Audit Report

[redacted]

2017

In [redacted], the [redacted] BMT program was audited by CIBMTR. While the overall error rate was 2.5%, below the 3% "pass" standard, a Corrective Action Plan was requested. This document outlines the corrective action implemented and the evaluable results to date.

Systemic errors identified in the audit:

- Reporting in the disease status and latest disease assessment data fields
- Reporting the HCT product and infusion data fields

Overview of the corrective action plan

[redacted] BMT's corrective action plan, submitted in [redacted] 2015, had three major components:

1. Disease assessment/status worksheets for accurate disease staging/assessment pre- and post-transplant of each major disease reported on, listing the CIBMTR guidelines for disease assessment with a "yes/no" system of checkboxes for easy and accurate assessment.
2. A continuing education program, designed and implemented by the CIBMTR reporting team members, with each monthly topic researched and presented by one of the CIBMTR reporting staff. Thus each major topic presented also creates a local 'expert' in that topic, in the person doing the research and presentation.
3. An intensive and systematic new program of auditing CIBMTR forms submitted. Previously our CIBMTR reporting staff aimed at performing a QA audit on 10% of the forms

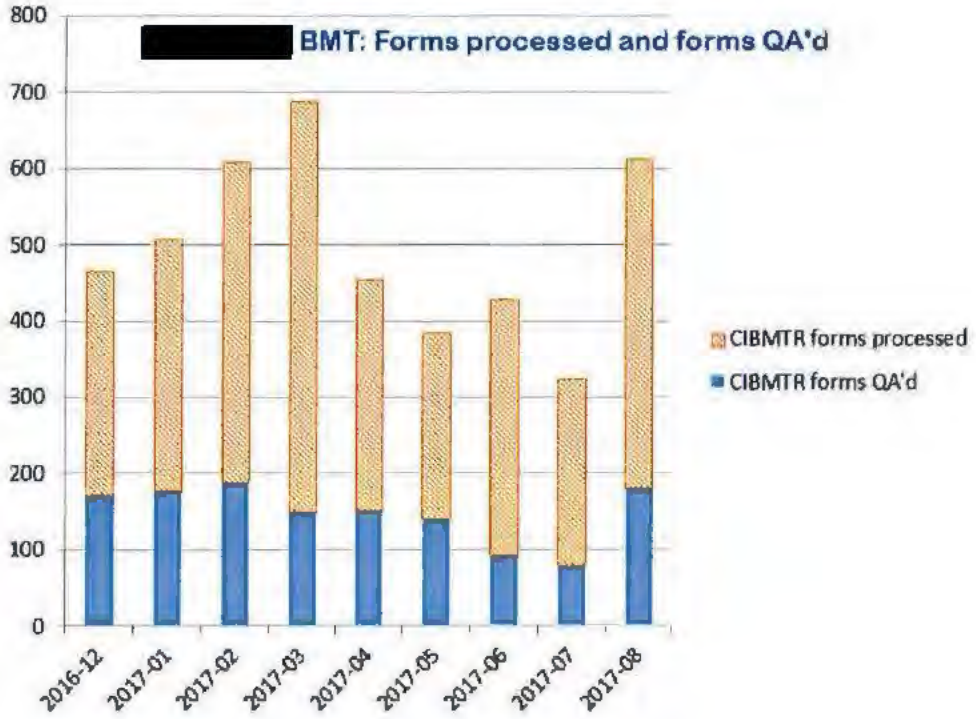


Figure 1: CIBMTR forms processed and forms audited [redacted]

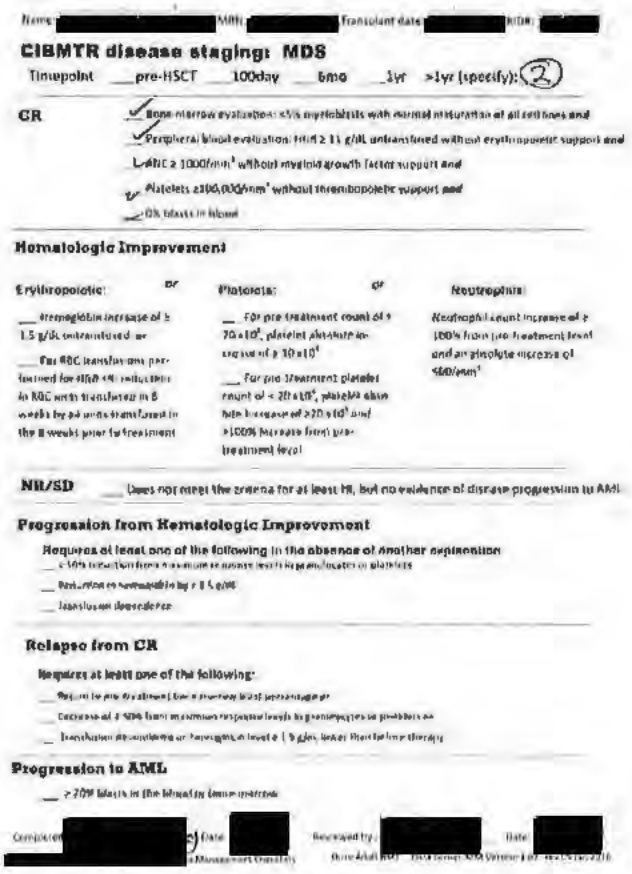
submitted, some of which were only audited for some specific fields. The goal for this corrective action program was to increase to 20% monitoring, and after some discussion and experimentation, it was decided to audit every field on every form selected for audit.

