (kappa) free light chain level was "known" or "unknown" at the time of evaluation for the reporting period. This value should reflect the quantity of serum **free** light chains, not a quantification of total light chains. If "known," report the value and unit of measure documented on the laboratory report in question 121. If "unknown" or "not applicable," continue with question 123.

Question 122: Upper limit of normal for *κ* free light chain:
Indicate the upper limit of normal for *κ* (kappa) free light chains value and unit of measure used at your institution.

Questions 123-124: Serum free light chain – *λ* (lambda)
Indicate whether the serum *λ* (lambda) free light chain level was "known" or "unknown" at the time of evaluation for the reporting period. This value should reflect the quantity of serum **free** light chains, not a quantification of total light chains. If "known," report the value and unit of measure documented on the laboratory report in question 124. If "unknown" or "not applicable," continue with question 126.

Question 125: Upper limit of normal for *λ* free light chain:
Indicate the upper limit of normal for *λ* (lambda) free light chains value and the unit of measure used at your institution.

Question 126: Was the disease status assessed by cytogenetic testing (conventional or FISH)?
Cytogenetic assessment involves testing blood or bone marrow for the presence of a known cytogenetic abnormality that reflects the recipient's disease. FISH is categorized with cytogenetics. Although often used for finding specific features in DNA, FISH is not as sensitive as molecular methods, even though the markers identified may be the same.

If a cytogenetic assessment was performed at the time of evaluation for this reporting period, select "yes" and continue with question 127.

If no cytogenetic assessments were performed, check "no" and continue with question 135.

Question 127: Was the disease status assessed via FISH?
FISH, fluorescence *in situ* hybridization, is a sensitive technique that assesses a large number of cells. This technique uses special probes that recognize and bind to fragments of DNA commonly found in plasma cell disorders. These probes are mixed with cells from the recipient's blood. A fluorescent "tag" is then used to visualize the binding of the probe to the diseased cells.

Indicate if FISH studies were obtained at the time of evaluation for this reporting period. If FISH studies were obtained, select "yes" and continue with question 128.

If no FISH studies were obtained, select "no"" and continue with question 131.

Question 128: Date assessed:
Enter the date of FISH assessment at the time of evaluation for the reporting period. Report the date the sample was collected for the laboratory.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Question 129: Was disease detected?
Indicate if evidence of disease was detected on the sample sent for FISH assessment. If FISH results were consistent with evidence of disease, check "yes" and continue with question 130.
If FISH results were not consistent with evidence of disease, check "no" and continue with question 131.

Question 130: Was the status considered a disease relapse or progression?
Indicate if the FISH abnormalities were considered to be relapsed or progressive disease. Criteria for cytogenetic relapse or progression are established by clinical judgment, and should reflect the clinical decision of the transplant physician. A recipient may be reported to have cytogenetic relapse or progression even in the setting of hematologic CR. Criteria for complete remission are based on hematologic (biochemical markers) and pathologic (marrow) characteristics and are independent of cytogenetic markers of disease.

If the recipient has FISH abnormalities that the physician considers to be consistent with cytogenetic relapse, check "yes" and continue with question 131.

If the recipient has FISH abnormalities that the physician does not consider to be consistent with molecular relapse, check "no" and continue with question 131.

Question 131: Was the disease status assessed via conventional cytogenetics?
Cytogenetics is the study of chromosomes. Cytogenetic assessment involves testing blood or bone marrow for the presence of a known chromosomal abnormality that reflects the recipient's disease. Cytogenetics may also be referred to as karyotyping or g-banding.

Indicate if cytogenetic studies were obtained at the time of evaluation for this reporting period. If cytogenetic studies were obtained, select "yes" and continue with question 132.

If no cytogenetic studies were obtained, select "no" and continue with question 135.

Question 132: Date assessed:
Enter the date of conventional cytogenetic assessment at the time of evaluation for this reporting period. Report the date the sample was collected for the laboratory.

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Question 133: Was disease detected?
Indicate if evidence of disease was detected on the sample sent for conventional cytogenetic assessment. If conventional cytogenetic results were consistent with evidence of disease, check “yes” and continue with question 134.

If conventional cytogenetic results were not consistent with evidence of disease, check “no” and continue with question 135.

