



**CIBMTR**<sup>®</sup>

CENTER FOR INTERNATIONAL BLOOD  
& MARROW TRANSPLANT RESEARCH

**Instructions for Waldenström’s  
Macroglobulinemia/Lymphoplasmacytic Lymphoma (MAC)  
Pre-HCT Data (Form 2019)**

This section of the CIBMTR Forms Instruction Manual is intended to be a resource for completing the Waldenström’s Macroglobulinemia and Lymphoplasmacytic Lymphoma Pre-HCT Form.

E-mail comments regarding the content of the CIBMTR Forms Instruction Manual to: [CIBMTRFormsManualComments@nmdp.org](mailto: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.

**TABLE OF CONTENTS**

Key Fields .....	2
Subsequent Transplant .....	3
Disease Assessment at Diagnosis .....	3
Clinical Features Present at Diagnosis .....	4
Laboratory Studies at Diagnosis .....	5
Pre-HCT Therapy .....	10
Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen .....	14
Disease Status at Last Evaluation Prior to the Preparative Regimen .....	17

**Waldenström’s Macroglobulinemia &  
Lymphoplasmacytic Lymphoma Pre-HCT Data**

Lymphoplasmacytic lymphoma (LPL) and subtype Waldenström’s macroglobulinemia (WM) are specific presentations of Non-Hodgkin lymphoma that are characterized by abnormal cellular populations containing small B-cells, plasma cells, and plasmacytoid lymphocytes. Additional hallmarks of Waldenström’s macroglobulinemia are bone marrow involvement (which may be present in lymphoplasmacytic lymphoma) and IgM paraprotein. Patients typically present with symptoms associated with anemia, such as weakness and fatigue. Workup often reveals normocytic, normochromatic anemia. Additional findings

© 2013 National Marrow Donor Program<sup>®</sup> and The Medical College of Wisconsin

may include IgM paraprotein, clinical hyperviscosity syndrome, and neuropathy. LPL will generally involve the bone marrow and, in some cases, the lymph nodes and other extranodal sites. A significant number of patients with WM will also have organomegaly and adenopathy. Advanced age, decreased performance status, anemia, and elevated  $\beta_2$  microglobulin have been associated with poorer outcomes, though there is no validated staging system to establish prognosis.

The Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma Pre-HCT Data Form is one of the Comprehensive Report Forms. This form captures WM/LPL-specific pre-HCT data such as: the recipient's clinical and genetic findings at the time of diagnosis and prior to the start of the preparative regimen, pre-HCT treatments administered, and disease manifestations prior to the preparative regimen.

This form must be completed for all recipients randomized to the Comprehensive Report Form (CRF) track whose primary disease is reported on Form 2400, question 357 as Non-Hodgkin lymphoma and question 583 as Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma.

World Health Organization. (2008). *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues* (4<sup>th</sup> ed.). Lyon, France.

## 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<sup>SM</sup> 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.

## Subsequent Transplant

If this is a report of a second or subsequent transplant for the same disease subtype and if this baseline disease insert was not completed for the previous transplant (e.g., patient was on TED track for the prior HCT, prior HCT was autologous with no consent, etc.), begin at question 1.

If this is a report of a second or subsequent transplant for a different disease (e.g., patient was previously transplanted for a disease other than WM/LPL), begin at question 1.

If this is a report of a second or subsequent transplant for the same disease and this baseline disease insert was completed previously, check yes and continue with the next question.

For the next question, indicate if this form is being completed for a relapse or a progression of the same disease. If "yes," continue with question 76; if "no," continue with question 121.

## Disease Assessment at Diagnosis

### Question 1: What is the diagnosis?

Waldenström's macroglobulinemia (WM) and lymphoplasmacytic lymphoma (LPL) are two closely related neoplasms. They are both characterized by an abnormal population of small B-cells, lymphoplasmacytoid cells, and plasma cells. WM is characterized by an IgM paraprotein and bone marrow involvement, whereas these two features may be absent in LPL.<sup>1</sup>

Indicate if the patient was diagnosed with WM or LPL.

<sup>1</sup>World Health Organization. (2008). *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues* (4<sup>th</sup> ed.). Lyon, France.

