

Instructions for Multiple Myeloma / Plasma Cell Leukemia Post-HSCT Data (Form 2116)

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Multiple Myeloma / Plasma Cell Leukemia Post-HSCT 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 liaison.

TABLE OF CONTENTS

Key Fields	3
Disease Assessment at the Time of Best Response to HSCT	4
Laboratory Studies at the Time of Best Response to HSCT	12
Post-HSCT Treatment for Multiple Myeloma/Plasma Cell Leukemia	15
Disease Status at the Time of Evaluation for This Reporting Period.....	25

Multiple Myeloma / Plasma Cell Leukemia Post-HSCT Data

NOTE:

Many references are included from the “Clinical Research Professionals Data Management – Multiple Myeloma” presentation from February 23, 2010, at the BMT Tandem Meetings. This presentation is available at:

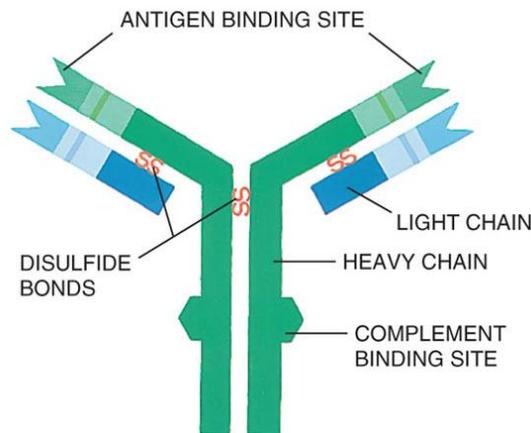
<http://www.cibmtr.org/Meetings/Materials/CRPDMC/Pages/fen10Hari.aspx>

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 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 Antibody



Secretory Multiple Myeloma:

Healthy plasma cells make immunoglobulins 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
<i>Source of monoclonal proteins</i>	
Serum monoclonal proteins	80%
Urine monoclonal proteins	75%
<i>Type of monoclonal proteins</i>	
IgG	50-54%
IgA	20%
Monoclonal light chain (light chain only disease)	20%
IgD	2%

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.

The Multiple Myeloma/Plasma Cell Leukemia (PCL) Post-HSCT Data Form is one of the Comprehensive Report Forms. This form captures multiple myeloma/PCL-specific post-HSCT data such as: 1) the recipient’s best response to HSCT, 2) laboratory studies at the time of best response, 3) planned treatments post-HSCT, and 4) disease status for the reporting period.

This form must be completed for all recipients whose primary disease, reported on Form 2000 question 9, is Multiple Myeloma/Plasma Cell Disorder. The Multiple Myeloma / PCL Post-HSCT Data (Form 2116) must be completed in conjunction with each Post-HSCT follow-up form (Forms 2100, 2200, and 2300) and capture specific data occurring within the timeframe of the reporting period of the follow-up form.

Key Fields

Accuracy of the Key Fields is essential for ensuring that:

- Data are being reported for the correct recipient.
- Transplant centers have access to their data.
- Data are being shared with the correct donor center, cord blood bank, cooperative registry, or other agency.

For instructions regarding the completion of the Key Fields, see [Appendix K](#). Key fields include all fields listed in the box found in the upper right-hand corner of the first page of the paper form, or on the “key page” in the FormsNet2™ application.

Disease Assessment at the Time of Best Response to HSCT

For multiple myeloma, the best response to HSCT includes the whole “therapy package.” For example, a myeloma patient was initially treated with lenalidomide/ dexamethasone for six cycles and achieved a partial response (PR). The patient then had high dose cyclophosphamide to mobilize PBSCs, followed by an autologous HSCT. In this case, use the labs obtained at diagnosis to determine the best response to HSCT. [Table 2](#) can be used to determine which values should be used to determine the best response to transplant. Identify the recipient’s best disease status within the reporting period, even if relapse or progression followed the best response. If the best response was achieved in a previous reporting period, report this response again and indicate that it was previously reported.

For more information regarding reporting best response, see [Appendix V](#) and [Appendix W](#).