Question 134: Was the status considered a disease relapse or progression?
Indicate if the conventional cytogenetic abnormalities were considered to be relapsed or progressive disease. Criteria for cytogenetic relapse or progression are established by clinical judgment, and should reflect the clinical decision of the transplant physician. A recipient may be reported to have cytogenetic relapse or progression even in the setting of hematologic CR. Criteria for complete remission are based on hematologic (biochemical markers) and pathologic (marrow) characteristics, and are independent of cytogenetic markers of disease.

If the recipient has conventional cytogenetic abnormalities that the physician considers to be consistent with cytogenetic relapse, select “yes” and continue with question 135.

If the recipient has conventional cytogenetic abnormalities that the physician does not consider to be consistent with molecular relapse, check “no” and continue with question 135.

Question 135: What is the disease status?
Report the disease status at the time of evaluation for this reporting period.

Table 14. Disease Status

Disease Status	Definition
Stringent Complete Remission (sCR)	Follow criteria for CR as defined below, **plus all of the following**: • Normal free light chain ratio, • Absence of clonal cells in the bone marrow by immunohistochemistry or immunofluorescence (confirmation with repeat bone marrow biopsy not needed). (Presence and/or absence of clonal cells is based upon the κ/λ ratio. An abnormal κ/λ ratio by immunohistochemistry and/or immunofluorescence requires a minimum of 100 plasma cells for analysis. An abnormal ratio reflecting the presence of an abnormal clone is κ/λ of > 4:1 or < 1:2.) sCR requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy sCR requirements.
Complete Remission (CR)	A treatment response where **all** of the following criteria are met: • Negative immunofixation on serum and urine samples • Disappearance of any soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) **NOTE: CR Requirements** For recipients with light chain only myeloma, **all** of the following criteria must be met: • Normal serum free light chain ratio • Negative immunofixation on urine samples • Disappearance of any soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) For recipients with non-secretory myeloma, **all** of the following criteria must be met: • Disappearance of all soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) CR requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy CR requirements.

Table 14. Disease Status *(cont.)*

Disease Status	Definition
Near Complete Remission (nCR)	A treatment where **all** of the following criteria met: • Serum and urine M-protein detectable by immunoelectrophoresis (immunofixation, IFE) but not on electrophoresis (SPEP and UPEP) • ≤ 5% plasma cells in bone marrow. nCR requires two consecutive assessments (by the same method) made at any time prior to the initiation of any new therapy and no known evidence of progressive or new bone lesions if radiographic studies were performed; radiographic studies are not required to satisfy nCR requirements.
Very Good Partial Response (VGPR)	**One or more** of the following must be present: • Serum and urine M-protein detectable by immunofixation but not on electrophoresis • ≥ 90% reduction in serum M-protein and urine M-protein level < 100 mg/24 hours. If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis): • Serum M-protein ≥ 1 g/dL • Urine M-protein ≥ 200 mg/24 hours; then a ≥ 90% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria. VGPR requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy VGPR requirements.

Table 14. Disease Status *(cont.)*

Disease Status	Definition
Partial Response (PR)	**Both** of the following must be present: • ≥ 50% reduction in serum M-protein • Reduction in 24-hour urinary M-protein by ≥ 90% or to < 200 mg/24 hours. If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria): • Serum M-protein ≥ 1 g/dL • Urine M-protein ≥ 200 mg/24 hours; then a ≥ 50% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria (provided the serum free light chain assay shows involved level > 10 mg/dL and the serum free light chain is abnormal). If serum and urine M-protein *and* serum-free light assay are not measurable, a ≥ 50% reduction in bone marrow plasma cells is required in place of M-protein, provided the baseline bone marrow plasma cell percentage was ≥ 30%. In addition to the above-listed criteria, a ≥ 50% reduction in the size of any soft tissue plasmacytomas that were present at baseline is also required.
Partial Response (PR) *(cont.)*	PR requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy PR requirements.
Stable Disease (SD)	Does not meet the criteria for CR, VGPR, PR, or PD. SD requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy SD requirements.

