



DATE: March 12, 2020

TO: Daniel Cline, OMB Desk Officer

FROM: Lisa Wright-Solomon, HRSA Information Collection Clearance Officer

Request: The Health Resources and Services Administration (HRSA) Division of Transplantation requests approval for non-substantive changes to the Stem Cell Therapeutic Outcomes Database (SCTOD) Collection (OMB 0915-0310 expiration date 10/31/2022).

Purpose: The purpose of this request is to make changes to the Pre-Transplant Essential Data (Pre-TED) and disease classification forms to maintain current and effective data collection. This memo explains the changes and supporting rationale.

The **Pre-TED Form 2400** is being modified to add one additional question to the form to determine whether patients received specific pre-transplant treatments associated with post-transplant complications. Certain immune-based cancer therapies are associated with serious complications following allogeneic hematopoietic cell transplant (HCT), and this question will help to identify exposure to those treatments. It is important to understand these associations as immunotherapy for cancer expands.

The Disease Classification Form 2402 is being modified to split the combined Myelodysplastic (MDS)/myeloproliferative (MPN) diseases section into two separate sections. Since the last change to this section of the form, there have been some changes in disease classification, and substantial changes in medical understanding of risk factors and response criteria for the myeloproliferative diseases. These changes make it appropriate to clearly separate the two disease groups, with distinct and relevant question sets identifying risk factors and response criteria for each. The changes we are proposing have been guided by the updated 2016 World Health Organization (WHO) classifications¹ and International

¹Arber, Daniel A., Orazi, Attilio, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*, 2016; 127 (20): 2391–2405. doi: <https://doi.org/10.1182/blood-2016-03-643544>.

Working Group (IWG)^{2,3} response criteria for these indications and input from our physician scientist working committees and clinical research professionals (CRPs).

We believe separating the sections will **decrease form complexity** by maintaining one set of questions applicable to each disease, **making information easier to find** and **removing ambiguity** for CRPs who complete the forms. Once CRPs become familiar with these changes, we believe specific purpose-built questions and answers by disease will result in **neutral or reduced time burden** of completing these sections. Additionally, the information gathered, particularly for MPN, will be more accurate, and more appropriate for risk adjustment to fulfill the requirements of the HRSA C.W. Bill Young Cell Transplantation Program (CWBYCTP).

The overall scope of change in data collected for MDS is minimal, representing an update of existing content. A new distinct section devoted to MPN has been created, with questions specific and appropriate to MPN added to capture transfusion dependence, constitutional symptoms, splenomegaly, and hepatomegaly data. Capturing this information is consistent with current assessment standards. The relative burden to completing this section for MPN will be similar to that of Acute Myeloid Leukemia (AML), Acute Lymphocytic Leukemia (ALL) or MDS, and we have received feedback from CRP stakeholders suggesting the clarity of content is improved, and the time to complete the new MPN section should be similar to those mentioned above. Respondents will only complete one of these two sections based on the patient's diagnosis. Importantly, MPN represents a relatively small portion (3.5 percent) of allogeneic HCT performed in the United States annually.

Time Sensitivity: The SCTOD data collection changes must be completed in a timely manner to fulfill CWBYCTP requirements. Approval of these changes is needed by April 1, 2020, to implement the changes in the data collection system by mid-April scheduled release. If this timeline is not met, the next release for data collection forms is scheduled approximately three months later.

²MDS: Platzbecker, U., Fenaux, P., et al. Proposals for revised IWG 2018 hematological response criteria in patients with MDS included in clinical trials. *Blood*, 2019; 133 (10): 1020–1030. doi: <https://doi.org/10.1182/blood-2018-06-857102>.

³MPN: Tefferi Ayalew, Cervantes Francisco, et al. Revised response criteria for myelofibrosis: International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN) consensus report. *Blood*, 2013; 122 (8): 1395–1398. doi: <https://doi.org/10.1182/blood-2013-03-488098>.

Burden: The non-substantive changes included herein do not substantially change the estimated reporting burden for patients with these indications, and may lead to reductions in the burden.

PROPOSED CLARIFICATIONS AND NON-SUBSTANTIVE CHANGES FOR STEM CELL THERAPEUTIC OUTCOMES DATABASE FORMS:

Form 2400 Pre-Transplant Essential Data (Pre-TED)

a. Question 144, page 22 – Addition

New question “Specify if the recipient received any of the following (at any time prior to HCT / infusion) (check all that apply).”