### Question 2: What was the date of diagnosis?

Report the date of the first pathological diagnosis (e.g., bone marrow biopsy) of WM or LPL. Enter the date the sample was collected for examination. If the diagnosis was determined at an outside center and no documentation of a pathological or laboratory assessment is available, the dictated date of diagnosis within a physician note may be reported. Do not report the date symptoms first appeared. The date of diagnosis is important because the interval between diagnosis and HCT is often a significant indicator for the recipient's prognosis post-HCT.

If the exact pathological diagnosis date is not known, use the process for reporting partial or unknown dates as described in General Instructions, [Guidelines for Completing Forms](#).

## Clinical Features Present at Diagnosis

### Question 3: Was peripheral neuropathy present?

Peripheral neuropathy often starts as tingling or burning in the distal extremities, and may progress to extremity numbness and weakness. The etiology of peripheral neuropathy in WM/LPL is not well understood in the absence of associated autoimmunity (such as cold agglutinin disease). Indicate if the patient reported peripheral neuropathy at diagnosis.

### Questions 4-5: Did the recipient have known nodal involvement?

The majority of patients with WM or LPL will have bone marrow and, in some cases, lymph nodes involved by disease. Indicate if the patient had known nodal involvement at diagnosis. If "yes," continue with question 5 and specify the size of the largest nodal mass. If "no," continue with question 6.

### Question 6: Was there any known extranodal or splenic involvement?

Additional sites of extranodal disease (e.g., splenomegaly, hepatomegaly, etc.) have been noted in the literature, especially in more advanced disease stages. Indicate if the patient had any known extranodal or splenic involvement at diagnosis. If "yes," continue with question 7. If "no" or "unknown," continue with question 15.

### Questions 7-14: Specify the site(s) of involvement

Indicate "yes" or "no" for each site specified in questions 7-13. Do not leave any response blank. If "yes" is indicated for "other site," specify the site in question 14. If extranodal or splenic involvement was indicated in question 6, at least one of the questions 7-13 must be answered "yes."

### Question 15: Were systemic symptoms (B symptoms) present?

Systemic or constitutional symptoms, often referred to as B symptoms, include fevers, drenching night sweats, and unintentional weight loss. Indicate if the patient reported B symptoms at diagnosis.

### Question 16: Was clinical hyperviscosity syndrome present?

The clinical signs and symptoms of hyperviscosity syndrome include skin and mucosal bleeding, dizziness, retinopathy with visual disturbance, fatigue, and neurological dysfunction. Ophthalmologic examination often reveals characteristic venous engorgement of the retina. Indicate if hyperviscosity syndrome was clinically present at the time of diagnosis. If "yes," continue with question 17. If "no" or "unknown," continue with question 23.

**Questions 17-22: Specify clinical symptoms present at diagnosis**

Indicate “yes,” “no,” or “unknown” for each clinical symptom specified in questions 17-21. If clinical hyperviscosity syndrome was present (question 16), at least one of the questions 17-21 must be answered “yes.” If “yes” is indicated for “other,” specify clinical symptom in question 22.

**Question 23: Was plasmapheresis or plasma exchange required?**

Elevation of IgM paraprotein is associated with hyperviscosity. In an acute setting, plasmapheresis or plasma exchange may be used to rapidly reduce IgM paraprotein levels. Indicate if the patient required plasmapheresis or plasma exchange at diagnosis.

**Laboratory Studies at Diagnosis**

Report findings at the time of diagnosis. If multiple studies were performed prior to beginning therapy, report the latest values prior to the start of treatment.

**Questions 24-25: Absolute lymphocyte count**

Indicate whether the lymphocyte count was “known” or “unknown” at the time of WM or LPL diagnosis. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 25. If “unknown,” continue with question 26.

**Questions 26-27: Hemoglobin**

Indicate whether the hemoglobin was “known” or “unknown” at the time of WM or LPL diagnosis. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 27. If “unknown,” continue with question 28.

**Questions 28-29: Platelets**

Indicate whether the platelet count was “known” or “unknown” at the time of WM or LPL diagnosis. If “known,” report the laboratory count and unit of measure documented on the laboratory report in question 29. If “unknown,” continue with question 30.

**Questions 30-31: Bone marrow aspirate (examined for histologic involvement)**

Indicate whether the extent of histologic involvement in the bone marrow aspirate was “known” or “unknown” at the time of diagnosis. If bone marrow aspirate was not examined, report “not applicable.” If “known,” report the extent of aspirate histologic involvement in question 31. If “unknown” or “not applicable,” continue with question 32.

