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Management Review and Responsibility

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COMM-QA-075
MANAGEMENT REVIEW AND RESPONSIBILITY

1 PURPOSE

1.1 This Standard Operating Procedure (SOP) provides an overview of how management reviews the quality management systems (QMS).

2 INTRODUCTION

2.1 This procedure outlines how management reviews the quality systems to ensure continuing adequacy, suitability, effectiveness and to evaluate the need for changes to the systems at planned intervals. Management reviews are also used to identify and assess opportunities to change quality policy and quality objectives to address resource needs and to look for opportunities to improve products.

3 SCOPE AND RESPONSIBILITIES

3.1 This SOP applies to all members of management with responsibilities related to the quality management system and processes.

3.2 Management Representative: Communicates with employees, as needed, regarding scheduled management reviews. Reviews and signs off on reports or minutes, if applicable.

3.3 QSU: Facilitates the development, implementation, and maintenance of effective QMS. Provides and compiles data related to the quality management systems, as needed, for the management reviews. Reviews and signs off on reports or minutes, if applicable.

4 DEFINITIONS/ACRONYMS

4.1 Adequacy: Sufficient to satisfy a requirement or meet a need. A quality management system should be capable of satisfying applicable requirements including those specified by the organization, the customer, and any applicable standards and/or regulations.

4.2 APBMT: Adult and Pediatric Blood and Marrow Transplant Program

4.3 BLA: Biologics License Application

4.4 CAP: College of American Pathologists

4.5 CCBB: Carolinas Cord Blood Bank

4.6 Complaint: An event in which customer expectations are not met. Complaints are also documented when a vendor or supplier fails to meet the expectations of the program/manufacturer. Complaints may or may not also be classified as deviations.

4.7 DCO: Document Control Operations

4.8 Effectiveness: Adequate to accomplish a purpose; producing the intended or expected result. A quality management system should enable the organization

to meet its own needs, those of the customer and those of other interested parties.

4.9 FACT: Foundation for the Accreditation of Cellular Therapy

4.10 FDA: Food and Drug Administration

4.11 GvHD: Graft versus Host Disease

4.12 JMR: Joint Management Review

4.13 MasterControl: An electronic 21 CFR compliant document management system.

4.14 Out of Specification Result: Any measurement or assay result that falls outside of established specifications or other established acceptance criteria as defined by the Program.

4.15 QA: Quality Assurance

4.16 QMP: Quality Management Plan

4.17 Quality Management System (QMS): Set of interrelated or interacting elements used to direct and control how quality policies are implemented and quality objectives are achieved.

4.18 QSU: Quality Systems Unit

4.19 SOP: Standard Operating Procedure

4.20 STCL: Stem Cell Laboratory

4.21 Suitability: The quality of having properties that are right for the specific purpose. A quality management system should be able to sustain the current performance levels of the organization utilizing an acceptable amount of organizational resources.

5 MATERIALS

5.1 N/A

6 EQUIPMENT

6.1 Computer access to MasterControl

7 SAFETY

7.1 N/A

8 PROCEDURE

8.1 General

8.1.1 Management and Program Director(s) review information at multiple time-points throughout the year. These reviews are done via quarterly reports, and/or regular meetings, and/or through annual process and product reviews.

8.1.2 At a minimum, QSU and the Program Director(s) will document these reviews through signed reports and/or meeting minutes.

8.1.3 Should corrective or preventive actions result from these reviews/reports/meetings, these action items will be documented in the Event Management System per COMM-QA-076 *Corrective and Preventive Actions*.

8.1.4 It is the ultimate responsibility of Management to ensure that action items are addressed and that the in-place processes and systems are functioning appropriately with respect to the program.

8.2 Adult and Pediatric Blood and Marrow Transplant Program (APBMT)

8.2.1 The APBMT clinical program is accredited by the Foundation for the Accreditation of Cellular Therapy (FACT). The program reviews its clinical quality indicators in quarterly meetings with the APBMT Quality Assurance (QA) Committee comprised of the Program Director(s) and Management Representatives or designees. These meetings are documented with minutes, which are reviewed and signed by the Program Director(s) and QSU.

8.2.2 The QSU provides annual summary reports on the performance of the Quality Management Plan (QMP) to the QA Committee. Annual summary reports are reviewed and signed by the Program Director(s) and QSU.

8.2.3 The following clinical and nonclinical inputs are reviewed:

Clinical (at defined time points):

Time to engraftment

Catheter infections

Acute and chronic Graft versus Host Disease (GvHD)

Overall mortality and survival

Treatment related, non-relapse, mortality (TRM)

Incidence of Cytokine Release Syndrome (CRS)

Incidence of Neurotoxicity

Event Free Survival (EFS)

Non-Clinical:

Facilities

Equipment Management

Inventory Control/Supply Management

Document Control/Records Management

Event Management

Process Management and Control

Quality System Audits and Supported Inspections

8.2.4 It is expected that the Program Director(s) and Management Representatives in this meeting will disseminate information from the quarterly meetings and annual reports to applicable staff.