Rationale: Capture data on treatments in which specific safety issues have been raised in the post-allogeneic transplant setting.

Form 2402 Disease Classification

b. Question 2, Primary Disease for HCT / Cellular Therapy, page 1 – Change/Addition

Split the combined MDS/MPN category into two separate options: one for myelodysplastic syndrome and another for myeloproliferative neoplasms.

Rationale: Decrease form complexity to capture one set of questions applicable to each disease.

c. Questions 179 - 180, MDS classification, page 34 – Change/Addition

Updated subtypes to align with 2016 WHO classifications.

Rationale: To capture accurate disease subtypes based on published criteria.

d. Q181, page 34 – Addition

New question “Was documentation submitted to the CIBMTR (e.g., pathology report used for diagnosis)?” to be asked for subtypes “MDS-unclassifiable” and “MDS/MPN unclassifiable.”

Rationale: To prompt attachment of supporting documentation for “unclassifiable” subtypes.

e. Question 184, page 35 – Change/Addition

Modified the list of predisposing conditions.

Rationale: To capture an updated list of predisposing conditions.

f. Question 186, page 35 – Addition

New question “Date CBC drawn” at diagnosis.

Rationale: To capture the date of laboratory studies obtained at diagnosis.

g. Questions 191- 192, Blasts in Blood, page 36 – Addition

New questions to capture “Blasts in blood” at diagnosis, previously collected on the MDS Pre-Infusion F2014 R4.

Rationale: To capture essential data earlier upstream.

h. Questions 202 – 217, Cytogenetic Results at diagnosis, pages 37-40 – Change/Addition

Karyotyping and fluorescence in situ hybridization (FISH) results broken down into separate questions. Cytogenetic abnormality list is now a “check all that apply.” Added questions to capture sample source (Q203 and Q211) and if documentation was submitted to CIBMTR (Q209 and Q217).

Rationale: To improve the data professionals’ experience when completing the form. To capture the sample source of the cytogenetic results at diagnosis and to prompt attachment of supporting documentation.

i. Question 219, page 40-41 – Change/Addition

Updated subtypes to capture only those an MDS recipient would transform to, in alignment with 2016 WHO classifications.

Rationale: To capture applicable, updated classifications based on published criteria.

j. Question 223, page 41 – Addition

New question “Date CBC drawn” at last evaluation prior to the start of the preparative regime.

Rationale: To capture the date of laboratory studies obtained at last evaluation prior to the start of the preparative regimen.

k. Questions 228 – 229, Blasts in blood, pages 41-42 – Addition

New questions to capture “Blasts in blood” at last evaluation prior to the start of the preparative regimen, previously collected on the MDS Pre-Infusion F2014 R4.

Rationale: To capture essential data earlier upstream.

l. Questions 239 – 254, Cytogenetic Results at last evaluation prior to the start of the preparative regimen, pages 42-46 – Change/Addition

Karyotyping and FISH results broken down into separate questions. Cytogenetic abnormality list is now a “check all that apply.” Added questions to capture sample source (Q240 and Q248) and if documentation was submitted to CIBMTR (Q246 and Q254).

Rationale: To improve the data professionals’ experience when completing the form. To capture the sample source of the cytogenetic results at last evaluation prior to the start of the preparative regimen and to prompt attachment of supporting documentation.