**Questions 32-33: Bone marrow biopsy (examined for histologic involvement)**

Indicate whether the extent of histologic involvement in the bone marrow biopsy was “known” or “unknown” at the time of diagnosis. If bone marrow biopsy was not examined, report “not applicable.” If “known,” report the extent of biopsy histologic involvement in question 33. If “unknown” or “not applicable,” continue with question 34.

**Question 34: Specify the type of histological involvement in marrow**

WM and LPL are often characterized by histologic involvement of the bone marrow. However, there are variations in the type of involvement:<sup>2</sup>

- *Lymphoplasmacytoid*: This variant is primarily defined by small lymphocytes with some plasmacytoid lymphocytes and rare mature plasma cells. Lymphoplasmacytoid cells (plasmacytoid lymphocytes) are mononuclear cells with dark, irregular nuclei. They are slightly larger than a small lymphocyte. Additionally, mitotic and large cells are rare.
- *Lymphoplasmacytic*: In this variant, the involved cells are a mix of small lymphocytes, plasmacytoid lymphocytes, and mature plasma cells. Mitotic and large cells are rare.
- *Polymorphous*: This variant can resemble either lymphoplasmacytoid or lymphoplasmacytic variants, but mitotic and large cells are more common. Large cells are still less common than in large cell lymphomas.

Specify the type of histologic involvement as indicated by the pathology report or transplant physician. Report “unknown” if the bone marrow was not examined, there was no bone marrow involvement, or if the type of histologic involvement cannot be specified.

<sup>2</sup>Ioachim HL, Medeiros LJ. (2009) *Lymph Node Pathology, 4<sup>th</sup> edition*. Philadelphia, PA: Lippincott Williams & Wilkins.

**Question 35: Was flow cytometry (immunophenotyping) performed?**

Flow cytometry assessment is a method of analyzing peripheral blood, bone marrow, or tissue preparations for multiple unique cell characteristics. Its primary clinical purpose in the setting of WM or LPL is to identify unique cell populations through immunophenotyping.

Indicate if flow cytometry was performed at diagnosis. If flow cytometry was performed, check “yes” and continue with question 36.

If flow cytometry was not performed or it is unknown if flow cytometry was performed, indicate “no” or “unknown” and continue with question 43.

**Questions 36-41: Specify cell population phenotype**

Flow cytometry utilizes fluorescent-tagged monoclonal antibodies to identify cell marker expression by binding to cell surface antigens. Certain cell or disease panels use different combinations of monoclonal antibodies to identify cell markers that typically characterize that population, either by their presence or absence. Flow cytometry report formatting is highly variable among labs. However, most laboratories will summarize significant findings, including characteristics of the neoplastic cell population. Indicate if the cell population was "positive" or "negative" for each marker. If certain monoclonal antibodies were not part of the panel used, indicate "not done."

**Question 42: Was documentation submitted to the CIBMTR? (e.g., flow cytometry report)**

Indicate if a copy of the flow cytometry report at diagnosis is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the report. Attaching a copy of the report may prevent additional queries.

**Questions 43-44: Serum  $\beta$ 2 microglobulin**

Elevation in  $\beta$ 2 microglobulin at diagnosis is considered a negative prognostic indicator. Indicate whether  $\beta$ 2 microglobulin was "known" or "unknown" at the time of WM or LPL diagnosis. If "known," report the laboratory count and unit of measure documented on the laboratory report in question 44. If "unknown," continue with question 45.

**Question 45: Serum heavy chain - IgM**

Immunofixation is used to detect abnormal immunoglobulins in serum or urine, and to identify the heavy and/or light chain characterizing the clonal population. WM is generally characterized by an IgM monoclonal protein. Indicate whether an IgM paraprotein was identified on serum immunofixation.

**Question 46: Urine heavy chain – IgM**

Immunofixation is used to detect abnormal immunoglobulins in serum or urine, and to identify the heavy and/or light chain characterizing the clonal population. WM is generally characterized by an IgM monoclonal protein. Indicate whether an IgM paraprotein was identified on urine immunofixation.