This corrective action plan was implemented in early 2016 and is ongoing at this time. [redacted] CIBMTR reporting staffing has varied significantly since then, but is currently able to keep up with the workload both for forms submission requirements (CPI) and QA load; see Figure 1.

Audit plan implementation

1. ***Disease assessment worksheets:*** This was the first item on our Corrective Action Plan, and the first to be implemented. The program works in this way: For each disease staging or assessment timepoint (baseline, post-therapies, timepoints 100 days, 6 months, and years 1 through the end of follow-up), records are consulted and the applicable worksheet is completed. If needed, the patient's clinical team is questioned on interpretation of scans and labs. The worksheets are completed, signed and dated, and scanned into the archives with the rest of the CIBMTR forms' documentation.

   There are currently five targeted worksheets in use in the CIBMTR reporting group. These include the three originally planned (AML, multiple myeloma, and MDS) and two others (general Pre-TED datapoints, and lymphoma staging & assessment.) Our intent is to create worksheets for each of the diseases that bring people to transplant here at [redacted]


CIBMTR disease staging: MDS

Timepoint pre-HSCT 100day 6mo 1yr >1yr (specify): 2

CR

Hematologic Improvement

Erythropoietic: Platelets: Neutrophils:

NR/SD

Progression from Hematologic Improvement

Relapse from CR

Progression to AML

Figure 2: example disease assessment worksheet

Regular use of these worksheets not only ensures accurate disease assessment, but also will help inculcate the relevant guidelines for each major disease in reporting staff. The worksheets are attached in Appendix A. The worksheets are:

- Pre-TED assessments and data (comorbidities, chemo regimen, etc.)
- Myeloma staging and status at assessment
- MDS staging and status at assessment
- Lymphoma staging and status at assessment
- AML staging and status at assessment

Continuing education for CIBMTR reporting staffers:

a. Training sessions occur approximately monthly, and are scheduled for 90 minutes per topic. This allows 60 minutes for the presentation, a bit extra for running long, and then 15-20 minutes for questions and discussion.

b. Following each presentation, the slides and notes, plus any written materials, are stored in a server subdirectory every staffer has access to, for future reference. These materials will also be used for training new staffers.

c. The presentations to date have been:

- CD34+ counts in infusion reporting [redacted]17
- Timelines for CIBMTR reporting [redacted]17
- FISH assays [redacted]2017
- Standard cytogenetics ([redacted]/17
- Date of diagnosis reporting [redacted]/17
- Infusion forms: key points [redacted]/17
- AML reporting [redacted]17
- MDS and MPN reporting ([redacted]17

2. *Data audit program*

This has been the most intensive part of the corrective action plan. Every month, each CIBMTR reporting staff member is given a pseudo-randomly selected group of patients who had transplants in the desired time range. The director of the CIBMTR reporting group selects the forms to be audited from a list generated by the database analyst, picking from a new month or CPI period of completion, to ensure review across all the relevant form submission dates.

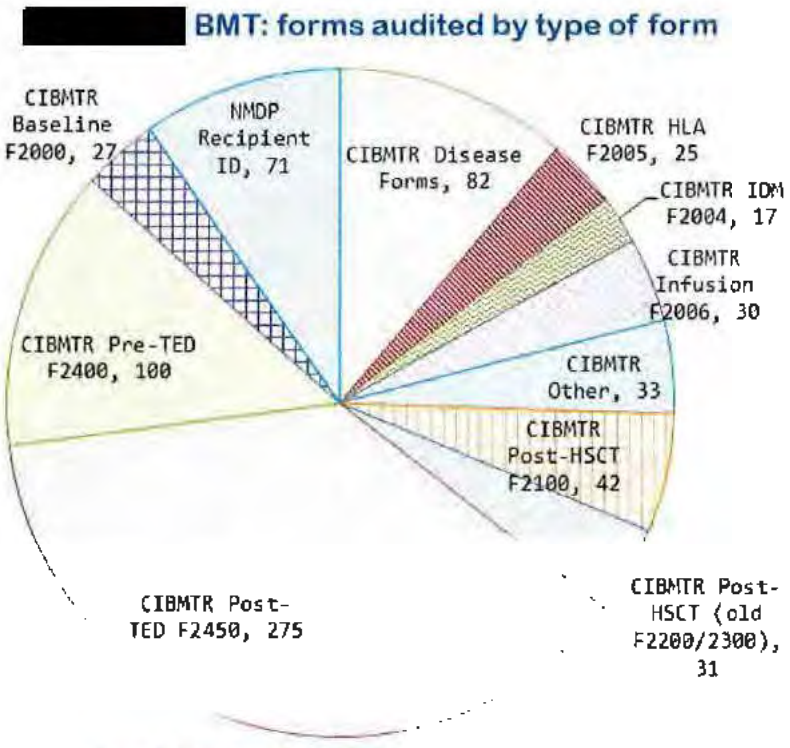


Figure 3: forms audited in 2017

Each staffer is responsible for auditing every CIBMTR form submitted for each patient on his or her list. An overview of the number of forms audited per month is presented on the first page, in Figure 1, along with the number of CIBMTR forms submitted/processed in the same month.