Table 14. Disease Status *(cont.)*

Disease Status	Definition
Progressive Disease (PD)	Requires **one or more** of the following: Increase of ≥ 25% from the lowest response value achieved in: • Serum M-component with an absolute increase ≥ 0.5 g/dL (for progressive disease, serum M-component increases of ≥ 1 g/dL are sufficient if the starting M-component is ≥ 5 g/dL); **and/or** • Urine M-component with an absolute increase ≥ 200 mg/24 hours; **and/or** • For recipients without measurable serum and urine M-protein levels, the difference between involved and uninvolved free light chain levels with an absolute increase > 10 mg/dL; **and/or** • Bone marrow plasma cell percentage with absolute percentage ≥ 10%; **and/or** • Definite development of new bone lesions or soft tissue plasmacytomas, or definite increase in the size of any existing bone lesions or soft tissue plasmacytomas; **and/or** • Development of hypercalcemia (corrected serum calcium > 11.5 mg/dL or 2.65 mmol) that can be attributed solely to the plasma cell proliferative disorder. PD requires two consecutive assessments (by the same method) made at any time before classification as disease progression, and/or the start of a new therapy.
Relapse from CR (untreated)	Requires **one or more** of the following: • Reappearance of serum or urine M-protein by immunofixation or electrophoresis; **and/or** • Development of ≥ 5% plasma cells in the bone marrow; **and/or** • Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia). Relapse requires two consecutive assessments (by the same method) made at any time before classification as relapse, and/or the start of a new therapy.

At any response level, if some but not all criteria met, the disease status should be downgraded to next lower level of response.

The percentage of plasma cells in the bone marrow aspirate and/or biopsy may also be identified on a flow cytometry report. A flow cytometry report may **NOT** be used to confirm CR (e.g., < 5% plasma cells in the bone marrow).

If the disease response prior to transplant is unknown, select "unknown" and continue with the signature lines.

If the recipient had amyloidosis, but no evidence of myeloma, select "Not Applicable (Amyloidosis with no evidence of myeloma)."

Question 136: Date assessed:
Enter the date of the most recent disease evaluation. Report the date the blood/urine was collected for the laboratory evaluations (e.g., SPEP/UPEP, serum/urine immunofixation) or report the date the bone marrow was collected for pathological evaluation. A PET scan may be used ***if*** a PET scan was previously obtained and ***only*** in limited circumstances (e.g., plasmacytomas, lytic lesions).

If the exact date is not known, use the process described for reporting partial or unknown dates in General Instructions, Guidelines for Completing Forms.

Current Status of Amyloidosis for this Reporting Period (for Amyloid Patients Only)

Complete questions 137-162 for Amyloid patients only. If diagnosis was other than amyloidosis or there is no history of it, continue with signature line.

Specify the recipient's current disease status for each of the following hematologic and organ systems:

Question 137: Specify the recipient's current hematologic status:
Indicate the recipient's current hematologic status at the time of evaluation for this reporting period.

Table 15. Hematologic Response

Disease Response	Description
Complete response (CR)	Requires **all** of the following: • Serum and urine negative for monoclonal proteins by immunofixation • Normal free light chain ratio • Plasma cells in marrow < 5%
Partial response (PR)	Requires **any** of the following: • ≥ 50% reduction in current serum monoclonal protein levels > 0.5 g/dL • ≥ 50% reduction in current urine light chain levels > 100 mg/day with a visible peak • ≥ 50% reduction in current free light chain levels > 10mg/dL
No response (NR)/stable disease (SD)	Does not meet the criteria for CR, PR, or progressive disease.
Progressive disease (PD)	Requires **any** of the following: • If progressing from CR, any detectable monoclonal protein or abnormal free light chain ratio (light chain must double) • If progressive from PR or SD, ≥ 50% increase in the serum M protein to > 0.5 g/dL, or ≥ 50% increase in urine M protein to > 200mg/day with visible peak present. • Free light chain increase of ≥ 50% to > 10 mg/dL (100 mg/L)

If the recipient's hematologic status was CR, PR, NR, or progressive disease, continue with question 138.

If the recipient's hematologic status was not assessed during the reporting period, select "not assessed" and continue with question 140. "Not applicable" should rarely, if ever, be chosen.

Questions 138-139: Date assessed:
Indicate if the date of hematologic assessment is "known" or "unknown." If the date of assessment for hematologic status is known, report the date in question 139. If the date is unknown, select "unknown" and continue with question 140.

Question 140: Specify the recipient's current cardiac status:
Indicate the recipient's current cardiac status at the time of evaluation for this reporting period.