Table 2. Determining Baseline Values to Evaluate Best Response to HSCT

Disease Course	Which values to use to evaluate best response
The HSCT was performed as part of initial therapy for a recipient with no disease progression at any time prior to HSCT	Diagnostic laboratory values
The HSCT was performed for a recipient with disease relapse or progression prior to HSCT and who was treated to reduce the myeloma burden prior to the start of the preparative regimen	Laboratory values obtained at time of last relapse or progression
The HSCT was performed for a recipient who has not received any chemotherapy within six months of HSCT or has untreated relapse or progression	Laboratory values obtained immediately prior to preparative regimen
The HSCT was performed as part of a planned tandem autologous transplant for a recipient with no disease progression at any time prior to the first HSCT or the second HSCT	Diagnostic laboratory values should be used to assess best response to transplant for both the first and second HSCT
The HSCT was performed after relapse or progression from a previous HSCT (this includes planned tandem transplants or unplanned second transplant)	Laboratory values obtained at time of last relapse or progression

NOTE:

The following sentence in the instruction box will be updated to reflect the correct baseline to use: “If the HSCT was performed later in the disease course for a recipient with disease relapse or progression at any time prior to HSCT (see Form 2016, question 131, option 2), determine best response by comparing to the disease status immediately prior to the start of the preparative regimen.”

The updated instructions will read as follows: “If the HSCT was performed later in the disease course (see Form 2016, question 131, option 2) for a patient who has not received any chemotherapy within 6 months of HSCT or has untreated relapse or progression, determine best response to HSCT by comparing to 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 HSCT (see Form 2016, question 131, option 2) and was treated to reduce the myeloma burden prior to the start of the preparative regimen, determine best response to HSCT by comparing to the disease status at the time of relapse or progression.” So, the baseline is reset to the time of relapse or progression.

Question 1: Compared to the disease status prior to the preparative regimen, what was the best response to HSCT since the date of last report?

The wording of this question can be misleading. The best response to HSCT is not necessarily determined based on the disease status prior to the start of the preparative regimen. The intent of this question is to determine the best overall response to HSCT, 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-HSCT 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 2 to indicate that this disease status was previously reported.

Table 3. Best Response Definitions

Best Response	Definition
Stringent Complete Remission (sCR)	<p>Follow criteria for CR as defined below, plus all of the following:</p> <ul style="list-style-type: none"> • 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 $< 1:2$.) <p>sCR requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy sCR requirements.</p>
Complete Remission (CR)	<p>A treatment response where all of the following criteria are met:</p> <ul style="list-style-type: none"> • 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) <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> <p style="text-align: center;">NOTE: CR Requirements</p> <p>For recipients with light chain only myeloma, all of the following criteria must be met:</p> <ul style="list-style-type: none"> • 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) <p>For recipients with non-secretory myeloma, all of the following criteria must be met:</p> <ul style="list-style-type: none"> • Disappearance of all soft tissue plasmacytomas • $< 5\%$ plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) </div>

<p>Complete Remission (CR) (cont.)</p>	<p>CR requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy CR requirements.</p>
<p>Very Good Partial Response (VGPR)</p>	<p>One or more of the following must be present:</p> <ul style="list-style-type: none"> • Serum and urine M-protein detectable by immunofixation but not on electrophoresis • $\geq 90\%$ reduction in serum M-protein and urine M-protein level < 100 mg/24 hours. <p>VGPR requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy VGPR requirements.</p>
<p>Partial Response (PR)</p>	<p>Both of the following must be present:</p> <ul style="list-style-type: none"> • $\geq 50\%$ reduction in serum M-protein • Reduction in 24-hour urinary M-protein by $\geq 90\%$ or to < 200 mg/24 hours. <p>If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria):</p> <ul style="list-style-type: none"> • Serum M-protein ≥ 1 g/dL, and • Urine M-protein ≥ 200 mg/24 hours; <p>then a $\geq 50\%$ 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 ratio is abnormal).</p> <p>If serum and urine M-protein <i>and</i> serum-free light assay are not measurable, a $\geq 50\%$ reduction in plasma cells is required in place of M-protein, provided the baseline bone marrow plasma cell percentage was $\geq 30\%$.</p> <p>In addition to the above listed criteria, a $\geq 50\%$ reduction in the size of soft tissue plasmacytomas is also required, if present at baseline.</p> <p>PR requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy PR requirements.</p>

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<p>Stable Disease (SD)</p>	<p>Does not meet the criteria for CR, VGPR, PR, or PD. SD requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy SD requirements.</p>
<p>Progressive Disease (PD)</p>	<p>Requires one or more of the following:</p> <p>Increase of $\geq 25\%$ from the lowest response value achieved in:</p> <ul style="list-style-type: none"> • 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 $\geq 10\%$; 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. <p>PD requires two consecutive assessments (of the same method) made at any time before classification as disease progression, and/or the institution of any new therapy.</p>
<p>Relapse from CR (untreated)</p>	<p>Requires one or more of the following:</p> <ul style="list-style-type: none"> • Reappearance of serum or urine M-protein by immunofixation or electrophoresis; and/or • Development of $\geq 5\%$ plasma cells in the bone marrow (relapse from CR has a 5% cutoff vs. 10% for other categories); and/or • Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia). <p>Relapse requires two consecutive assessments (of the same method) made at any time before classification as relapse, and/or the institution of any new therapy.</p>