**Question 47: Serum light chain**

Immunofixation is used to detect abnormal immunoglobulins in serum or urine, and to identify the heavy and/or light chain characterizing the clonal population. Report the light chain that was identified on serum immunofixation.

**Question 48: Urine light chain**

Immunofixation is used to detect abnormal immunoglobulins in serum or urine, and to identify the heavy and/or light chain characterizing the clonal population. Report the light chain that was identified on urine immunofixation.

**Questions 49-51: Relative serum viscosity**

Hyperviscosity syndrome is a common manifestation of WM and LPL. Indicate if relative serum viscosity was "known" or "unknown" at diagnosis. If "known," report the laboratory value in question 50 and laboratory upper limit of normal in question 51. If "unknown," continue with question 52.

**Questions 52-53: Serum monoclonal protein (M-spike) (only from electrophoresis)**

Indicate whether serum monoclonal protein quantification from electrophoresis was "known" or "unknown" at diagnosis. If "known," report the laboratory value and unit of measure in question 53. If serum electrophoresis was done and did not show monoclonal protein, report "0." If "unknown," continue with question 54.

**Questions 54-55: Urinary monoclonal protein (M-spike)**

Indicate whether 24-hour urine monoclonal protein quantification from electrophoresis was "known" or "unknown" at diagnosis. If "known," report the laboratory value and unit of measure in question 55. If urine electrophoresis was done and did not show monoclonal protein, report "0." If "unknown," continue with question 56.

**Questions 56-58: LDH**

LDH elevation at diagnosis is considered a negative prognostic indicator. Indicate whether LDH was "known" or "unknown" at diagnosis. If "known," report the laboratory count and unit of measure documented on the laboratory report in question 57; report the laboratory upper limit of normal and unit of measure in question 58. If "unknown," continue with question 59.

**Question 59: Cold agglutinins**

Cold agglutinin disease is a common manifestation of WM and LPL. Cold agglutinins are autoantibodies that bind to the red blood cells, manifesting as autoimmune hemolytic anemia. Indicate if cold agglutinins were "positive" or "negative" at diagnosis. If cold agglutinins were not tested or it is unknown if cold agglutinins were tested, report "unknown."

**Question 60: Cryoglobulin**

Cryoglobulins are immunoglobulins that aggregate as a gel at temperatures below 37°C. Cryoglobulins may be mixed immunoglobulins or a single component; the majority of cryoglobulin in WM or LPL patients will be mixed IgM-

IgG. Indicate if cryoglobulin was “present” or “absent” at diagnosis. If cryoglobulin was not tested or it is unknown if cryoglobulin was tested, report “unknown.”

**Questions 61-63: IgG**

Indicate whether IgG level was “known” or “unknown” at diagnosis. If “known,” report the laboratory value and unit of measure in question 62; report the laboratory upper limit of normal value and unit of measure in question 63. If “unknown,” continue with question 64.

**Questions 64-66: IgA**

Indicate whether IgA level was “known” or “unknown” at diagnosis. If “known,” report the laboratory value and unit of measure in question 65; report the laboratory upper limit of normal value and unit of measure in question 66. If “unknown,” continue with question 67.

**Questions 67-69: IgM**

Indicate whether IgM level was “known” or “unknown” at diagnosis. If “known,” report the laboratory value and unit of measure in question 68; report the laboratory upper limit of normal value and unit of measure in question 69. If “unknown,” continue with question 70.

**Question 70: Were cytogenetics tested (conventional or FISH)?**

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. Testing methods include conventional chromosome analysis (karyotyping) and fluorescence *in situ* hybridization (FISH) testing. For more information about cytogenetic testing and terminology, see [Appendix R](#), Cytogenetic Abbreviations and Terminology.

Indicate if cytogenetic studies were obtained at the time the recipient was diagnosed with WM or LPL, or prior to the start of treatment.

If cytogenetic studies were obtained, check “yes” and continue with question 71.

If cytogenetic studies were not obtained or it is unknown if cytogenetic studies were performed, indicate “no” or “unknown” and continue with question 76.

**Question 71: Results of tests**

If cytogenetic studies identified abnormalities (any karyotype other than 46XX or 46XY), indicate “abnormalities identified” and continue with question 72.

If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, indicate this and continue with question 76.