Figure 3 shows the forms audited as part of this process, with the number of each form audited. As mentioned above, rather than checking only certain datapoints, every question on each audited form is checked against the source documentation.

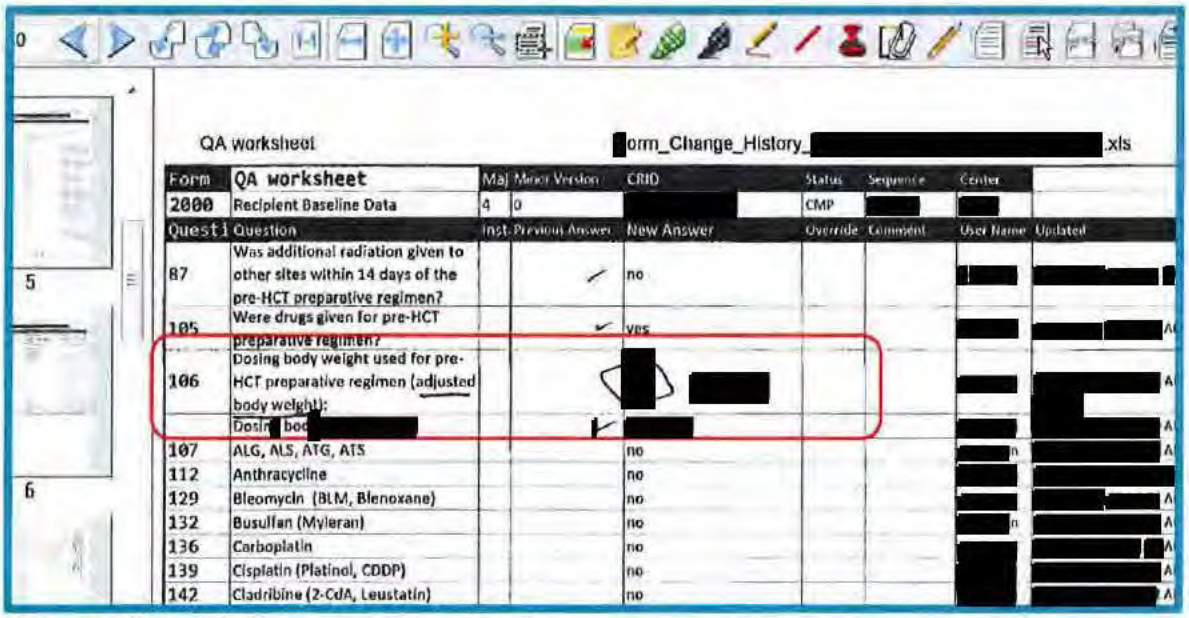
When errors or potential errors are found during the audit process, CIBMTR resources (the Forms Instruction Manual and/or the Retired Forms Manual) are consulted, and, clinicians are consulted when needed, and any necessary changes are made to the report in Formsnet3. After this, the changes and any needed documentation are scanned into our document archiving system (see Figure 3.) Then an entry in our internal database is made to indicate that the form was audited, the extent of the audit, and whether errors were unnecessary, or were found and corrected.

As part of our ongoing improvement efforts, each CIBMTR reporting staffer reports on the general results and findings of his/her monthly audits at our monthly CIBMTR Group staff meetings (which are separate from the continuing education presentations.) This group discussion allows staffers to identify problem areas in our reporting, and helps ensure that all staffers are aware of CIBMTR reporting guidelines for different situations (disease assessment, assay methods, onset dates, infection & GVHD reporting, etc.)

The increased data-audit plan thus increases both the quality of the data that has been reported, and, by the educational effect of using the worksheets and having every staffer's audits subject to discussion and review at meetings, increases the quality of future reporting by the CIBMTR group.

Data audit example:

Step 1: Possible error is identified (screenshot below shows typical QA worksheet; error is circled in pen by the person doing the audit but is outlined in red for clarity in this document.)