Table 16. Cardiac Response

Disease Response	Description
Cardiac response	Requires **any** of the following: • ≥ 2 mm decrease in mean intraventricular septal wall thickness by echocardiogram • ≥ 20% increase in left ventricular ejection fraction • ≥ 2 grade decrease in New York Heart Association functional class without an increase in diuretic use and no increase in wall thickness • Reduction (≥ 30% and ≥ 300ng/L) of NT-proBNP in patients whom the eGFR is ≥ 45 ml/minute/1.73m^2
No response/stable disease	Does not meet the criteria for cardiac response or progressive disease
Progressive disease	Requires **any** of the following: • ≥ 2 mm increase from baseline in the intraventricular wall thickness by echocardiogram • ≥ 10% decrease in the left ventricular ejection fraction. • ≥ 1 grade increase in New York Heart Association functional class

If the recipient's cardiac status was not assessed during the reporting period, select "not assessed." If the recipient never had evidence of cardiac involvement in their disease, select "not applicable."

Table 17. New York Heart Association Function Classification

Class	Description
Class I	Able to perform ordinary activities without symptoms; no limitation of physical activity
Class II	Ordinary physical activity produces symptoms; slight limitation of physical activity
Class III	Less-than-ordinary physical activity produces symptoms; moderate limitation of physical activity
Class IV	Symptoms present even at rest; severe limitation of physical activity.

Questions 141-142: Date assessed:
Indicate if the date of cardiac assessment is "known" or "unknown." If the date of assessment for cardiac status is known, report the date in question 142. If the date is unknown, select "unknown" and continue with question 143.

Question 143: Was there clinical improvement in GI involvement since the date of last report?
Indicate if there was clinical improvement of GI involvement at the time of evaluation for this reporting period. Judgment is required by a clinician to determine if there is evidence of improvement. If "yes" or "no," continue with question 144. If "unknown," continue with question 146.

Questions 144-145: Date assessed:
Indicate if the date the GI involvement was assessed is "known" or "unknown." If the date the GI response was assessed is known, report the date in question 145. If the date is unknown, select "unknown" and continue with question 146.

Question 146: Specify the recipient's current hepatic status:
Indicate the recipient's current hepatic status at the time of evaluation for this reporting period.

Table 18. Hepatic Response

Disease Response	Description
Hepatic response	Requires **all** of the following: • ≥ 2 cm decrease in liver span if hepatomegaly present (liver > 15 cm) • ≥ 50% decrease and/or normalization of serum alkaline phosphatase (ALP) level
No response/stable disease	Does not meet the criteria for hepatic response or progressive disease
Progressive disease	Requires the following: • ≥ 50% increase in the serum alkaline phosphatase (ALP) level

If the recipient's hepatic status was not assessed during the reporting period, select "not assessed." If the recipient never had evidence of hepatic involvement in their disease, select "not applicable."

Questions 147-148: Date assessed:
Indicate if the date of hepatic assessment is "known" or "unknown." If the date of assessment for hepatic status is known, report the date in question 148. If the date is unknown, select "unknown" and continue with question 149.

Question 149: Specify the current status of autonomic neuropathy:
Indicate the recipient's current autonomic neuropathy status at the time of evaluation for this reporting period.

Table 19. Autonomic Neuropathy Response

Disease Response	Description
Autonomic neuropathy response	Resolution of symptomatic orthostatic hypotension
No response/stable disease	Does not meet the criteria for autonomic neuropathy response or progressive disease
Progressive disease	Worsening of symptomatic orthostatic hypotension

If the recipient's autonomic neuropathy was not assessed during the reporting period, select "not assessed." If the recipient never had evidence of disease related autonomic neuropathy, select "not applicable."

Questions 150-151: Date assessed:
Indicate if the date of autonomic neuropathy assessment is "known" or "unknown." If the date of assessment for autonomic neuropathy status is known, report the date in question 151. If the date is unknown, select "unknown" and continue with question 152.

Question 152: Specify the current status of peripheral neuropathy:
Indicate the recipient's current peripheral neuropathy status at the time of evaluation for this reporting period.

Table 20. Peripheral Neuropathy Response

Disease Response	Description
Peripheral neuropathy response	Requires **any** of the following: • Resolution of abnormal physical findings • Resolution or improvement of abnormal EMG and/or NCV findings
No response/stable disease	Does not meet the criteria for peripheral neuropathy response or progressive disease
Progressive disease	Requires **any** of the following: • Worsening of physical findings • Worsening of EMG and/or NCV findings

If the recipient's peripheral neuropathy was not assessed during the reporting period, select "not assessed." If the recipient never had evidence of disease related peripheral neuropathy, select "not applicable."

Questions 153-154: Date assessed:
Indicate if the date of autonomic neuropathy assessment is "known" or "unknown." If the date of assessment for autonomic neuropathy status is known, report the date in question 154. If the date is unknown, select "unknown" and continue with question 155.