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 VGPR 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 HSCT 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 To HSCT	Q2. Date the best response first began
Pre-transplant	PR	---	---
100-Days Post-HSCT	VGPR	VGPR	<i>[date of first confirmatory labs]</i>
6-Months Post-HSCT	Progression	VGPR	Previously reported
1-Year Post-HSCT	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 To HSCT	Q2. Date the best response first began
Pre-transplant	CR	---	---
100-Days Post-HSCT	CR	CR	<i>[date of labs that first confirmed a continued CR]</i>
6-Months Post-HSCT	Relapsed	CR	Previously reported
1-Year Post-HSCT	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 To HSCT	Q2. Date the best response first began
Pre-transplant	PR	---	---
100-Days Post-HSCT	PR	PR	[date of labs that first confirmed a continued PR]
6-Months Post-HSCT	Progression	PR	Previously reported
1-Year Post-HSCT	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 To HSCT	Q2. Date the best response first began
Pre-transplant	VGPR	---	---
100-Days Post-HSCT	VGPR	VGPR	[date of labs that first confirmed a continued VGPR]
6-Months Post-HSCT	CR	CR	[date of labs that first confirmed CR]
1-Year Post-HSCT	CR	CR	Previously reported

Include response to any post-HSCT 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 be considered “planned therapy;” however, bisphosphonate therapy administered post-HSCT will not be reported in question 20. **Do not include any treatment administered as a result of relapse or progression.**

Question 2: Specify the date the best response first began

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 exam.

If the best response is the same as the pre-transplant disease status, report the date of the first assessment that confirmed the ongoing disease status post-HSCT and continue with question 3.

If the date was reported in a prior period, check “date previously reported” and continue with question 20.

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 had been 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 was not available when completing the form. 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 was not available when completing the form. 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.

Laboratory Studies at the Time of Best Response to HSCT

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 3-5.
- 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.

Question 3: Plasma cells in bone marrow aspirate

If "known," report the percentage of plasma cells from bone marrow **aspirate** documented on the pathology report. Question 5 should then be answered "not known." If "not known," continue with question 4.

Question 4: Plasma cells in bone marrow biopsy

If "known," report the percentage of plasma cells from bone marrow **biopsy** documented on the pathology report. Question 5 should then be answered "not known." If "not known," continue with question 5.

Question 5: Plasma cells in bone marrow, sample source unknown

Question 5 is to be answered when it is unclear from the source documentation whether the sample source was the marrow aspirate or the marrow biopsy. If that is the case, then indicate "known," report the percentage of plasma cells as documented, and verify that questions 3-4 are answered "not known." If "not known," continue with question 6.

NOTE: Serum Monoclonal Ig

Question 6 is intended to capture the M-protein value identified on the serum electrophoresis (SPEP) at the time of best response post-HSCT.

Do not report immunofixation results here.

Sometimes the SPEP will report an M-protein is present, but cannot be quantified. In these cases, it should be reported as follows:

Question 6: "not known"

Question 7: "known"

Question 8: "present"

Question 9: "yes, original monoclonal bands"

NOTE: Oligoclonal Reconstitution

Oligoclonal reconstitution is the emergence of a new M-protein that was not present at diagnosis. The M-protein is identified on serum immunofixation and occurs during immune function recovery post transplant.

Example: A recipient was originally diagnosed with IgG kappa with a serum M-protein of 3.2 g/dL. In the 100-day reporting period post-transplant, the SPEP/SIFE reveals 0.14 g/dL (IgG kappa), nonquantifiable IgA lambda, and free lambda light chains. Report 0.14 g/dL (IgG) in Q6 and indicate "yes" to Q10 for the new monoclonal bands.

Question 6: Serum monoclonal Ig (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. If serum monoclonal Ig is "known," report the value and unit of measure documented on the laboratory report. If "not known" or "non-secretory," continue with question 7.

For recipients with biclonal myeloma, report the serum monoclonal Ig with the largest quantity.

Question 7: Serum immunofixation

Serum immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the blood. If "known," continue with question 8. If "not known," continue with question 11.

