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Deviations and Investigations

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## **COMM-QA-042**

### **DEVIATIONS AND INVESTIGATIONS**

#### **1 PURPOSE**

- 1.1 To describe the procedure for reporting, documenting, approving, and tracking events occurring outside of Standard Operating Procedure (SOP), current Good Manufacturing Practices (cGMP), current Good Laboratory Practices (cGLP), Good Tissue Practices (cGTP), and/or current Good Clinical Practices (cGCP).

#### **2 INTRODUCTION**

- 2.1 An event management system is necessary to promptly alert the Quality Systems Unit (QSU) and applicable parties of the event, document details of the event including root cause, risk assessment, investigation, and action(s) taken, and facilitate timely closure of events.

#### **3 SCOPE AND RESPONSIBILITIES**

- 3.1 This procedure is referenced when reporting, investigating, documenting, approving, and tracking the event(s) via MasterControl, for the Carolinas Cord Blood Bank (CCBB), Stem Cell Laboratory (STCL), Adult and Pediatric Blood and Marrow Transplant (APBMT) Programs, and the Robertson GMP Laboratory.
- 3.2 Refer to program-specific OOS procedures (e.g., *CCBB-QA-020 Handling Out of Specifications (OOS) and Unexpected Results*; *STCL-QA-007 Non-Conforming Products – Receipt, Processing, Distribution, and Disposition*; *GMP-QA-003 Non-Conforming Products and Out of Specification Results*; *GMP-QA-016 Out of Specification Investigations for RETHYMIC*) for details on evaluating and documenting these types of events.
- 3.3 Refer to program-specific procedures for handling Adverse Experiences (AEs) (e.g., *CCBB-QA-026 Postmarketing Receipt of Adverse Experiences*; *GMP-QA-005 Evaluation of Complaints and Adverse Experiences*; *STCL-DIST-006 FRM2 Adverse Event Reporting Form*).
- 3.4 Program personnel are responsible for promptly notifying their Supervisor/Manager when an event or deviation from a policy, process, or procedure is identified, to allow the initiation of the event to occur within three business days of discovery.
- 3.5 Trained personnel are responsible for completing *COMM-QA-042 FRM4 Deviation and Investigation Report* and modifying step routes as needed to ensure applicable Supervisor/Manager, Medical/Program Director, relevant SMEs, and program-specific approving physician, when applicable, are included. Responsibilities also include bracketing of product(s) and external sponsor notification consistent with the current quality agreement, in conjunction with input from QSU and Medical Director, as applicable.
- 3.6 The Medical/Program Director reviews and approves or rejects, for further clarification, all Deviations/Investigations.

### 3.7 QSU responsibilities include:

- 3.7.1 Review and approval of all Deviations/Investigations for completeness and appropriate level of detail.
- 3.7.2 Verify bracketing as necessary to assess quality impact to product(s).
  - 3.7.2.1 Verify appropriate quarantine of associated product(s), as applicable, until the investigation is complete and the product(s) are approved by QSU to be released from quarantine.
  - 3.7.2.2 Utilize available databases (i.e., EMMES, CordSource, MasterControl) to prevent release/upload of associated product(s), as necessary, while an investigation is ongoing.
- 3.7.3 QSU must ensure there is no product impact from any deviations/investigations before releasing a product and/or signing a Certificate of Analysis. Although most commonly the events are fully closed and approved, it is acceptable for this process to occur outside of MasterControl if necessary due to time constraints. A MasterControl event must be initiated for reference, and QSU should be consulted to identify an appropriate way to document the situation and assessments in real time. The documentation, such as a Memo or an expanded description in the associated batch record, must include a product impact assessment, prior to issuing final quality assurance (QA) approval for release.
- 3.7.4 Monitor the Deviation/Investigation system to facilitate timely closure of reports.
- 3.7.5 Perform quarterly tracking and trending Initiate investigations based on identified trends, as applicable.
- 3.7.6 Provide status updates to applicable Supervisor/Managers, Project Coordinators, and Medical/Program Directors, in an effort to facilitate thorough and timely closure of Deviations/Investigations and CAPAs and to communicate identified trends.

## 4 DEFINITIONS/ACRONYMS

- 4.1 **AEs:** Adverse Experiences
- 4.2 **APBMT:** Adult and Pediatric Blood and Marrow Transplant
- 4.3 **BPDR:** Biological Product Deviation Report
- 4.4 **Bracketing:** The practice of performing an expanded product impact assessment on all products that were manufactured during the timeframe in which the deviation occurred; e.g., failures in critical equipment, such as leaks and repairs to a HEPA filter. Bracketing will include tracking of products manufactured back to the last successful equipment monitoring to determine impact on product.
- 4.5 **CAPA:** Corrective and Preventive Action
- 4.6 **Corrective Action:** Action taken to eliminate the cause of a detected event or deviation. Corrective action is taken to prevent the recurrence of a problem.

Please note that any action taken to address the cause of a problem is part of a CAPA (ex. additional training or changes to procedures, processes or systems).