QA worksheet [redacted]orm_Change_History_[redacted].xls

Form	QA worksheet	Ma	Minor Version	CRID	Status	Sequence	Center	
2000	Recipient Baseline Data	4	0	[redacted]	CMP	[redacted]	[redacted]	
Questi	Question	Inst	Previous Answer	New Answer	Override	Comment	User Name	Updated
87	Was additional radiation given to other sites within 14 days of the pre-HCT preparative regimen?			no			[redacted]	[redacted]
105	Were drugs given for pre-HCT preparative regimen?			yes			[redacted]	[redacted]
106	Dosing body weight used for pre-HCT preparative regimen (adjusted body weight):			[redacted]			[redacted]	[redacted]
	Dosin[redacted] boc[redacted]			[redacted]			[redacted]	[redacted]
107	ALG, ALS, ATG, ATS			no			[redacted]	[redacted]
112	Anthracycline			no			[redacted]	[redacted]
129	Bleomycin (BLM, Blenoxane)			no			[redacted]	[redacted]
132	Busulfan (Myleran)			no			[redacted]	[redacted]
136	Carboplatin			no			[redacted]	[redacted]
139	Cisplatin (Platinol, CDDP)			no			[redacted]	[redacted]
142	Cladribine (2-CdA, Leustatin)			no			[redacted]	[redacted]