Question 8: Specify monoclonal immunoglobulin result

If monoclonal immunoglobulin is "present/positive," continue with question 9. If "absent/negative," continue with question 11.

Question 9: Original monoclonal bands

Indicate "yes" if the original monoclonal band was present or "no" if it was not present.

Question 10: New monoclonal bands

Indicate “yes” if a new monoclonal band was present or “no” if it was not present.

NOTE: Urinary Monoclonal Light Chains

Question 11 is intended to capture the 24-hour urine light chain results, not the 24-hour protein excretion at the time of best response post-HSCT. The results will be reported as XX g in 24-hour of kappa or lambda light chains, 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 light chains.

For example:

(total in g/dL of the light chain) x (total urine volume) = urinary monoclonal light chains/24 hours
(0.145 g/dL of lambda light chains) x (1500 mL total urine) = 2.175 g/24 hours

Do not report immunofixation results here.

Sometimes the UPEP will report that an M-protein is present but cannot be quantified. In these cases, it should be reported as follows:

Question 11: “not known”

Question 12: “known”

Question 13: “present”

Question 14: “original monoclonal bands”

NOTE: Oligoclonal Reconstitution

Oligoclonal reconstitution is the emergence of a new M-protein that was not present at diagnosis. The M-protein is identified on urine immunofixation and occurs during immune function recovery post transplant.

Example: A recipient was originally diagnosed with IgG kappa with a serum M-protein of 4.6 g/dL and a urine M-protein of .36 g/24 hr. In the 100-day reporting period post-transplant, the SPEP/SIFE reveals no M-protein and the immunofixation is negative. The UPEP/UIFE reveals 0.1 g/24 hr (IgG kappa) and nonquantifiable IgA lambda. Report 0.1 g/24 hr (IgG) in Q11 and indicate “yes” to Q15 for the new monoclonal bands.

Question 11: Urinary monoclonal light chains

The value reported here should be based on a 24-hour urine collection. If “known,” report the urinary monoclonal light chains value. If “not known,” continue with question 12.

Question 12: Urinary immunofixation

Urine immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the urine. If “known,” continue with question 13. If “not known,” continue with question 16.

Question 13: Specify monoclonal immunoglobulin result

If monoclonal immunoglobulin is “present/positive,” continue with question 14. If “absent/negative,” 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 bands

Indicate “yes” if a new monoclonal band was present or “no” if it was not present.

Question 16: Serum free light chains – κ (kappa)

If “known,” report the serum free light chains – κ (kappa) value and unit of measure documented on the laboratory report. If “not known,” continue with question 18.

Question 17: Upper limit of normal for κ free light chain

Report the upper limit of normal for κ (kappa) free light chains value and unit of measure documented on the laboratory report (it may or may not be from “your institution”).

Question 18: Serum free light chains – λ (lambda)

If “known,” report the serum free light chains – λ (lambda) value and unit of measure documented on the laboratory report. If “not known,” continue with question 20.

Question 19: Upper limit of normal for λ free light chain

Report the upper limit of normal for λ (lambda) free light chains value and unit of measure documented on the laboratory report (it may or may not be from “your institution”).

Post-HSCT Treatment for Multiple Myeloma / Plasma Cell Leukemia

NOTE: Paper forms submission

When submitting the paper version of the form for more than two lines of therapy, copy the “Post-HSCT Treatment for Multiple Myeloma / Plasma Cell Leukemia” section to report the additional lines of therapy administered. Check the “additional pages” box after question 91/129. The FormsNet2™ application allows for multiple lines of therapy to be reported. Complete a “Line of Therapy” section for each planned line of therapy administered in the reporting period.

Question 20: Was planned treatment per protocol given since the date of the last report? (Include any maintenance therapy, but exclude any treatment given for relapse or progressive disease.)

Indicate if the recipient received planned treatment post-HSCT since the date of last report. If “yes,” continue with question 21. If “no” or “unknown,” continue with question 83.

Recipients are generally transplanted under a specific protocol that defines the radiation and/or systemic therapy the recipient is intended to receive as a preparative regimen prior to the HSCT; infection and GVHD prophylaxis to be administered pre- and/or post-HSCT; and any systemic therapy, radiation, and/or other treatments to be administered post-HSCT as planned (or maintenance) therapy. Planned (maintenance or consolidation) therapy is given to assist in prolonging 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.

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 starts when a new agent is (or agents are) added/changed due to relapse, progression, and/or toxicity.

Example A: 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 lenalidomide therapy at 15 mg/day. However, during the one-year reporting period, the dose was reduced to 10 mg/day due to toxicity. This would be reported as two lines of therapy.