**Questions 72-74: Specify abnormalities.**

Deletion of the long arm of chromosome 6 is the most common structural abnormality in WM and LPL. However, other structural and numeric abnormalities have been noted.

If question 71 indicates that abnormalities were identified at the time of WM or LPL diagnosis, questions 72-73 must be answered as "yes" or "no." Do not leave either response blank. If the patient had any abnormality other than del(6q), select "yes" for "other abnormality," and specify in question 74.

**Question 75: Was documentation submitted to the CIBMTR? (e.g., cytogenetic or FISH report)**

Indicate if a copy of the cytogenetic or FISH report is attached. Use the Log of Appended Documents (Form 2800) to attach a copy of the cytogenetic or FISH report. Attaching a copy of the report may prevent additional queries.

## **Pre-HCT Therapy**

Complete a "Line of Therapy" section for each line of therapy administered prior to the start of the preparative regimen. If multiple lines of therapy are administered, copy and complete questions 77-120 for each line of therapy.

**Question 76: Was therapy given (including chemotherapy used to mobilize stem cells)?**

Indicate if the recipient received treatment for WM or LPL after diagnosis and before the start of the preparative regimen. If "yes," continue with question 77. If "no," continue with question 121.

**Question 77: Systemic therapy**

Systemic therapy refers to a delivery mechanism where a therapeutic agent is delivered orally or intravenously, enters the bloodstream, and is distributed throughout the body.

Indicate "yes" if the patient received systemic therapy and continue with question 78. If the patient did not receive systemic therapy, indicate "no" and continue with question 109.

**Questions 78-79: Date therapy started**

Indicate "known" if the therapy start date is documented and specify the start date in question 79. If the date is unknown, indicate this and continue with question 80.

**Questions 80-81: Date therapy stopped**

Indicate “known” if the therapy completion date is documented, and specify the date therapy stopped in question 81. If the patient received systemic therapy in cycles, specify the *first day of the last cycle* of systemic therapy. If the patient received a single line or single administration, indicate the last day systemic therapy was administered.

If the date is unknown, indicate this and continue with question 82.

**Question 82: Number of cycles**

Indicate if the number of cycles is “known” or “unknown.” If the number of cycles is known, continue with question 83 and specify the number of cycles of chemotherapy administered. If the patient received a single administration or one line of chemotherapy, indicate a single cycle. If the patient received a long-term maintenance therapy consisting of a single agent, indicate “known” for question 82; leave question 83 blank and override the error as “not applicable.”

If the number of cycles is unknown, continue with question 84.

**Questions 84-107: Specify systemic therapy agents**

Systemic therapy agents and treatment regimens vary based on disease, prognosis, and protocol. Drugs may be administered in an inpatient or outpatient setting, and treatment may consist of one or multiple drugs. Additionally, drugs may be administered on a single day, over consecutive days, or continuously.

Indicate “yes” or “no” for each therapeutic agent listed. Do not leave any response blank. If the recipient received an agent that is not listed, check “yes” for “other systemic therapy” and specify the treatment in question 107.

**Question 108: Was this line of therapy given for stem cell mobilization (priming)?**

Systemic therapy may be given for stem cell priming. For example, mobilization occurs during the recovery phase after cyclophosphamide administration. As such, it may be administered with cytokines to overcome the suppressive effect of previous therapeutic agents. Indicate if this line of therapy was given for stem cell mobilization.

**Question 109: Radiation therapy**

Radiation therapy uses high-energy, ionizing radiation to kill malignant cells. Much like non-targeted systemic therapy, radiation therapy does not specifically target malignant cells and does have significant side effects. For that reason, high-dose radiation often targets a limited field.

Indicate if the recipient received radiation treatment for WM or LPL after the time of diagnosis and before the start of the preparative regimen. If "yes," continue with question 110. If "no," continue with question 117.

**Questions 110-111: Date therapy started**

Indicate "known" if the radiation therapy start date is documented, and specify the first date of radiation administration in question 111. If the date is unknown, indicate this and continue with question 112.

**Questions 112-113: Date therapy stopped**

Indicate "known" if the radiation therapy completion date is documented, and specify the last date of radiation administration in question 113. If the date is unknown, indicate this and continue with question 114.

**Questions 114-116: Specify site(s) of radiation therapy**

Specify radiation site(s). If question 109 is answered "yes," at least one site of radiation therapy must be specified in questions 114-116.