8.2.5 Conversely, it is expected that the Management Representative's staff will alert them of concerns in the program/process, and the Management Representative will bring those concerns to the meetings for discussion.

8.2.6 Flowchart 1 describes how reporting information moves through the APBMT program.

8.3 Stem Cell Laboratory (STCL)

8.3.1 The STCL program is accredited by the Foundation for the Accreditation of Cellular Therapy (FACT), College of American Pathologists (CAP), and is a processing laboratory for the clinical program. The STCL is also CLIA certified. The program reviews some inputs in quarterly meetings with the APBMT QA Committee. These meetings are documented with minutes, which are reviewed and signed by the Program Director(s) and QSU.

8.3.2 The QSU provides annual summary reports on the performance of the QMP to the QA Committee. Annual summary reports are reviewed and signed by the Program Director(s) and QSU.

8.3.3 The following inputs are reviewed:

Facilities

Equipment Management

Inventory Control/Supply Management

Document Control/Records Management

Event Management

Process Management and Control

Quality System Audits and Supported Inspections

8.3.4 It is expected that the Program Director(s) and Management Representatives will disseminate information from the quarterly meetings and annual reports to applicable staff.

8.3.5 Conversely, it is expected that the Management Representative's staff will alert them of concerns in the program/process, and the Management Representative will bring those concerns to the meetings for discussion.

8.3.6 Flowchart 1 describes how reporting information moves through the STCL program.

8.4 Robertson GMP Laboratory

8.4.1 The Robertson GMP Laboratory is a cGMP manufacturing facility accredited by the Foundation for the Accreditation of Cellular Therapy (FACT). This program reviews its inputs, including clinical quality indicators, such as adverse events and outcome analysis, as applicable,

quarterly. These reviews occur in quarterly meetings and/or minutes/reports, which are reviewed by the Program Director(s) and QSU.

8.4.2 The following inputs are reviewed:

Personnel/Training

Facilities

Environmental Monitoring

Equipment Management

Inventory Control/Supply Management

Document Control/Records Management

Process Management and Control

Adverse Events

Outcome Analysis

Product Release

Event Management

Quality System Audits and Supported Inspections

8.4.3 It is expected that the Program Director(s) and Management Representatives will disseminate information from the quarterly meetings, metrics, and key performance indicators to applicable staff.

8.4.4 Conversely, it is expected that the Management Representative's staff will alert them of concerns in the program/process, and the Management Representative will elevate those concerns for discussion, as applicable.

8.4.5 Flowchart 1 describes how reporting information moves through the Robertson GMP Laboratory.

8.4.6 If required, Joint Management Review (JMR) meetings with a Sponsor shall be held. Content and frequency will be agreed upon with the entities (MC3 and the Sponsor) and documented either in the Quality Agreement or a product-specific SOP.

8.4.6.1 JMR meetings for the Robertson GMP Laboratory are currently required for the RETHYMIC® project. Key performance indicators and metrics will be assessed and analyzed per SOP GMP-QA-024 *Metrics and Key Performance Indicators (KPI) for RETHYMIC*.

8.4.6.2 Environmental monitoring data is trended and analyzed per GMP-SOP-099 *Environmental Monitoring Data Trending in the Robertson GMP Laboratory*. Summaries of these outcomes are shared during JMR.

8.4.6.3 JMR meetings with Sumitomo Pharma America, Inc. also include other topics and processes beyond those required in

GMP-QA-024 *Metrics and Key Performance Indicators (KPI) for RETHYMIC.*

8.4.6.4 Minutes will be documented.

8.5 Carolinas Cord Blood Bank (CCBB)

8.5.1 The Carolinas Cord Blood Bank (CCBB) is a cGMP manufacturing facility accredited by the Foundation for the Accreditation of Cellular Therapy (FACT), College of American Pathologists (CAP), and approved by the United States Food and Drug Administration (FDA) to manufacture DUCORD under a Biologics License Application (BLA). The program reviews its inputs in regular meetings between QSU and executive management, quarterly reports, and an annual product review (per *CCBB-QA-021 Annual Product Review*).