- 4.7 **cGCP:** current Good Clinical Practices
- 4.8 **cGLP:** current Good Laboratory Practices
- 4.9 **cGMP:** current Good Manufacturing Practices
- 4.10 **cGTP:** current Good Tissue Practices
- 4.11 **CBUs:** Cord Blood Units
- 4.12 **CCBB:** Carolinas Cord Blood Bank
- 4.13 **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.
- 4.14 **Containment Actions:** Sorting or immediate assessment to segregate nonconforming parts from conforming parts.
- 4.15 **Correction:** Action to eliminate a detected nonconformity.
- 4.16 **DCO:** Document Control Operations
- 4.17 **Deviation and Investigation Report:** Form used to document the findings of an initiated deviation
- 4.18 **Events:** Examples may include planned and unplanned deviations from SOP, customer complaints, out of specification or unexpected results, internal and external audit findings, or reoccurring problems/trends.
- 4.19 **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.
- 4.20 **Final Quality Approval:** The point in the review and approval process after which a Deviation and Investigation report is considered to be complete/final and in a form that may be disseminated to an outside party as a complete/final document.
- 4.21 **HEPA:** high-efficiency particulate air
- 4.22 **Investigation:** A thorough and comprehensive collection of information to support resolution of the event identified with the goal to identify the root cause of the event.
- 4.23 **ISBT label:** is a standard labeling format that ensures a consistent layout of critical information for product labels.
- 4.24 **MasterControl:** An electronic 21 CFR compliant data management system that maintains all events and associated investigations.
- 4.25 **Nonconformity:** A departure of a quality characteristic from its intended level or state that occurs with severity sufficient to cause an associated product or service not to meet a specification requirement. A nonconformance may or may not be classified as a deviation.

- 4.26 **Out of Specification (OOS) Result:** Any measurement or assay result that falls outside of established specifications or other established acceptance criteria as defined by product specifications.
- 4.27 **PBMT:** Pediatric Blood and Marrow Transplant
- 4.28 **Planned Deviation:** A deviation from a policy, process, or procedure that is anticipated and requires prior approval by a designated Physician or Medical/Program Director and QSU.
- 4.29 **Preventive Action:** An activity or step implemented to prevent the initial occurrence of a problem, based on an understanding of the product or process. Please note that any action taken to prevent initial occurrence of a problem is part of a CAPA (ex. additional training or changes to procedures, processes or systems)
- 4.30 **QA:** Quality Assurance. The sum of activities planned and performed to provide confidence that systems and their elements that influence the quality of a product are functioning as expected and relied upon.
- 4.31 **QC:** Quality Control. Includes the activities and controls used to determine the accuracy of the establishment's equipment and operations in manufacturing and product release.
- 4.32 **QSU:** Quality Systems Unit
- 4.33 **Repeat Deviation:** A deviation that re-occurs within a 2-year period. Repeat deviations indicate that the root cause of previous, similar deviations have not been correctly identified or remediated, or actions had not been taken in a timely manner to effectively address the root cause.
- 4.34 **Root Cause:** An identified reason for the presence of a defect, problem, deviation, or nonconformity, the most basic reason which, if eliminated, would prevent recurrence. The root cause can also be defined as the source or origin of an event.
- 4.35 **SOP:** Standard Operating Procedures
- 4.36 **SQIPP:** Safety, Quality, Identity, Purity, Potency
- 4.37 **STCL:** Stem Cell Laboratory
- 4.38 **Unplanned Deviation:** An unexpected event or error that deviates from a policy, process, or procedure; e.g., written procedure or instructions not followed, failure to sample and test, improper material storage, use of equipment/reagents outside of calibration/expiration date.

## 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 Event Notification

- 8.1.1 Personnel notify their Supervisor/Manager upon discovery of an event or deviation from a policy, process, or procedure.
- 8.1.2 Supervisor/Manager ensures immediate containment action, if applicable, is initiated and notifies the QSU and Medical/Program Director, as necessary. Quality agreements should be consulted too, in conjunction with the QSU, in order to determine if immediate external sponsor reporting is required.
- 8.1.3 QSU will run reports weekly of all new events initiated in the preceding week. This report will minimally be distributed to QSU management.

### 8.2 Time Requirements and Report Monitoring

- 8.2.1 Trained personnel initiate *COMM-QA-042 FRM4 Deviation and Investigation Report* via MasterControl in a timely manner, within three business days, upon the discovery of a deviation.
  - 8.2.1.1 If more than 3 business days have elapsed before the initiation of a deviation/investigation report in MasterControl, an explanation of why the launching of the deviation/investigation report was delayed past the target timeframe, is required within the investigation section of the associated deviation/investigation report.
  - 8.2.1.2 For CCBB, cord blood units will be quarantined as appropriate per *CCBB-QA-032 Tracking and Traceability of CBUs* and a copy of the quarantine report will be attached to the deviation/investigation prior to submission for QA review.
- 8.2.2 *COMM-QA-042 FRM4 Deviation and Investigation Report* should be completed and submitted for review expediently, unless extenuating circumstances delay thorough investigation to identify root cause. The target timeframe for deviation/investigation resolution is 30 days.
  - 8.2.2.1 If more than 30 days have elapsed before the report is closed, written rationale for the delay is required within the investigation section of the associated deviation/investigation report.
- 8.2.3 Deviation/Investigation progress will be actively monitored by the QSU through a variety of mechanisms, which may include but are not limited to, regular QA meetings discussing open events, event management tracking meetings, and/or regular reports that are sent to applicable Department Managers, Quality Director and Medical Director(s). These meetings and reports will highlight key statistics such as discovery/initiation date and report duration.