**Question 117: Best response to line of therapy**

Indicate the patient's best response to this line of therapy.

**Table 1. Best response criteria for WM and LPL**

DISEASE STATUS	DEFINITION
<b>Complete response (CR)</b>	<ul style="list-style-type: none"> <li>• Disappearance of monoclonal protein on immunofixation (both serum and urine)</li> <li>• No histologic evidence of bone marrow involvement</li> <li>• Resolution of adenopathy and/or organomegaly on CT</li> <li>• Resolution of clinical signs or symptoms attributed to WM/LPL</li> </ul> <p>Complete response requires confirmatory immunofixation.</p>
<b>Partial response (PR)</b>	<ul style="list-style-type: none"> <li>• ≥ 50% reduction of serum monoclonal IgM spike on serum electrophoresis</li> <li>• ≥ 50% reduction of adenopathy and organomegaly on physical exam or CT</li> <li>• No new symptoms and no clinical signs of active disease</li> </ul>

**Table 1. Best response criteria for WM and LPL (cont.)**

DISEASE STATUS	DEFINITION
<b>Minor response/stable disease (MR/SD)</b>	<ul style="list-style-type: none"> <li>• 25–49% reduction of serum monoclonal IgM spike on serum electrophoresis</li> <li>• No new symptoms and no clinical signs of active disease</li> </ul> <p><i>Or</i></p> <ul style="list-style-type: none"> <li>• &lt; 25% reduction <u>and</u> &lt; 25% increase of serum monoclonal IgM spike on serum electrophoresis</li> <li>• No progression of adenopathy, organomegaly, cytopenias, or clinically significant symptoms attributed to WM/LPL</li> </ul>
<b>Progressive disease (PD)</b>	<ul style="list-style-type: none"> <li>• ≥ 25% increase in serum monoclonal IgM spike from lowest nadir on serum electrophoresis</li> <li>• Progression of clinically significant findings or symptoms (for example, anemia, adenopathy, constitutional symptoms, amyloidosis, etc.) attributed to WM/LPL</li> </ul> <p>Progression identified by increasing monoclonal protein on serum electrophoresis requires confirmatory test.</p>
<b>Not assessed</b>	Patient's disease was not assessed by any method, including physical examination.

**Question 118: Date assessed**

Enter the date the best response to the line of therapy was established. Report the date of the pathological (e.g., bone marrow biopsy) or radiological (e.g., CT scan) evaluation; if neither was reported, report the date of blood/serum assessment (e.g., CBC, peripheral blood smear). Enter the date the sample was collected for pathological and/or laboratory evaluation. If the recipient was treated for extramedullary disease and a radiological assessment (e.g., X-ray, CT scan, MRI scan, PET scan) was performed to assess disease response, enter the date the imaging took place for radiologic assessment. If no pathological, radiographic, or laboratory assessment was performed to establish the best response to the line of therapy, report the office visit in which the physician clinically assessed the recipient's response.

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

**Question 119: Did disease relapse/progress following this line of therapy?**

Relapse is the recurrence of disease after CR. WM or LPL relapse is demonstrated by reappearance of disease characteristics including IgM paraprotein, lymphadenopathy and/or organomegaly, and bone marrow histologic involvement.

WM or LPL progression criteria are specified in Table 1 above. Indicate if relapse or progression occurred following the line of therapy being reported. If question 117 is answered "progressive disease," question 119 must be "yes."

**Question 120: Date of relapse/progression**

Enter the date of the assessment that identified relapse or progression following the line of therapy. Enter the date the sample was collected for pathological and laboratory evaluation or enter the date the imaging took place. If the physician determined evidence of relapse in a clinical assessment during an office visit, report the date of assessment.

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

## Laboratory Studies at Last Evaluation Prior to the Start of the Preparative Regimen

These questions are intended to determine the status of the recipient prior to the preparative regimen. Testing may be performed multiple times within the pre-transplant workup period (approximately 30 days) prior to the start of the preparative regimen; report the most recent laboratory value. Laboratory values obtained on the first day of the preparative regimen may be reported as long as the sample was drawn before any radiation or systemic therapy was administered.

**Questions 121-122: Absolute lymphocyte count**

Indicate whether the lymphocyte count was "known" or "unknown" immediately prior to the start of the preparative regimen. If "known," report the laboratory count and unit of measure documented on the laboratory report in question 122. If "unknown," continue with question 123.