- m. Questions 255 – 258, Disease status at transplant, page 46 – Change/Addition**
Updated the response criteria in alignment with IWG criteria. Expanded to capture transfusion dependence and major/ minor response.
Rationale: To align with IWG criteria.
- n. Questions 260 - 261, MPN classification, page 47 – Change/Addition**
New question to capture MPN subtype classification at diagnosis.
Rationale: Collect MPN classification aligned with 2016 WHO classifications.
- o. Q262, page 47 – Addition**
New question “Was documentation submitted to the CIBMTR (e.g., pathology report used for diagnosis?” to be asked for single subtype “MPN-unclassifiable.”
Rationale: To prompt attachment of supporting documentation for an “unclassifiable” subtype.
- p. Question 263, page 47 – Addition**
New question to capture if the recipient had constitutional symptoms in six months before diagnosis.
Rationale: To capture prognostic scoring information.
- q. Question 264, page 48 – Addition**
New question “Date CBC drawn” at diagnosis.
Rationale: To capture the date of laboratory studies obtained at diagnosis.
- r. Questions 269 – 270, Blasts in Blood, page 48 – Addition**
New questions to capture “Blasts in blood” at diagnosis.
Rationale: To capture essential data early upstream.
- s. Questions 279 – 289, Driver Mutations, pages 49-50 - Addition**
Added new questions to capture driver mutation results for JAK2, CALR, MPL, CSF3, and to ask if documentation was submitted to CIBMTR.
Rationale: To capture critical molecular marker results and to prompt attachment of supporting documentation.
- t. Questions 291 – 306, Cytogenetic Results at diagnosis, pages 50-53 – Change / Addition**
Karyotyping and FISH results broken down into separate questions. Cytogenetic abnormality list is a “check all that apply.” Added questions to capture sample source (Q292 and Q300) and if documentation was submitted to CIBMTR (Q298 and Q306).

Rationale: To improve the data professionals' experience when completing the form. To capture the sample source of the cytogenetic results at diagnosis and to prompt attachment of supporting documentation.

u. Question 308, page 54 – Change

Updated to capture only those subtypes an MPN recipient would transform to.

Rationale: Modified to capture MPN applicable subtypes after transformation.

v. Question 311, page 54 – Addition

New question to capture transfusion dependence at last evaluation prior to the start of the preparative regimen.

Rationale: Collect critical data element for all MPN recipients.

w. Question 312, page 54 – Addition

New question to capture constitutional symptoms at last evaluation prior to the start of the preparative regimen.

Rationale: To capture prognostic scoring information.

x. Questions 313 – 316, Splenomegaly, pages 54-55 – Addition

New questions to capture splenomegaly and spleen size at last evaluation prior to the start of the preparative regimen.

Rationale: Collect critical data elements for all MPN recipients.

y. Questions 317 – 320, Hepatomegaly, page 55 – Addition

New questions to capture hepatomegaly and liver size at last evaluation prior to the start of the preparative regimen.

Rationale: Collect critical data elements for all MPN recipients.

z. Question 321, page 55 – Addition

New question “Date CBC drawn” at last evaluation prior to the start of the preparative regimen.

Rationale: To capture the date of laboratory studies obtained at last evaluation prior to the start of the preparative regimen.

aa. Questions 326 – 327, Blasts in blood, page 56 – Addition

New questions to capture “Blasts in blood” at last evaluation prior to the start of the preparative regimen.

Rationale: To capture essential data early upstream.

bb. Questions 336 – 346, Driver Mutations, pages 56-58- Addition

New questions to capture driver mutation results for JAK2, CALR, MPL, and CSF3 molecular markers, in addition to asking for documentation submitted to CIBMTR.

Rationale: To capture critical molecular marker results and prompt attachment of supporting documentation.

cc. Questions 348 – 363, Cytogenetic Results at last evaluation prior to the start of the preparative regimen, pages 58-61 – Change/Addition

Karyotyping and FISH results broken down into separate questions. Cytogenetic abnormality list is a “check all that apply.” Added questions to capture sample source (Q349 and Q357) and if documentation was submitted to CIBMTR (Q355 and Q363).

Rationale: To improve the data professionals’ experience when completing the form. To capture the sample source of the cytogenetic results at last evaluation prior to the start of the preparation regimen and to prompt attachment of supporting documentation.

dd. Questions 364 – 372, Disease status at transplant, pages 6162– Change/Addition

Updated the response criteria in alignment with IWG criteria. Expanded to capture anemia, spleen, and symptom response for recipients in “Clinical Improvement.” Also expanded to capture cytogenetic and molecular response.

Rationale: To align with IWG criteria.

Attachments:

1. Pre-Transplant Essential Data F2400 R6. Current, approved form.
2. Pre-Transplant Essential Data F2400 R7. All changes highlighted in yellow are changes and changes highlighted in blue are additions to the attached document.
3. Disease Classification Form 2402 R4. Current, approved form.
4. Disease Classification Form 2402 R5. All changes highlighted in yellow are changes and changes highlighted in blue are additions to the attached document.