Figure 4: audit worksheet

Step 2: Source documentation is checked

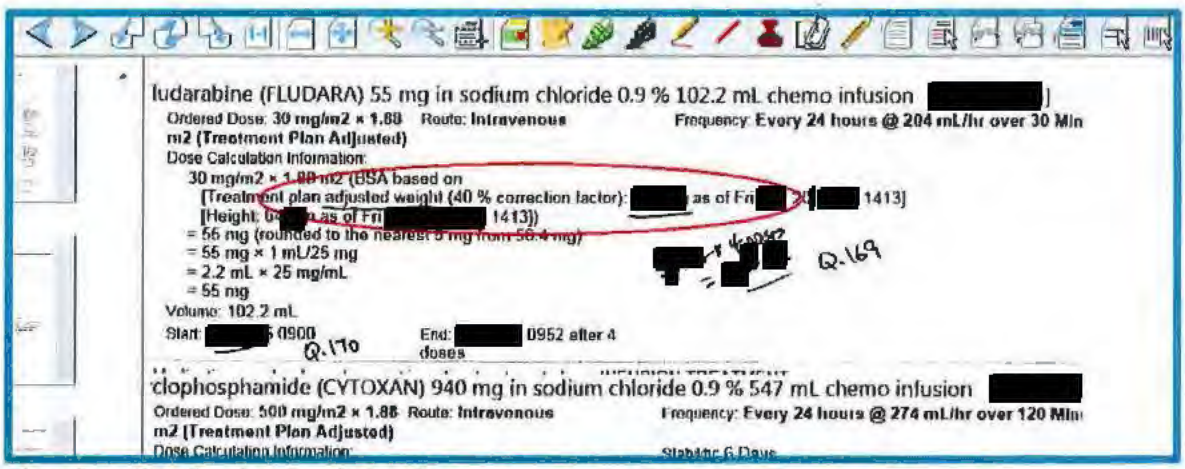


Figure 5: confirmation via source document

Step 3: Correction is made in Formsnet3

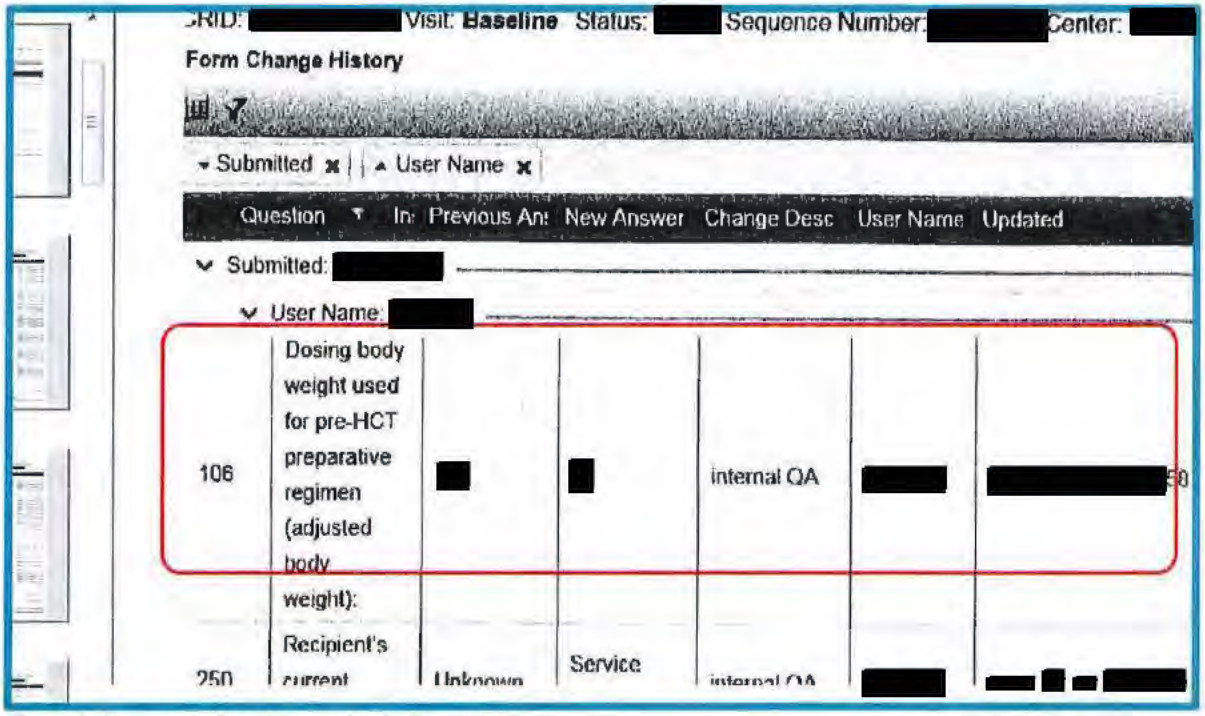


Figure 6: documentation of correction in Formsnet3

Step 4: Documents relating to the audit, including error correction and annotated source documentation, are scanned into our document archive. (Not shown but this document archive is the source of the three screenshots above, entered under the category "CIBMTR QA," with other documentation relating to this individual form's audit.)

(end of example)

Findings and recommendations

Our ongoing QA audits are (to date) entirely retrospective, in that CIBMTR reports previously submitted are being audited. Forms submitted since the enhanced quality action plan will begin to be audited in calendar 2018. Thus there are not specific findings to allow a conventional pre/post evaluation.

Figure 7 shows the number of forms audited per month in calendar 2017 to date by the number with and without detected errors. A calculated percentage of forms with errors appears in red. There appears to be no significance in the data presented in Figure 7, aside from a possibly low error-detection rate at the initiation of the program. (This finding is a guess based on the numbers and has not been tested statistically.)

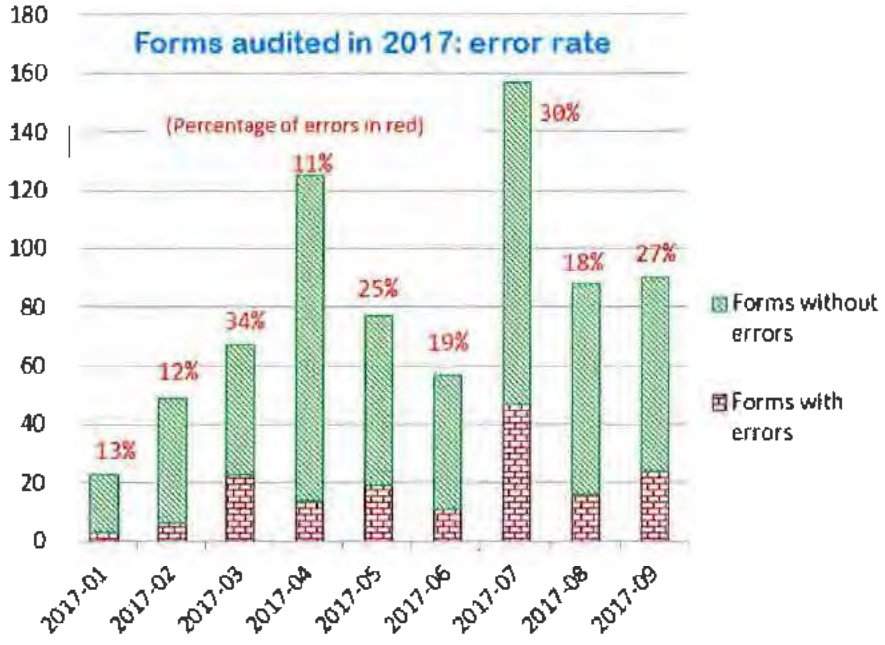


Figure 7

However, a number of non-quantifiable but notable results have arisen as our audit results are discussed in our monthly staff meetings.

These are:

❶ One of the most critical involves the large percentage of errors identified in the **infusion forms**, Form 2006, as noted in the 2015 audit. This is of particular concern as we begin to address the new cellular therapies infusion forms (Form 4006).

At the time of our Corrective Action Plan, we said "... the Stem Cell Lab will develop guidelines for staff to use in the accurate completion of infusion forms ... The Program (CIBMTR reporting staff) will utilize (the guidelines) to complete infusion forms in the future." The plan was for these guidelines to be available by the Spring of 2016. This has not yet been implemented, and while some progress has been made in this area, further improvements are being developed.

Another issue in the error-free completion of infusion forms turned out to be a problem with our recordkeeping for the CIBMTR Related Specimen Repository. We were aware of this issue previously, but we did not know the extent of the problem. This error was caused by poor communication

between reporting staff and the group responsible for taking the samples for shipment. This issue is being addressed and will no longer pose a problem.

❷ Another significant issue has been, as noted in the 2015 Audit Results, the **disease staging and assessment** in our reports. (These were noted as separate issues in the audit findings but the steps taken affect both issues.) In this area, the outlook is much more positive: the implementation of the disease staging/assessment worksheets designed by [redacted] (attached as an appendix) has resulted in a dramatic (though not as-yet quantified) improvement in the accuracy of our reporting, from Pre-TED through to yearly reports.