Question 155: Specify the recipient's current renal status:
Indicate the recipient's current renal status at the time of evaluation for this reporting period.

Table 21. Renal Response

Disease Response	Description
Renal response	• ≥ 50% decrease of at least 0.5 g/day (500mg/24hr) in 24 urine protein of > 0.5 g/day (500mg/24hr) pre-treatment • Creatinine clearance must not have worsened by ≥ 25% over baseline
No response/stable disease	Does not meet the criteria for renal response or progressive disease
Progressive disease	Requires **any** of the following: • ≥ 50% increase of at least 1 g/day (1000mg/24hr) for urine protein to > 1g/day (1000mg/24hr) • 25% worsening of serum creatinine or creatinine clearance

If the recipient's renal status was not assessed during the reporting period, select "not assessed." If the recipient never had evidence of renal involvement in their disease, select "not applicable."

Questions 156-157: Date assessed:
Indicate if the date of hepatic assessment is "known" or "unknown." If the date of assessment for hepatic status is known, report the date in question 157. If the date is unknown, select "unknown" and continue with question 158.

Questions 158-159: Was any other system assessed for current status?
Indicate if any other system was assessed at the time of evaluation for the reporting period. If the recipient had other site involvement reported in questions 179-185 of the Pre-HCT Plasma Cell Disorder form (Form 2016) and that site was assessed, the status should be reported here.

Indicate the involved system/site in question 159.

Question 160: Specify the current status of this system:
Indicate if the recipient's current response is "response," "no response/stable disease," "progressive disease," or "not applicable."

Questions 161-162: Date assessed:
Indicate if the date the other site/system was assessed at the time of evaluation for the reporting period is “known” or “unknown.” If the other site/system response is known, report the date in question 162. If the date is unknown, select “unknown” and continue with the signature lines.

Signature Lines
The FormsNet3^{SM} application will automatically populate the signature data fields, including name and email address of person completing the form and date upon submission of the form.

Manual Change History

Version Number	Date of Change	Type of Change (Add / Remove / Modify)	Description of Change
2.1	11/21/2013	Modify	Changed "Form 2016" to "Form 2116" in document header
2.1	11/21/2013	Add	Added "(Revision 3)" to title of document
2.2	03/28/2014	Add	Added a Note to Question 3: *NOTE:* *Currently there is an issue on Form 2116 regarding the number of plasma cells required for CR. CR requires less than (but **not** equal to) 5 % plasma cells in the bone marrow.*
2.2	03/28/2014	Modify	Question 61 – modified text to read: *Indicate if the recipient received therapy post-transplant for any reason other than relapse or progressive disease since the date of last report. If "yes," continue with question 62. If "no" or "unknown," continue with question ~~102~~ 100.*
2.3	06/01/2014	Modify	Updated formatting to match CIBMTR brand standards
2.3	06/01/2014	Modify	Updated explanatory text in question 61 to read: *Do not include any treatment administered as a result of relapse or progression.* *For the purposes of this question, a line of therapy is one or more cycles of a defined treatment program given to a patient with no progression of disease in between. A new line of therapy may be started for reasons including drug toxicities, planned changes to medications, etc. ~~starts when a new agent is (or agents are) added/changed due to relapse, progression, and/or toxicity~~ If a drug dose was changed due to toxicity, do not report this as a new line of therapy; however, if a drug is stopped and a new one started due to toxicity, report this as a new line of therapy.*

Version Number	Date of Change	Type of Change (Add / Remove / Modify)	Description of Change
2.4	07/11/2014	Add	Added text to Multiple Myeloma Disease Reponse Criteria for VGPR: ***One or more*** *of the following must be present:* • *Serum and urine M-protein detectable by immunofixation but not on electrophoresis* • *≥ 90% reduction in serum M-protein and urine M-protein level < 100 mg/24 hours.* *If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria at time of diagnosis):* • *Serum M-protein ≥ 1 g/dL* • *Urine M-protein ≥ 200 mg/24 hours;* *then a ≥ 90% decrease in the difference between involved and uninvolved free light chain levels is required in place of the M-protein criteria.* *VGPR requires two consecutive assessments (by the same method) made at any time before the start of a new therapy. If radiographic studies were performed, there must be no known evidence of new or progressive bone lesions. Radiographic studies are not required to satisfy VGPR requirements.*