**Questions 123-124: Bone marrow aspirate (examined for histologic involvement)**

Indicate whether the extent of histologic involvement in the bone marrow aspirate was "known" or "unknown" immediately prior to the start of the preparative

regimen. If bone marrow aspirate was not examined, report "not applicable." If "known," report the extent of aspirate histologic involvement in question 124. If "unknown" or "not applicable," continue with question 125.

**Questions 125-126: Bone marrow biopsy (examined for histologic involvement)**

Indicate whether the extent of histologic involvement in the bone marrow biopsy was "known" or "unknown" immediately prior to the start of the preparative regimen. If bone marrow biopsy was not examined, report "not applicable." If "known," report the extent of biopsy histologic involvement in question 126. If "unknown" or "not applicable," continue with question 127.

**Questions 127-128: Serum  $\beta$ 2 microglobulin**

Indicate whether  $\beta$ 2 microglobulin was "known" or "unknown" immediately prior to the start of the preparative regimen. If "known," report the laboratory count and unit of measure documented on the laboratory report in question 128. If "unknown," continue with question 129.

**Questions 129-130: Relative serum viscosity**

Hyperviscosity syndrome is a common manifestation of WM and LPL. Indicate if relative serum viscosity was "known" or "unknown" immediately prior to the start of the preparative regimen. If "known," report the laboratory value in question 130. If "unknown," continue with question 131.

**Questions 131-132: Serum monoclonal protein (M-spike) (only from electrophoresis)**

Indicate whether serum monoclonal protein quantification from electrophoresis was "known" or "unknown" immediately prior to the start of the preparative regimen. If "known," report the laboratory value and unit of measure in question 132. If serum electrophoresis was done and did not show monoclonal protein, report "0." If "unknown," continue with question 133.

**Questions 133-134: Urinary monoclonal protein (M-spike)**

Indicate whether 24-hour urine monoclonal protein quantification from electrophoresis was "known" or "unknown" immediately prior to the start of the preparative regimen. If "known," report the laboratory value in question 134. If urine electrophoresis was done and did not show monoclonal protein, report "0." If "unknown," continue with question 135.

**Question 135: Cold agglutinins**

Cold agglutinin disease is a common manifestation of WM and LPL. Cold agglutinins are autoantibodies that bind to the red blood cells, manifesting as autoimmune hemolytic anemia. Indicate if cold agglutinins were "positive" or "negative" immediately prior to the start of the preparative regimen. If cold

agglutinins were not tested or it is unknown if cold agglutinins were tested, report "unknown."

**Question 136: Cryoglobulin**

Cryoglobulins are immunoglobulins that aggregate as a gel at temperatures below 37°C. Cryoglobulins may be mixed immunoglobulins or a single component; the majority of cryoglobulin in WM or LPL patients will be mixed IgM-IgG. Indicate if cryoglobulin was "present" or "absent" immediately prior to the start of the preparative regimen. If cryoglobulin was not tested or it is unknown if cryoglobulin was tested, report "unknown."

**Questions 137-139: IgG**

Indicate whether IgG level was "known" or "unknown" immediately prior to the start of the preparative regimen. If "known," report the laboratory value and unit of measure in question 138; report the laboratory upper limit of normal value and unit of measure in question 139. If "unknown," continue with question 140.

**Questions 140-142: IgA**

Indicate whether IgA level was "known" or "unknown" immediately prior to the start of the preparative regimen. If "known," report the laboratory value and unit of measure in question 141; report the laboratory upper limit of normal value and unit of measure in question 142. If "unknown," continue with question 143.

**Questions 143-145: IgM**

Indicate whether IgM level was "known" or "unknown" immediately prior to the start of the preparative regimen. If "known," report the laboratory value and unit of measure in question 144; report the laboratory upper limit of normal value and unit of measure in question 145. If "unknown," continue with question 146.

**Question 146: Were cytogenetics tested (conventional or FISH)?**

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. Testing methods include conventional chromosome analysis (karyotyping) and fluorescence *in situ* hybridization (FISH) testing. For more information about cytogenetic testing and terminology, see [Appendix R](#), Cytogenetic Abbreviations and Terminology.