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 20-51.

Question 21 or 52: 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 22 or 53. If “no,” continue with question 45 or 76.

Question 22 or 53: Date therapy started

Enter the date the recipient began this line of therapy. If the start date was reported on a previous report, report the same date again when the start/stop dates overlap reporting periods.

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 23 or 54: Date therapy stopped

If the recipient is receiving therapy administered in cycles, report the date the recipient started the last cycle for this line of therapy.

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 23 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](#).

Question 24 or 55: 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. Report the number of cycles the recipient received during the line of therapy being reported, or check "unknown/not applicable."

Questions 25-44 or 56-75: Treatment

Chemotherapy 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 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 44 or 75. Report the generic name of the agent, not the brand name.

Question 45 or 76: Radiation Therapy

Radiation therapy utilizes 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-HSCT. If "yes," continue with question 46 or 77. If "no," continue with question 48 or 79.

Question 46 or 77: Date therapy started

Enter the date the line of radiation therapy began.

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 47 or 78: Date therapy stopped

Enter the date the line of radiation therapy ended.

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 48 or 79: 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 establish best response, see [Appendix V](#) and [Appendix W](#).

Table 4. Best Response Definitions

Best Response	Definition
Stringent Complete Remission (sCR)	<p>Follow criteria for CR as defined below, plus all of the following:</p> <ul style="list-style-type: none"> • 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 $< 1:2$.) <p>sCR requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy sCR requirements.</p>
Complete Remission (CR)	<p>A treatment response where all of the following criteria are met:</p> <ul style="list-style-type: none"> • 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)

<p>Complete Remission (CR) (cont.)</p>	<p style="text-align: center;">NOTE: CR Requirements</p> <p>For recipients with light chain only myeloma, all of the following criteria must be met:</p> <ul style="list-style-type: none"> • 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) <p>For recipients with non-secretory myeloma, all of the following criteria must be met:</p> <ul style="list-style-type: none"> • Disappearance of all soft tissue plasmacytomas • < 5% plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) <p>CR requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy CR requirements.</p>
<p>Very Good Partial Response (VGPR)</p>	<p>One or more of the following must be present:</p> <ul style="list-style-type: none"> • 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. <p>VGPR requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy VGPR requirements.</p>
<p>Partial Response (PR)</p>	<p>Both of the following must be present:</p> <ul style="list-style-type: none"> • ≥ 50% reduction in serum M-protein • Reduction in 24-hour urinary M-protein by ≥ 90% or to < 200 mg/24 hours.

<p>Partial Response (PR) (cont.)</p>	<p>If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria):</p> <ul style="list-style-type: none"> • Serum M-protein ≥ 1 g/dL, and • Urine M-protein ≥ 200 mg/24 hours; <p>then a $\geq 50\%$ 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 ratio is abnormal).</p> <p>If serum and urine M-protein and serum-free light assay are not measurable, a $\geq 50\%$ reduction in plasma cells is required in place of M-protein, provided the baseline bone marrow plasma cell percentage was $\geq 30\%$.</p> <p>In addition to the above listed criteria, a $\geq 50\%$ reduction in the size of soft tissue plasmacytomas is also required, if present at baseline.</p> <p>PR requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy PR requirements.</p>
<p>Stable Disease (SD)</p>	<p>Does not meet the criteria for CR, VGPR, PR, or PD.</p> <p>SD requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy SD requirements.</p>
<p>Progressive Disease (PD)</p>	<p>Requires one or more of the following:</p> <p>Increase of $\geq 25\%$ from the lowest response value achieved in:</p> <ul style="list-style-type: none"> • 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

<p>Progressive Disease (PD) (cont.)</p>	<ul style="list-style-type: none"> • Bone marrow plasma cell percentage with absolute percentage $\geq 10\%$; 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. <p>PD requires two consecutive assessments (of the same method) made at any time before classification as disease progression, and/or the institution of any new therapy.</p>
<p>Relapse from CR (untreated)</p>	<p>Requires one or more of the following:</p> <ul style="list-style-type: none"> • Reappearance of serum or urine M-protein by immunofixation or electrophoresis; and/or • Development of $\geq 5\%$ plasma cells in the bone marrow (relapse from CR has a 5% cutoff vs. 10% for other categories); and/or • Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia). <p>Relapse requires two consecutive assessments (of the same method) made at any time before classification as relapse, and/or the institution of any new therapy.</p>

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).

