STEM CELL LABORATORY (STCL)

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Stability Assessment of Clinical Products

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STCL-QA-008
STABILITY ASSESSMENT OF CLINICAL PRODUCTS

1 PURPOSE

1.1 The purpose of the STCL Stability Program is to annually monitor clinical products processed and cryopreserved in the Stem Cell Laboratory (STCL) to ensure that the thawed product continues to meet specifications for administration.

1.2 This procedure will define the samples, tests, and specifications used to monitor the stability of hematopoietic cellular products processed by the STCL. The stability assessment will be based on a comparison of analytical data before and after cryopreservation.

2 INTRODUCTION

2.1 The Stem Cell Laboratory was established in 1998 and is an integral part of the Adult and Pediatric Blood and Marrow Transplant Program (APBMT) at Duke University Medical Center. The STCL provides laboratory support for the recipients/donors being evaluated by these groups as well as preparation for administration of all hematopoietic cellular products including bone marrow, peripheral blood progenitor cells, cord blood, and donor lymphocytes.

2.2 The purpose of this stability program is to evaluate the cellular therapy products that have been administered and assess specific stability parameters. Two types of assessments are currently performed and included in this procedure: a **retrospective analysis** of products infused and a prospective analysis, of two specific products (see 2.3) that were dedicated to this aim, and will be preserved and then thawed at established intervals in the future.

NOTE: If the prospective stability program is successful, we may consider no longer do the retrospective analysis as part of the Stability Program.

2.3 Two different fresh clinical products were dedicated to be used in the stability program. One (1) sample came from an HPC, Apheresis product and one (1) sample came from an HPC, Marrow.

3 SCOPE AND RESPONSIBILITIES

3.1 This procedure applies when assessing stability for clinical products.

3.2 It is the responsibility of the STCL to provide stability data for review.

3.3 Quality Systems Unit (QSU) will review all data.

3.4 It is the responsibility of the Medical Director to review and approve the stability analysis.

4 DEFINITIONS/ACRONYMS

4.1	BM	Bone Marrow
4.2	CFU	Colony Forming Unit

4.3	DAT	Dextran Albumin Thaw
4.4	DLI	Donor Lymphocytes
4.5	HPC	Hematopoietic Progenitor Cells
4.6	N/A	Not Applicable
4.7	PBPC	Peripheral Blood Progenitor Cells
4.8	QSU	Quality Systems Unit
4.9	SCE	Stem Cell Enumeration
4.10	STCL	Stem Cell Laboratory
4.11	TNCC	Total Nucleated Cell Count

5 MATERIALS

5.1 N/A

6 EQUIPMENT

6.1 STCL EMMES Database

7 SAFETY

7.1 All laboratory employees must practice the rule of Universal Precautions, when handling all human blood, body fluids, and/or tissues as if they are infectious. The use of personal protective equipment (PPE) should provide appropriate protective measures to reduce or eliminate the risk of occupational exposure.

8 PROCEDURE

8.1 Retrospective Assessment of Stability

8.1.1 Hematopoietic cellular products used for the STCL stability program will include HPC, Marrow (BM) and Peripheral Blood Progenitor Cells (PBPC). These products will be assessed individually, by thaw type: 37°C Thaw or Dextran Albumin Thaw (DAT). The manner in which each product is thawed will determine which analytical assay data will be used to assess stability. Details on the analytical assays that will be used to assess stability are provided in **Table 8-1,** below:

Table 8-1: Analytical Methods and Specifications for Stability Testing

Assay	Comparison	Specification	Thaw Type
% Recovery TNCC	Comparing TNCC count (*post-thaw*) to data post-processing (*pre-cryo*)	Mean Recovery ≥70%	DAT and 37°C
CFU Growth	CFU growth of the thawed product	Mean Colony Number > 0	DAT
Post-Thaw Viability by Trypan blue ***(for information ONLY)***	Viability of the thawed product	Mean Viability ≥70%	DAT and 37°C
% Viability of the CD34 Population (SCE Flow Assay)	CD34 viability on the thawed unit	Mean Viability ≥50%	DAT

8.1.2 The Stem Cell Enumeration Assay (SCE) was implemented in the STCL in September 2012 to assess $CD34^+$ cells via flow cytometry, which includes reporting viability of the CD34 population. To ensure consistency in data reporting, only products infused in 2012 or later will be included in this stability assessment. Prior to 2012, products were assessed using the Procount Assay.

8.1.3 The mean, median, minimum, and maximum values for each of the parameters included in Table 8-1 will be reported by product and thaw type.

8.1.4 Results from these assays will also be examined in conjunction with product age range. For example, the mean % Recovery TNCC will be compared between products stored one to two years versus products stored two to three years.

NOTE: Most products are infused within a month of collection. The sample size for products stored for a longer duration is substantially smaller.

8.1.5 For all cellular products infused after five or more years of storage, engraftment data will be requested.

8.1.6 Review will be conducted of the data of all infusions for the previous year (retrospective) to look at engraftment*, as it is a informative parameter and provides valuable information regarding cellular therapy products. (*only ANC500, that is, days to engraftment or graft failure). Only the ANC500 parameter will be considered as it is a critical parameter of therapy efficacy).