Indicate if cytogenetic studies were obtained immediately prior to the start of the preparative regimen.

If cytogenetic studies were obtained, check "yes" and continue with question 147.

If cytogenetic studies were not obtained or it is unknown if chromosome studies were performed, indicate "no" or "unknown" and continue with question 151.

**Question 147: Results of tests**

If cytogenetic studies identified abnormalities (any karyotype other than 46XX or 46XY), indicate “abnormalities identified” and continue with question 148. If cytogenetic studies yielded no evaluable metaphases or there were no abnormalities identified, indicate this and continue with question 151.

**Question 148-150: Specify abnormalities**

Deletion of the long arm of chromosome 6 is the most common structural abnormality in WM and LPL. However, other structural and numeric abnormalities have been noted.

If question 147 indicates that abnormalities were identified immediately prior to the start of the preparative regimen, questions 148-149 must be answered as “yes” or “no.” Do not leave either response blank. If the patient had any abnormality other than del(6q), select “yes” for “other abnormality,” and specify in question 150.

**Disease Status at Last Evaluation Prior to the Preparative Regimen**

**Question 151: What was the disease status at the last evaluation prior to the preparative regimen?**

Indicate the disease status of WM or LPL at last evaluation prior to the start of the preparative regimen.

**Table 2. Disease status criteria for WM and LPL**

DISEASE STATUS	DEFINITION
<p><b>Complete response (CR)</b></p> <p><i>Continue with question 152.</i></p>	<ul style="list-style-type: none"> <li>• Disappearance of monoclonal protein on immunofixation (both serum and urine)</li> <li>• No histologic evidence of bone marrow involvement</li> <li>• Resolution of adenopathy and/or organomegaly on CT</li> <li>• Resolution of clinical signs or symptoms attributed to WM/LPL</li> </ul> <p>Complete response requires confirmatory immunofixation.</p>
<p><b>Partial response (PR)</b></p> <p><i>Continue with question 152.</i></p>	<ul style="list-style-type: none"> <li>• ≥ 50% reduction of serum monoclonal IgM spike on serum electrophoresis</li> <li>• ≥ 50% reduction of adenopathy and organomegaly on physical exam or CT</li> <li>• No new symptoms and no clinical signs of active disease</li> </ul>

**Table 2. Disease status criteria for WM and LPL (cont.)**

DISEASE STATUS	DEFINITION
<p><b>Minor response/stable disease (MR/SD)</b></p> <p><i>Continue with question 152.</i></p>	<ul style="list-style-type: none"> <li>• 25–49% reduction of serum monoclonal IgM spike on serum electrophoresis</li> <li>• No new symptoms and no clinical signs of active disease</li> </ul> <p><u>Or</u></p> <ul style="list-style-type: none"> <li>• &lt; 25% reduction <u>and</u> &lt; 25% increase of serum monoclonal IgM spike on serum electrophoresis</li> <li>• No progression of adenopathy, organomegaly, cytopenias, or clinically significant symptoms attributed to WM/LPL</li> </ul>
<p><b>Progressive disease (PD)</b></p> <p><i>Continue with question 152.</i></p>	<ul style="list-style-type: none"> <li>• ≥ 25% increase in serum monoclonal IgM spike from lowest nadir on serum electrophoresis</li> <li>• Progression of clinically significant findings or symptoms (for example, anemia, adenopathy, constitutional symptoms, amyloidosis, etc.) attributed to WM/LPL</li> </ul> <p>Progression identified by increasing monoclonal protein on serum electrophoresis requires confirmatory test.</p>
<p><b>Not assessed</b></p> <p><i>Continue with signature section.</i></p>	<p>Patient's disease was not assessed by any method, including physical examination.</p>

**Question 152: Date assessed**

Enter the date of the most recent assessment of disease status within the pre-transplant work-up period (approximately 30 days) prior to the start of the preparative regimen. Clinical and hematologic assessments include pathological evaluation (e.g., bone marrow biopsy), radiographic examination (e.g., X-ray, CT scan, MRI scan, PET scan), and laboratory assessment (e.g., SPEP), in addition to clinician evaluation and physical examination. Enter the date the sample was collected for pathological and laboratory evaluation; enter the date the imaging took place for radiographic assessment.

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

**Signature**

The FormsNet3<sup>SM</sup> 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.