Question 49 or 80: Date response established

Any response requires two consecutive assessments (of the same labs) made at any time before the institution of any 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 and 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.

For more information on determining the date best response was established, see [Appendix W](#).

Question 50 or 81: Did patient 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 51 or 82. Documentation of relapse or progression requires two consecutive assessments (of the same labs) made at any time before classification as relapse or progression, **and/or** the institution of any new therapy. Indicate “no” if the recipient did not relapse or progress following this line of therapy and continue with question 52 or 83.

Table 5. Relapse/Progression Definition

Disease Status	Definition
Progression	<p>Requires one or more of the following:</p> <p>Increase of $\geq 25\%$ from the lowest response value achieved in:</p> <ul style="list-style-type: none"> • Serum M-component with an absolute increase ≥ 0.5 g/dL (for progressive disease, serum M-component increases of ≥ 1 g/dL are sufficient to define relapse 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 $\geq 10\%$; 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. <p>PR requires two consecutive assessments (of the same method) made at any time before classification as disease progression, and/or the institution of any new therapy.</p>

<p>Relapse from CR</p>	<p>Requires one or more of the following:</p> <ul style="list-style-type: none"> • Reappearance of serum or urine M-protein by immunofixation or electrophoresis; and/or • Development of $\geq 5\%$ plasma cells in the bone marrow (relapse from CR has a 5% cutoff vs. 10% for other categories); and/or • Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia) <p>Relapse requires two consecutive assessments (of the same method) made at any time before classification as relapse, and/or the institution of any new therapy.</p>
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Question 51 or 82: 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 obtained prior to the start of new therapy, report the date the new therapy started as the date of relapse/progression. Continue with question 52 or 83.

If more than two lines of therapy were administered post-HSCT, continue reporting each line as described at the beginning of this section. Continue to question 83 when all lines of therapy have been reported.

NOTE:

It is possible that the relapse or progression would be reported twice if already reported in question 50. Question 50 is asking about relapse or progression following any planned/maintenance therapy. Question 83 is asking about relapse or progression at any time, regardless of whether therapy was given or not.

Question 83: Has the disease relapsed or progressed since the date of the last report?

Indicate “yes” if a relapse or progression occurred since the date of the last report. Documentation of relapse or progression requires two consecutive assessments (of the same method) made at any time before classification as relapse or progression, **and/or** the institution of any new therapy. Indicate “no” if the recipient did not relapse or progress since the date of the last report and continue with question 85.

Table 6. Relapse/Progression Definition

Disease Status	Definition
Progression	<p>Requires one or more of the following:</p> <p>Increase of $\geq 25\%$ from the lowest response value achieved in:</p> <ul style="list-style-type: none"> • Serum M-component with an absolute increase ≥ 0.5 g/dL (for progressive disease, serum M-component increases of ≥ 1 g/dL are sufficient to define relapse 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 $\geq 10\%$; 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. <p>PR requires two consecutive assessments (of the same method) made at any time before classification as disease progression, and/or the institution of any new therapy.</p>
Relapse from CR	<p>Requires one or more of the following:</p> <ul style="list-style-type: none"> • Reappearance of serum or urine M-protein by immunofixation or electrophoresis; and/or • Development of $\geq 5\%$ plasma cells in the bone marrow (relapse from CR has a 5% cutoff vs. 10% for other categories); and/or • Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia) <p>Relapse requires two consecutive assessments (of the same method) made at any time before classification as relapse, and/or the institution of any new therapy.</p>

Question 84: Specify the date of disease relapse or progression

Enter the date the relapse or progression was established since the date of the last report. 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 obtained prior to the start of new therapy, report the date the new therapy started as the date of relapse/progression.

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 85-87.
- 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.

Question 85: Plasma cells in bone marrow aspirate

If "known," report the percentage of plasma cells in bone marrow **aspirate** documented on the pathology report. Question 87 should then be answered "not known." If "not known," continue with question 86.

Question 86: Plasma cells in bone marrow biopsy

If "known," report the percentage of plasma cells in bone marrow **biopsy** documented on the pathology report. Question 87 should then be answered "not known." If "not known," continue with question 87.

Question 87: Plasma cells in bone marrow, sample source unknown

Question 87 is to be answered when it is unclear from the source documentation that the sample source was either the marrow aspirate or the marrow biopsy. If that is the case, then indicate “known” and report the percentage of plasma cells as documented; and verify that questions 85-86 are answered “not known.” If “not known,” continue with question 88.

NOTE: Serum Monoclonal Ig

Question 88 is intended to capture the M-protein value identified on the serum electrophoresis (SPEP) at the time of evaluation for this reporting period.