8.5.2 The following inputs are reviewed in the quarterly reports:

Personnel/Training

Facilities

Environmental Monitoring

Equipment Management

Inventory Control/Supply Management

Document Control/Records Management

Process Management and Control

Product Release

Event Management

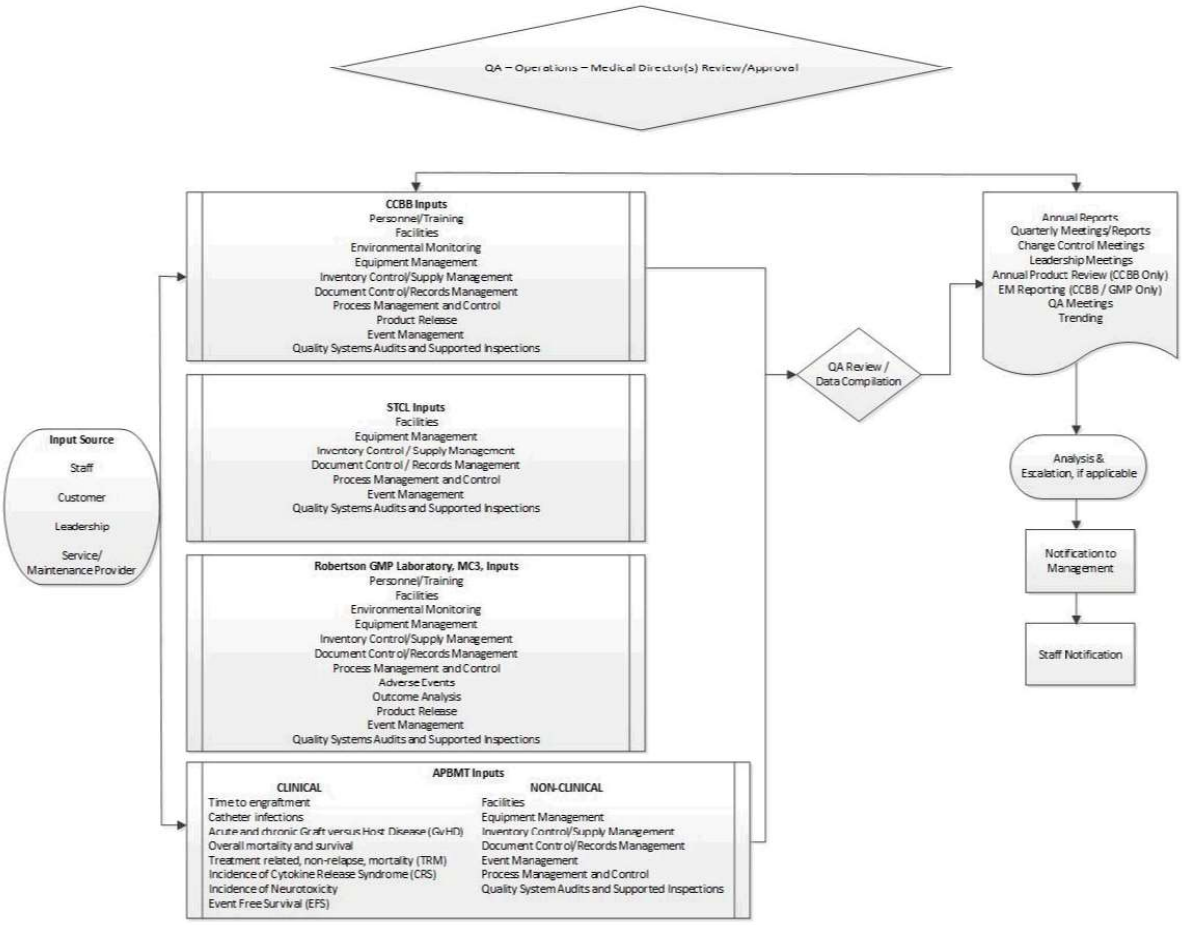
Quality System Audits and Supported Inspections

8.6 It is expected that the Program Director(s) and Management Representatives will disseminate information from the quarterly reports to applicable staff.

8.7 Conversely, it is expected that the Management Representative's staff will alert them of concerns in the program/process, and the Management Representative will elevate those concerns for discussion, as applicable.

8.8 Flowchart 1 describes how reporting information moves through the Carolinas Cord Blood Bank.

8.9 Flowchart 1 below describes how reporting information moves through each program.



9 RELATED DOCUMENTS/FORMS

9.1 APBMT-COMM-027 Adult and Pediatric Blood and Marrow Transplant Program Quality Management Plan

9.2 CCBB-QA-014 CCBB Quality Management Plan

9.3 CCBB-QA-021 Annual Product Review

9.4 COMM-QA-076 Corrective and Preventive Actions

9.5 GMP-SOP-099 Environmental Monitoring Data Trending in the Robertson GMP Laboratory

9.6 GMP-QA-001 Robertson GMP Laboratory Quality Management Plan

9.7 GMP-QA-024 Metrics and Key Performance Indictors (KPI) for RETHYMIC

9.8 STCL-QA-006 Stem Cell Laboratory Quality Management Plan

10 REFERENCES

10.1 FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration, Current Edition

10.2 NetCord-FACT International Standards for Cord Blood Collection, Banking, and Release for Administration, Current Edition

10.3 FACT Common Standards, Current Edition

11 REVISION HISTORY

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10	Carlos Cruz	Section 8.4.6.3 – Replaced “ENZYVANT” by “Sumitomo Pharma America, Inc.”

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