One reason for this is that staff new to CIBMTR reporting often used physicians' dictated notes for disease staging. The physicians' assessments are typically focused on patients' clinical status, not on CIBMTR reporting guidelines. Thus it has been common for, as an example, a multiple myeloma patient to be described as "in remission" in clinical notes when the patient's K/L ratio is well outside the normal range and no negative bone marrow biopsy has been obtained. Use of the disease staging worksheets has nearly eliminated such errors in ongoing reporting, and is currently being applied retrospectively in our audits of previously submitted reports.

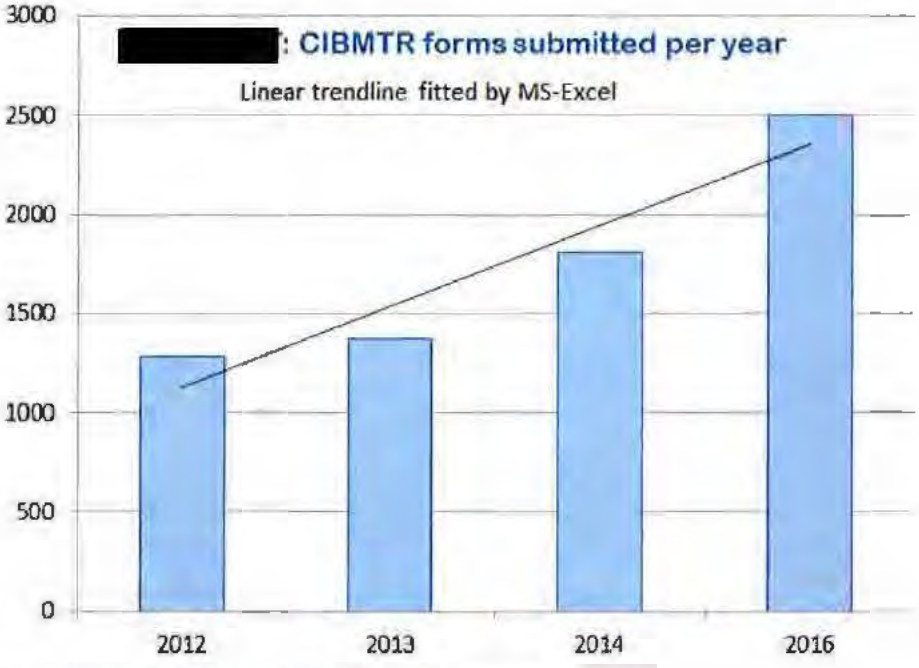


Figure 8: forms submitted/processed [redacted] by year

The CIBMTR reporting group's "continuing education" program of directed learning and follow-up lectures by and for staffers has also contributed significantly to staffers' awareness of key issues in reporting.

As noted above, our desired form-audit rate was 10% prior to the 2015 audit. Following the audit it was decided to audit at least 20% of forms as a beginning step. In our Corrective Action Plan we declared an intent to increase this to 30% in the future. Given our ongoing workload (see Figure 8, total forms newly submitted, and forms corrected and resubmitted during QA audits) this has not yet been implemented, though it is still actively planned.

❸ Again in the area of disease assessment and staging, but also directly relevant to a number of other key issues, is the familiarization of CIBMTR reporting staff with the **resources available** for guidance on the CIBMTR website. In the course of our monthly staff/quality assurance meetings, it became apparent that some newer staffers were unaware of the Forms Instruction Manual, the Data Management Guide, and the Retired Forms Manual.

Now these items are discussed often, both in the monthly staff meetings and in our new CIBMTR reporting continuing-education lectures. Staffers, even the newest, are now familiar with these reporting resources, which we are sure will significantly improve our data quality.

In summary:

Three major areas of systemic error were found during the 2015 audit and addressed in our 2015 Corrective Action Plan:

- Disease status
- Latest disease assessment
- HCT product and infusion

The first two, as described above, have been addressed through a vigorous three-part program of educational programs and reporting resources. While results are not yet quantifiable, we have no doubt that this has resulted in significant enhancement to our data quality. The data quality of our infusion reporting has been improved, but further enhancements remain to be developed and implemented.

Signatures

[redacted] Medical Director

[redacted] Nurse Manager, Operations; Clinic

Appendix A:

Disease staging/assessment worksheets:

- Pre-TED assessments and data
- Myeloma staging and status at assessment
- MDS staging and status at assessment
- Lymphoma staging and status at assessment
- AML staging and status at assessment

Name: _____ MRN: _____ Transplant date: _____ CRID#: _____

Pre-TED QA checklist

Height reported on the pre-ted:

_____ cm / in

SOURCE: _____

☐ QA'd by _____ QA date _____

CIBMTR wants the patient's height that was used for calculating doses of chemotherapy. If that height isn't documented in the chemotherapy treatment orders, report the patient's height just prior to the start of the preparative regimen (final pre-HSCT evaluation.) Report whole units, rounding as needed. Please note the SOURCE of the height reported.

Weight reported on the pre-ted:

_____ kg / lb

SOURCE: _____

☐ QA'd by _____ QA date _____

CIBMTR wants the actual weight of the patient immediately prior to the start of the preparative regimen, NOT the weight used in the chemo treatment orders. Report whole units (integers) and round if needed. Do not report adjusted body weight or ideal body weight. Please note the SOURCE of the weight reported.