8.1.7 As part of the *STCL-QA-008 (JA1) EMMES Stability Data Integrity Verification* process, a minimum of ten (10) laboratory files, in which data was included in the annual stability report that was generated and

provided by the EMMES Corporation, to check for accuracy in the STCL EMMES database.

8.1.7.1 The records selected will be checked for accuracy in the EMMES STCL database using source documentation for parameters that are used to generate the information in Table 8-1. (**NOTE**: A list of parameters is included in *STCL-QA-008 (JA1) EMMES Stability Data Integrity Verification)*

8.1.7.2 If corrections made are found to have a major effect on the data used to generate the annual report, a corrected report should be requested from the EMMES Corporation.

8.2 Annual Assessment of Stability (Prospective)

8.2.1 Two different fresh clinical products were obtained to be used in the stability program. One (1) sample came from an HPC, Apheresis product and one (1) sample came from an HPC, Marrow:

8.2.2 Each of the fresh products was diluted as follows:

8.2.2.1 **HPC, Apheresis** was diluted 1:1 containing 20 mL of apheresis sample + 16 mL of Plasmalyte-A + 4 mL of 25% human serum albumin +10% DMSO (*added before cryopreservation*). Total volume = 43 vials (*containing ~ 1 mL of sample/vial*).

8.2.2.2 **HPC, Marrow** was diluted 1:4 containing 5 mL of bone marrow (*post-processing on the SePAX 2 RM instrument*) + 16 mL of Plasmalyte-A + 4 mL of 25% human serum albumin + 10% DMSO (added before cryopreservation). Total volume = 25 vials (*containing ~ 1 mL of sample/vial*).

8.2.3 At the time the fresh samples were collected, testing was performed on each of the fresh samples to include cell count, viability (*trypan blue, for information only*), % viability of CD34+ population, and CFU assay.

8.2.4 All cryopreserved vials are stored in a designated vapor phase LN2 freezer.

8.2.5 One cryopreserved sample vial, from each product type (*HPC, Apheresis, and HPC, Marrow*), was dextran albumin thawed (DAT) to get baseline results (*after storage in vapor phase of LN2 for at least one month*).

8.2.6 Six months later, one cryopreserved sample vial, from each product type (*HPC, Apheresis, and HPC, Marrow*), was dextran albumin thawed (DAT) and tested to gather data for stability purposes.

8.2.7 Thereafter, one cryopreserved vial from one of the product types (*HPC, Apheresis or HPC, Marrow*) is DAT annually.

NOTE: Alternate the cellular product type that is thawed each year *(ie. thaw HPC, Apheresis sample one year than thaw HPC, Marrow sample the next year and so on).*

8.2.8 A final report will be generated following the annual assessment of stability. The report will summarize data and provide conclusions regarding the stability of clinical products.

8.2.9 Engraftment of all products cryopreserved and stored in the STCL, subsequently administered to patients, is also monitored on a continuous basis, reported and reviewed quarterly in the APBMT QA meeting.

Table 8-2: Analytical Methods and Specifications for Stability Testing

Assay	Comparison	Specification	Thaw Type
% Recovery TNCC	Comparing TNCC count (after thawing) to data post-processing (pre-cryopreservation)	Mean Recovery ≥70%	DAT and 37°C
CFU Growth	CFU growth of the thawed product	Mean Colony Number > 0	DAT
Post-Thaw Viability by Trypan blue *(for information ONLY)*	Viability of the thawed product	Mean Viability ≥70%	DAT and 37°C
% Viability of the CD34 Population (SCE Flow Assay)	CD34 viability on the thawed unit	Mean Viability ≥50%	DAT

8.3 Final Report

8.3.1 A final report will be generated following annual assessment of stability. The final report will include data analysis as described in this procedure.

8.3.2 Data in the final report will include mean, median, minimum, and maximum values for all parameters included in the analysis.

8.3.3 The "correction rate" calculated as a result of corrections identified during the data integrity verification process (STCL-QA-008 JA1), will be included in the final annual stability report.

9 RELATED DOCUMENTS/FORMS

9.1 STCL-QA-008 (JA1) EMMES Stability Data Integrity Verification

10 REFERENCES

10.1 FACT-Jacie International Standards for Hematopoietic Cellular Therapy. Product Collection, Processing, and Administration. 8th edition 8.0

11 REVISION HISTORY

Revision No.	Author	Description of Change(s)
04	B. Waters-Pick Isabel Storch	• Updated prospective procedure (8.2) to capture current practice and based on guidelines from the STCL's medical director • Engraftment revision of ANC500 only (section 8.1.6)

Signature Manifest

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Author

Name/Signature	Title	Date	Meaning/Reason
Barbara Waters-Pick (WATER002)		14 Mar 2023, 11:45:32 AM	Approved

Management

Name/Signature	Title	Date	Meaning/Reason
Barbara Waters-Pick (WATER002)		14 Mar 2023, 11:45:49 AM	Approved

Medical Director

Name/Signature	Title	Date	Meaning/Reason
Joanne Kurtzberg (KURTZ001)		14 Mar 2023, 05:12:27 PM	Approved

Quality

Name/Signature	Title	Date	Meaning/Reason
Isabel Storch De Gracia (IMS19)		28 Mar 2023, 11:57:47 AM	Approved

Document Release

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Sandra Mulligan (MULLI026)		29 Mar 2023, 09:56:25 AM	Approved