Do not report immunofixation results here.

Sometimes the SPEP will report an M-protein is present, but cannot be quantified. In these cases, it should be reported as follows:

Question 88: “not known”

Question 89: “known”

Question 90: “present”

Question 91: “yes, original monoclonal bands”

NOTE: Oligoclonal Reconstitution

Oligoclonal reconstitution is the emergence of a new M-protein that was not present at diagnosis. The M-protein is identified on serum immunofixation and occurs during immune function recovery post-transplant.

Example: A recipient was originally diagnosed with IgG kappa with a serum M-protein of 3.2 g/dL. In the 100-day reporting period post-transplant, the SPEP/SIFE reveals 0.14 g/dL (IgG kappa), nonquantifiable IgA lambda, and free lambda light chains. Report 0.14 g/dL (IgG) in Q88 and indicate “yes” to Q92 for the new monoclonal bands.

Question 88: Serum monoclonal Ig (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. If “known,” report the value and unit of measure documented on the laboratory report. If “not known” or “non-secretory,” continue with question 89.

For recipients with biclonal myeloma, report the serum monoclonal Ig with the largest quantity.

Question 89: Serum immunofixation

Serum immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the blood. If “known,” continue with question 90. If “not known,” continue with question 93.

Question 90: Specify monoclonal immunoglobulin result

If monoclonal immunoglobulin is “present/positive,” continue with question 91. If “absent/negative,” continue with question 93.

Question 91: Original monoclonal bands

Indicate “yes” if the original monoclonal band was present or “no” if it was not present.

Question 92: New monoclonal bands

Indicate “yes” if a new monoclonal band was present or “no” if it was not present.

NOTE: Urinary Monoclonal Light Chains

Question 93 is intended to capture the 24-hour urine light chain results, not the 24-hour protein excretion, at the time of best response post-HSCT. The results will be reported as XX g in 24-hour of kappa or lambda light chains, 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 light chains.

For example: (total in g/dL of the light chain) x (total urine volume) = urinary monoclonal light chains/24 hours
(0.145 g/dL of lambda light chains) x (1500 mL total urine) = 2.175 g/24 hours

Do not report immunofixation results here.

Sometimes the UPEP will report that an M-protein is present but cannot be quantified. In these cases, it should be reported as follows:

Question 93: “not known”

Question 94: “known”

Question 95: “present”

Question 96: “yes, original monoclonal bands”

NOTE: Oligoclonal Reconstitution

Oligoclonal reconstitution is the emergence of a new M-protein that was not present at diagnosis. The M-protein is identified on urine immunofixation and occurs during immune function recovery post-transplant.

Example: A recipient was originally diagnosed with IgG kappa with a serum M-protein of 4.6 g/dL and a urine M-protein of .36 g/24 hr. In the 100-day reporting period post-transplant, the SPEP/SIFE reveals no M-protein and the immunofixation is negative. The UPEP/UIFE reveals 0.1 g/24 hr (IgG kappa) and nonquantifiable IgA lambda. Report 0.1 g/24 hr (IgG) in Q93 and indicate “yes” to Q97 for the new monoclonal bands.

Question 93: Urinary monoclonal light chains

The value reported here should be based on a 24-hour urine collection. If “known,” report the urinary monoclonal light chains value. If “not known,” continue with question 94.

Question 94: Urinary immunofixation

Urine immunofixation is a laboratory technique that detects and types monoclonal antibodies or immunoglobulins in the urine. If “known,” continue with question 95. If “not known,” continue with question 98.

Question 95: Specify monoclonal immunoglobulin result

If monoclonal immunoglobulin is “present/positive,” continue with question 96. If “absent/negative,” continue with question 98.

Question 96: Original monoclonal bands

Indicate “yes” if the original monoclonal band was present or “no” if it was not present.

Question 97: New monoclonal bands

Indicate “yes” if a new monoclonal band was present or “no” if it was not present.

Question 98: Serum free light chains – κ (kappa)

If “known,” report the serum free light chains – κ (kappa) value and unit of measure documented on the laboratory report. If “not known,” continue with question 100.

Question 99: Upper limit of normal for κ free light chain

Report the upper limit of normal for κ (kappa) free light chains value and unit of measure documented on the laboratory report (it may or may not be from “your institution”).

Question 100: Serum free light chains – λ (lambda)

If “known,” report the serum free light chains - λ (lambda) value and unit of measure documented on the laboratory report. If “not known,” continue with question 102.

