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**DOCUMENT TITLE:**  
Risk Assessment Procedure  

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COMM-QA-077
RISK ASSESSMENT PROCEDURE

1 PURPOSE
1.1 The purpose of this procedure is to describe the assessment of risk and resulting mitigation activities/control actions for events, including but not limited to, Deviations/Investigations, Product Complaints, and Customer Complaints.

2 INTRODUCTION
2.1 A risk assessment system is necessary to adequately assess the potential impact of an event and what (if any) corrective and preventive actions (CAPA) may be necessary to effectively address the event.

3 SCOPE AND RESPONSIBILITIES
3.1 This procedure is referenced when assessing risk for events associated with the Carolinas Cord Blood Bank (CCBB), Stem Cell Laboratory (STCL), Adult and Pediatric Blood and Marrow Transplant Programs, Molecular Products and Cellular Therapies (MPACT), and the Robertson GMP Laboratory.

3.2 Responsibilities for assessing risk are shared among all staff involved in writing or reviewing Deviations/Investigations, Product Complaints, and Customer Complaints. Approval of any associated risk assessment is implicit with electronic signatures in MasterControl. Section 3.3 below details specific responsibilities for the different aspects of risk assessment.

3.3 Responsibilities
3.3.1 Operations/Manufacturing
The Operations department is responsible for:
- Participating in risk management assessments and discussions.
- Reviewing/approving planned CAPA and recommending changes, as necessary.
- Reporting new risks, which may result from a suggested CAPA.
- Completing assigned CAPA tasks and reporting the status/completion of CAPA.
- Reviewing and recommending changes on the overall CAPA based on review of effectiveness checks.
- Participate in determining if any external reporting is required to outside vendors/sponsors of events that may impact products related to their organization.

3.3.2 Quality Systems Unit (QSU)
Quality Assurance (QA) is responsible for:
- Participating in risk management assessments and discussions.
- Maintaining this risk management procedure.
- Tracking open CAPA.
- Facilitating risk assessment activities.
- Coordinating with Subject Matter Experts (SME) to review and recommend changes on CAPA, as applicable.
- Reviewing and recommending changes on the overall CAPA based on review of effectiveness checks.
- Ensuring implementation of CAPA recommendations.
- Determining if any external reporting is required to outside vendors/sponsors of events that may impact products related to their organization.

3.3.3 Medical Director (MD)

Medical Director is responsible for:
- Participating in risk management assessments and discussions.
- Reporting new risks that can adversely affect a patient's health or medical outcome as the result of a planned CAPA.
- Reviewing/approving planned CAPA and recommending changes as necessary.
- Completing assigned CAPA tasks and reporting the status/completion of assigned CAPA.
- Reviewing and recommend changes on the overall CAPA based on review of effectiveness checks.

3.3.4 Subject Matter Experts (SME)

Subject Matter Experts are responsible for:
- Participating in risk management assessments and discussions as needed based on their expertise of the product and topic of evaluation.

3.3.5 Executive Management (Operations/Medical Director and Quality Director)

Executive Management is responsible for:
- Reviewing and approving final CAPA plans.
- Reviewing and approving additional resources that may be requested.
- Reviewing and approving effectiveness checks.

4 DEFINITIONS/ACRONYMS

4.1 CAPA: Corrective and Preventive Action
4.2 CBU: Cord Blood Unit
4.3 CCBB: Carolinas Cord Blood Bank
4.4 Corrective Action: Action to eliminate the cause of a detected event or deviation. Corrective action is taken to prevent the recurrence of a problem
4.5 DCO: Document Control Operations
4.6 Effectiveness Check: Method or data used to determine effectiveness of a CAPA.
4.7 **Events**: Examples may include planned and unplanned deviations from SOP, customer complaints, out of specification or unexpected results, internal and external audit findings, reoccurring problems/trends.

4.8 **External Reporting**: The dissemination of information to an outside party as required by any applicable regulation, standard, contract or quality agreement. This could include reporting to FDA, an external sponsor, or another entity.

4.9 **Final Quality Approval**: The point in the review process after which an event report is considered to be complete/final and in a form that may be disseminated to an outside party as a complete/final document.

4.10 **MasterControl**: An electronic 21 CFR compliant data management system.

4.11 **MD**: Medical Director

4.12 **Preventive Action**: An activity or step implemented to prevent the initial occurrence of a problem, based on an understanding of the product or process.