KPS reported on the pre-ted:

_____ 100-0 in units of ten

SOURCE: _____

☐ QA'd by _____ QA date _____

If the patient was worked-up for transplant within one month of Day 0, report the KPS as of the workup date. If the workup is more than one month from Day 0, report the last documented KPS prior to the start of the prep regimen. Be sure to note the SOURCE of the KPS that is reported on the pre-TED.

Disease status prior to transplant :

Status reported: _____

☐ QA'd by _____ QA date _____

Each disease has specific grading/staging criteria; see the CIBMTR data management manual for full criteria. An abbreviated version is given on the disease-specific pages of the pre-TED. There are worksheets for multiple myeloma, AML, and MDS to ensure the correct status is chosen.

Chemo/XRT treatment orders :

Reported on pre-TED _____

_____

SOURCE: _____

☐ QA'd by _____ QA date _____

On the pre-TED, the **total prescribed** dosage of XRT and each chemo agent should be reported. Do not include support drugs (steroids for nausea, mesna, etc.) Drug doses must be reported in whole numbers. Example: busulfan at 0.8 mg/kg x 16 doses = 12.8 mg/kg total prescribed dose; we report 13 mg/kg. Report as either "mg/m^2," or "mg/kg." Convert if needed *(example: 80mg Campath in a pt with BSA of 1.9m^2 would be reported as 40mg/m^2)* If a drug is given before and after Day 0, only the dose given before Day 0 should be reported under "prep regimen." Doses given after Day 0 should be reported in 'Post-HSCT Therapy Planned.'

Name: _____ MRN: _____ Transplant date: _____ CRID#: _____

CIBMTR disease staging: multiple myeloma

Timepoint ___pre-HSCT ___100day ___6mo ___1yr >1yr (specify):_____

> ☆ **NOTE:** All criteria listed for the various response levels must be met PRIOR to the initiation of any new treatment for active, residual, or progressive disease (but not including maintenance medications.)
>
> ☆ Where criteria say "serum/urine," serum is needed. Urine tests are not necessary, but if done, they must be negative.

sCR

___ Normal FLC ratio (two consecutive tests) ***and***

___ No clonal cells in BM by IHC or IFE ***and***

___ Negative IFE, serum/urine (two consecutive tests) ***and***

___ Disappearance of soft tissue plasmacytomas ***and***

___ Less than 5% plasma cells in BM

CR

Standard MM

___ Negative IFE and serum/urine (two consecutive tests) ***and***

___ Disappearance of any soft tissue plasmacytomas (2 consecutive) ***and***

___ Less than 5% plasma cells in BM

Light-chain only

___ Normal FLC ratio (2 consecutive) ***and***

___ Neg urine IFE (2 consecutive) ***and***

___ Disappearance of any soft tissue plasmacytomas (2 consecutive) ***and***

___ No more than 5% plasma cells in BMBX

Non-secretory MM

___ Disappearance of any soft tissue plasmacytomas (2 consecutive) ***and***

___ No more than 5% plasma cells in BMBX

nCR

___ If bone survey was done (not required), no new/progressive bone lesions ***and***

___ M-protein detected on serum/urine by IFE, but NOT on SPEP/UPEP (two consecutive tests) ***and***

___ No more than 5% plasma cells in BM

VGPR

IF M-protein was measurable at DX

___ M-protein detected on serum/urine by IFE, but NOT on SPEP & UPEP (two consecutive) ***or***

___ At least 90% reduction in serum M-protein (two consecutive tests)

IF M-protein was NOT measurable at DX

___ At least 90% decrease in FLC ratio (two consecutive tests) ***or***

___ At least 90% reduction in serum M-protein (two consecutive tests)

PR

___ At least 50% reduction in serum M-protein ***and***

___ At least 90% reduction in urine M-protein OR less than 200mg/24hrs

SD

___ Does not meet criteria for CR, VGPR, or PR, and is not progressive/relapsed disease

Completed by: _____ Date: _____ Reviewed by: _____ Date: _____

Name: _____ MRN: _____ Transplant date: _____ CRID#: _____

CIBMTR disease staging: MDS

Timepoint ___pre-HSCT ___100day ___6mo ___1yr >1yr (specify):_____

CR

___ Bone marrow evaluation: <5% myeloblasts with normal maturation of all cell lines ***and***

___ Peripheral blood evaluation: HGB ≥ 11 g/dL untransfused without erythropoietic support ***and***

___ ANC ≥ 1000/mm^3 without myeloid growth factor support ***and***

___ Platelets ≥100,000/mm^3 without thrombopoietic support ***and***

___ 0% blasts in blood

All of these for minimum 4 weeks

Hematologic Improvement

Erythropoietic: ***or***

___ Hemoglobin increase of ≥ 1.5 g/dL untransfused ***or***

___ For RBC transfusions performed for HGB ≤9: reduction in RBC units transfused in 8 weeks by ≥4 units transfused in the 8 weeks prior to treatment