Question 101: Upper limit of normal for λ free light chain

Report the upper limit of normal for λ (lambda) free light chains value and unit of measure documented on the laboratory report (it may or may not be from “your institution”).

Question 102: What is the current disease status?

Indicate whether the current disease status of multiple myeloma or PCL is in “complete remission” or “not in complete remission” based on the most recent assessment during this reporting period. The only response codes that are included in “complete remission” are stringent complete remission (sCR) or complete remission (CR).

Table 7. Disease Status Definition

Disease Status	Definition
Stringent Complete Remission (sCR)	<p>Follow criteria for CR as defined below, plus all of the following:</p> <ul style="list-style-type: none"> • 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 $< 1:2$.) <p>sCR requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy sCR requirements.</p>
Complete Remission (CR)	<p>A treatment response where all of the following criteria are met:</p> <ul style="list-style-type: none"> • 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) <div style="border: 1px solid black; padding: 5px; margin: 10px 0;"> <p style="text-align: center;">NOTE: CR Requirements</p> <p>For recipients with light chain only myeloma, all of the following criteria must be met:</p> <ul style="list-style-type: none"> • 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) <p>For recipients with non-secretory myeloma, all of the following criteria must be met:</p> <ul style="list-style-type: none"> • Disappearance of all soft tissue plasmacytomas • $< 5\%$ plasma cells in the bone marrow (confirmation with repeat bone marrow biopsy not needed) </div> <p>CR requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy CR requirements.</p>

<p>Very Good Partial Response (VGPR)</p>	<p>One or more of the following must be present:</p> <ul style="list-style-type: none"> • Serum and urine M-protein detectable by immunofixation but not on electrophoresis • $\geq 90\%$ reduction in serum M-protein and urine M-protein level < 100 mg/24 hours. <p>VGPR requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy VGPR requirements.</p>
<p>Partial Response (PR)</p>	<p>Both of the following must be present:</p> <ul style="list-style-type: none"> • $\geq 50\%$ reduction in serum M-protein • Reduction in 24-hour urinary M-protein by $\geq 90\%$ or to < 200 mg/24 hours. <p>If the serum and urine M-protein are not measurable (i.e., do not meet the following criteria):</p> <ul style="list-style-type: none"> • Serum M-protein ≥ 1 g/dL, and • Urine M-protein ≥ 200 mg/24 hours; <p>then a $\geq 50\%$ 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 ratio is abnormal).</p> <p>If serum and urine M-protein <i>and</i> serum-free light assay are not measurable, a $\geq 50\%$ reduction in plasma cells is required in place of M-protein, provided the baseline bone marrow plasma cell percentage was $\geq 30\%$.</p> <p>In addition to the above listed criteria, a $\geq 50\%$ reduction in the size of soft tissue plasmacytomas is also required, if present at baseline.</p> <p>PR requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy PR requirements.</p>
<p>Stable Disease (SD)</p>	<p>Does not meet the criteria for CR, VGPR, PR, or PD.</p> <p>SD requires two consecutive assessments (of 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 progressive or new bone lesions. Radiographic studies are not required to satisfy SD requirements.</p>

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<p>Progressive Disease (PD)</p>	<p>Requires one or more of the following: Increase of $\geq 25\%$ from the lowest response value achieved in:</p> <ul style="list-style-type: none"> • 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 has an absolute increase > 10 mg/dL; and/or • Bone marrow plasma cell percentage with absolute percentage $\geq 10\%$; 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. <p>PD requires two consecutive assessments (of the same method) made at any time before classification as disease progression, and/or the institution of any new therapy.</p>
<p>Relapse from CR (untreated)</p>	<p>Requires one or more of the following:</p> <ul style="list-style-type: none"> • Reappearance of serum or urine M-protein by immunofixation or electrophoresis; and/or • Development of $\geq 5\%$ plasma cells in the bone marrow (relapse from CR has a 5% cutoff vs. 10% for other categories); and/or • Appearance of any other sign of progression (e.g., new plasmacytoma, lytic bone lesion, hypercalcemia). <p>Relapse requires two consecutive assessments (of the same method) made at any time before classification as relapse, and/or the institution of any new therapy.</p>

At any response level if some but not all criteria met, the current 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).

Question 103: Date the current disease status was established in this reporting period

Enter the date of the most recent assessment of disease status during this reporting period. 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 previous PET scan had been 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](#).

Question 104: Signed

The person completing the form must sign the form, print his/her name, and provide a phone number, fax number, and e-mail address where he/she can be reached.