4.13 **QA**: Quality Assurance

4.14 **QSU**: Quality Systems Unit

4.15 **Risk**: The combination of the probability of occurrence (Rate of Occurrence and/or Likelihood of Recurrence) of harm and the impact (Risk Severity) of that harm.

4.16 **Risk Assessment**: A systematic process comprised of a Risk Analysis and Risk Evaluation.

4.17 **Risk Classification**: The process of categorizing the risk against established criteria.

4.18 **Risk Evaluation**: The process of comparing the estimated risk against given risk criteria to determine the acceptability of the risk.

4.19 **Risk Management**: A systematic application of management policies, procedures and practices to the tasks of analyzing, evaluating, controlling and monitoring the risk.

4.20 **STCL**: Stem Cell Laboratory

4.21 **Subject Matter Expert**: A person who is an authority in a particular area or topic, based on training and experience.

4.22 **SQIPP**: An acronym referring to Safety, Quality, Identity, Potency, Purity of a product.

5 **MATERIALS**

5.1 Supporting reports/documents; e.g., product recall notification, email correspondences.

6 **EQUIPMENT**

6.1 Computer access to MasterControl

7 **SAFETY**

7.1 N/A
8 PROCEDURE

8.1 Risk Matrix

8.1.1 The following tables should be used, as described in this procedure, to identify the risk associated with an applicable event or investigation.

8.1.1.1 When a risk assessment is performed for out of compliance events (ex. Deviations/Investigations, Complaints), the risk score associated with that event is captured on the relevant form (Deviation and Investigation Report, Complaint).

### Risk Classification Matrix

<table>
<thead>
<tr>
<th>Rate of Occurrence and/or Likelihood of Recurrence</th>
<th>Negligible - 1</th>
<th>Marginal - 2</th>
<th>Moderate - 3</th>
<th>Serious - 4</th>
<th>Critical - 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequent - 5</td>
<td>5</td>
<td>10</td>
<td>15</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>Probable - 4</td>
<td>4</td>
<td>8</td>
<td>12</td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>Occasional - 3</td>
<td>3</td>
<td>6</td>
<td>9</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Low - 2</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Improbable - 1</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

Table 1
Risk Severity or Risk Consequence

<table>
<thead>
<tr>
<th>Severity</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical - 5</td>
<td>Resulted in or contributed to death; Could have resulted in death had the event not been caught. SQIPP likely to be affected</td>
</tr>
<tr>
<td>Serious - 4</td>
<td>Resulted in or could have resulted in a severe reaction or injury that is life threatening which may lead to permanent impairment, surgical or other medical intervention, extensive trauma and/or hospitalization had the event not been caught. SQIPP likely to be affected</td>
</tr>
<tr>
<td>Moderate - 3</td>
<td>Resulted in or could have resulted in transient or persistent medical reaction or injury that is not life threatening but required monitoring and/or intervention to prevent harm had the event not been caught. SQIPP not likely to be affected</td>
</tr>
<tr>
<td>Marginal - 2</td>
<td>Resulted in or would have resulted in no more than minimal harm to patient nor additional monitoring of patient had the event not been caught. SQIPP not likely to be affected</td>
</tr>
<tr>
<td>Negligible - 1</td>
<td>Resulted in or would have resulted in no harm to patient nor additional monitoring of patient had the event not been caught. SQIPP not affected</td>
</tr>
</tbody>
</table>

*If the event did not reach the patient, consider potential patient impact had the event not been caught and assign risk accordingly.

Table 2

<table>
<thead>
<tr>
<th>Rate of Occurrence and/or Likelihood of Recurrence</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequent - 5</td>
<td>Occurs at a high rate or likely to recur at a high rate.</td>
</tr>
<tr>
<td>Probable - 4</td>
<td>Occurs at a moderate rate or likely to recur at a moderate rate.</td>
</tr>
<tr>
<td>Occasional - 3</td>
<td>Occurs at a low rate or likely to recur at a low rate.</td>
</tr>
<tr>
<td>Low - 2</td>
<td>Unlikely to occur or recur.</td>
</tr>
<tr>
<td>Improbable - 1</td>
<td>Extremely unlikely to occur or recur.</td>
</tr>
</tbody>
</table>