Platelets: ***or***

___ For pre-treatment count of > 20 x10^9, platelet absolute increase of ≥ 30 x10^9

___ For pre-treatment platelet count of < 20 x10^9, platelet absolute increase of ≥20 x10^9 ***and*** ≥100% increase from pre-treatment level

Neutrophils:

Neutrophil count increase of ≥ 100% from pre-treatment level *and* an absolute increase of 500/mm^3

One maintained at least 8 weeks

NR/SD

___ Does not meet the criteria for at least HI, but no evidence of disease progression to AML.

Progression from Hematologic Improvement

Requires at least one of the following in the absence of another explanation

___ ≥ 50% reduction from maximum response levels in granulocytes or platelets

___ Reduction in hemoglobin by ≥ 1.5 g/dL

___ Transfusion dependence

Relapse from CR

Requires at least one of the following:

___ Return to pre-treatment bone marrow blast percentage ***or***

___ Decrease of ≥ 50% from maximum response levels in granulocytes or platelets *or*

___ Transfusion dependence or hemoglobin level ≥ 1.5 g/dL lower than before therapy

Progression to AML

___ ≥ 20% blasts in the blood or bone marrow

Completed by: _____ Date _____ Reviewed by: _____ Date _____

Name: _____ MRN: _____ Transplant date: _____ CRID#: _____

CIBMTR Disease Staging: Lymphoma

Timepoint ___ pre-HSCT ___ 100day ___ 6mo ___ 1yr >1yr (specify): _____

CR

____ Complete disappearance of all known disease. For typically PET-avid lymphoma, a post treatment residual mass of any size is permitted as long as it is PET negative.
For variably PET-avid lymphoma, all lymph nodes and nodal masses must have regressed as measured by CT to < 1.5 cm (for nodes > 1.5 cm before therapy) or < 1 cm (for nodes 1.1 cm to 1.5 cm before therapy.

____ *Spleen/Liver*: not palpable; nodules disappeared

____ *Bone Marrow*: infiltrate cleared on repeat biopsy. If indeterminate by morphology, immunohistochemistry should be negative.

PR

____ ≥ 50% reductions in the greatest diameter of up to six of the largest dominant nodes or nodal masses and no new sites. For typically PET-avid lymphoma, post-treatment PET should be positive in at least one site. For variably PET-avid lymphoma, use CT criteria.

____ *Spleen/Liver*: ≥ 50% reduction in SPD of nodules; for single nodule, ≥ 50% reduction in greatest transverse diameter. No increase in size of liver or spleen.

____ *Bone Marrow*: irrelevant if positive prior to therapy. Cell type should be specified.

Stable Disease

____ Failure to attain CR, PR or PD

Progressive Disease

____ Any new lesion and/or > 50% increase in the least diameter of previously involved sites

____ *Spleen/Liver*: > 50% increase from nadir of any previous lesions

____ *Bone Marrow*: new or recurrent involvement

Not Tested / Unknown

____ The results from the line of therapy are unknown.

Not Assessed

____ No evaluation was performed for the line of therapy prior to the initiation of a new line of therapy or the start of the preparative regimen.

Completed by: _____ Date: _____ Reviewed by : _____ Date: _____

Name: _____ MRN: _____ Transplant date: _____ CRID#: _____

CIBMTR Disease Staging: (AML) acute myelogenous leukemia

Timepoint ___ pre-HSCT ___ 100day ___ 6mo ___ 1yr >1yr (specify): _____

PIF

____ The patient received treatment for AML but **never achieved complete remission at anytime.** PIF is not limited by the number of unsuccessful treatments; this disease status only applies to recipients who have *never been in complete remission.*

CR

Hematologic complete remission is defined as meeting all of the following response criteria for **at least four weeks.***

____ < 5% blasts in the bone marrow ***and***

____ No blasts with Auer rods ***and***

____ Normal maturation of all cellular components in the bone marrow ***and***

____ No extramedullary disease (e.g., CNS, soft tissue disease) ***and***

____ Neutrophils ≥ 1,000/µL ***and***

____ Platelets ≥ 100,000/µL ***and***

____ Transfusion independent

*If there is not a 4 week interval between completion of therapy and the pre-transplant disease assessment, CR should be reported as the status at transplant since it represents the "best assessment" prior to HSCT.

For recipients with MDS that transformed to AML

If the recipient has residual MDS following treatment for AML, report the AML disease status as either PIF or relapse.

Relapse (REL)

Relapse is defined as the recurrence of disease after CR, meeting the following criteria:

____ ≥ 5% blasts in the marrow or peripheral blood ***and***

____ Extramedullary disease ***and***

____ Disease presence determined by a physician upon clinical assessment

No Treatment

____ The recipient was diagnosed with acute leukemia and never received therapeutic agents; include patients who have received only supportive therapy, including growth factors and/or blood transfusions.

For Recipients with MDS that transformed to AML

"No treatment" may apply if the recipient's MDS was treated, then transformed to AML, and the recipient proceeded directly to transplant without receiving treatment for their AML.

Completed by: _____ Date: _____ Reviewed by : _____ Date: _____