Table 3
### Table 4

<table>
<thead>
<tr>
<th>Risk Score (Severity Multiplied by Rate)</th>
<th>Recommended Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>No further action is necessary.</td>
</tr>
<tr>
<td></td>
<td>No CAPA required but acceptable if deemed necessary.*</td>
</tr>
<tr>
<td>4-6</td>
<td>Evaluate the current controls and determine whether additional efforts can be made to bring the risk of harm to as low as reasonably possible.</td>
</tr>
<tr>
<td></td>
<td>CAPA optional but recommended if severity is Serious/Critical and CAPA is feasible for the root cause identified.*</td>
</tr>
<tr>
<td>8-10</td>
<td>Additional effort should be considered to bring risk of harm as low as reasonably possible.</td>
</tr>
<tr>
<td></td>
<td>CAPA optional but recommended if severity is Serious/Critical and CAPA is feasible for the root cause identified.*</td>
</tr>
<tr>
<td>12-15</td>
<td>Additional efforts should be made to reduce the risk of harm to as low as reasonably possible.</td>
</tr>
<tr>
<td></td>
<td>CAPA Mandatory</td>
</tr>
<tr>
<td>16-25</td>
<td>Additional efforts are required to reduce the risk of harm to as low as reasonably possible.</td>
</tr>
<tr>
<td></td>
<td>CAPA Mandatory</td>
</tr>
</tbody>
</table>

*When determining if a CAPA is necessary, consideration should also be given to how likely a subsequent event is to be detected.

#### 8.2 Risk Evaluation

8.2.1 Trained personnel, when completing and/or reviewing MasterControl documentation for events, including but not limited to Deviations/Investigations, Product Complaints and Customer Complaints, will use the Risk Classification Matrix (Table 1) to make an evaluation of risk and determine the potential need for a CAPA.

8.2.2 Definitions for each category under Severity and Occurrence in the Risk Classification Matrix are provided Tables 2 and 3.

8.2.3 As defined in Table 4, the score on each side of the Risk Classification Matrix is multiplied to define the overall risk score and categorize the event. This table also provides recommended actions, including when CAPAs are necessary.

8.2.4 Action(s) taken to address the root cause of a problem or prevent initial occurrence of a problem is a CAPA regardless of the risk evaluation score assigned (ex. additional training or changes to procedures, processes or systems). Specific consideration for a CAPA should be made for any event scored as critical even if the rate of occurrence or recurrence is minimized. If no CAPA is deemed necessary, an explanation with rationale should be provided in the associated event form.
8.2.5 In addition to risk driven CAPA initiation, a CAPA may be initiated in response to internal/external audit findings and identified trends.

8.2.6 If a CAPA is determined to be warranted, a specific plan for the implementation, monitoring, and follow-up (effectiveness checks) will be drafted for approval by Executive Management, using COMM-QA-076 FRM1 CAPA Report.

8.2.7 Refer to procedure COMM-QA-076 Corrective and Preventive Actions for details on completing the MasterControl CAPA form.

8.3 Maintenance of Records

8.3.1 All records are maintained according to the associated Program Records Management or Records Retention procedure(s).

9 RELATED DOCUMENTS/FORMS

9.1 CCBB-QA-011 Licensed Biological Product Deviation (BPD)
9.2 CCBB-QA-020 Handling Out of Specifications and Unexpected Results
9.3 CCBB-QA-026 Post-marketing Receipt of Adverse Experiences
9.4 COMM-QA-042 Deviations and Investigations
9.5 COMM-QA-076 Corrective and Preventive Actions
9.6 COMM-QA-076 FRM1 CAPA Report
9.7 STCL-QA-007 Non-Conforming Products – Receipt, Processing, Distribution, and Disposition

10 REFERENCES

10.1 21 CFR 211.22(a) – Responsibilities of a Quality Control Unit
10.2 21 CFR 211.100 – Written Procedures; Deviations
10.3 21 CFR 1271 – Human Cells, Tissues, and Cellular and Tissue-Based Products
10.4 FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration; Current Edition
10.5 FACT Common Standards for Cellular Therapies; Current Edition
10.6 NetCord-FACT International Standards for Cord Blood Collection, Banking and Release for Administration; Current Edition

11 REVISION HISTORY

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<th>Revision No.</th>
<th>Author</th>
<th>Description of Change(s)</th>
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<tr>
<td>04</td>
<td>R. Bryant</td>
<td>Updated to align with concurrent changes to CAPA and Deviation and Investigation SOPs and associated forms.</td>
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## Signature Manifest

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All dates and times are in Eastern Time.

### COMM-QA-077 Risk Assessment Procedure

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#### Medical Director

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