- 8.2.3.1 At a target frequency of monthly, QSU convenes a meeting with applicable facility management to monitor deviation/investigation progress. Specifically, this meeting includes reporting on all deviation/investigations that are open greater than 30 days. If facility management or management representatives are unable to attend the meeting or due to scheduling, an in-person meeting is not practical, updates for the corresponding deviation/investigation progress may be provided electronically.
- 8.3 Completing *COMM-QA-042 FRM4 Deviation and Investigation Report*
  - 8.3.1 See *COMM-QA-042 Appendix A* for guidance on completing the form.
  - 8.3.2 If the initiator of *COMM-QA-042 FRM4 Deviation and Investigation Report* is not the Supervisor/Manager, modify step routes, as applicable, to include the Supervisor/Manager for review and approval.
  - 8.3.3 Verify that the appropriate Medical/Program Director or physician, as applicable, is selected for review and approval routes. Modify step routes as necessary.
- 8.4 Unplanned Deviations
  - 8.4.1 Refer to *COMM-QA-042 Appendix A* for instructions on completing an unplanned deviation.
  - 8.4.2 Refer to *COMM-QA-077 Risk Assessment Procedure* for assistance on evaluating and determining how to assess risk to facilitate completion of a risk assessment that is captured within *COMM-QA-042 FRM4 Deviation and Investigation Report* and if a CAPA is required due to this risk assessment.
    - 8.4.2.1 Within *COMM-QA-042 FRM4 Deviation and Investigation Report*, risk assessments should be expanded to include potential, related outcomes that could occur in the future despite not having occurred in this specific event so that any potential preventive actions can be evaluated and captured appropriately as a CAPA. To accomplish this, a systemic view should be taken when looking at the event/issue to help determine if any changes can be made to facilitate reduced risk of a similar event occurring in the future.
    - 8.4.2.2 Additionally, during the risk assessment, any program risk report(s) conducted per *COMM-QA-080 Quality Risk Management* should be reviewed/consulted to ensure that no updates are necessary.
  - 8.4.3 Refer to procedure *COMM-QA-076 Corrective and Preventive Actions* for additional information and instructions on completing a CAPA, if deemed necessary.
    - 8.4.3.1 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, equipment, or systems). Specific consideration for a CAPA should be made for any event scored as a 5 on any risk parameter (severity, probability, or detectability) even if the overall risk score is low. If no CAPA is deemed necessary when a single parameter is scored a 5, rationale should be provided within the Risk Assessment Summary/Conclusion field of the Report, as described in Appendix A, addressing specifically how the risk was evaluated to be at an acceptable level.

- 8.4.3.2 If a CAPA is warranted, a specific plan for the implementation, monitoring, and follow-up (effectiveness checks) will be drafted for approval using *COMM-QA-076 FRM1 CAPA Report*.
- 8.4.3.3 If a change/action occurred during the course of the associated Deviation/Investigation Report and the actions are completed before closure of the associated COMM-QA-042 FRM4 *Deviation and Investigation Report*, actions that fulfill the requirements stated within *COMM-QA-076 Corrective and Preventive Actions* should still be captured as a CAPA on a corresponding *COMM-QA-076 FRM1 CAPA Report*.
- 8.4.3.4 If a CAPA is implemented, ensure the corrective and/or preventive actions are noted in the designated CAPA section of *COMM-QA-042 FRM4 Deviation and Investigation Report*. Details and the effectiveness check will be documented and monitored per *COMM-QA-076 Corrective and Preventive Actions*.
- 8.4.4 Bracketing of any possible broad impact of the event beyond the immediately affected products/situation should be conducted.
  - 8.4.4.1 Unless otherwise specified by a specific equipment SOP, documentation of unplanned deviations is required if an “as found” result is out of specification for re-qualified/calibrated critical equipment or supplies, including leaks and repairs to supply HEPA filters. For these events, an expanded product impact assessment (bracketing) is required. These investigations require a quality assessment on all products processed since the last successful equipment or environmental monitoring.
- 8.4.5 Documentation of an unplanned deviation is required when an equipment change/repair results from an issue that could not be captured solely by *COMM-QA-019 Change Control*, which may be due to the need for an expanded product impact assessment. Qualification status of the equipment should be assessed during the investigation.
- 8.4.6 Thorough investigations using all available data at the time of the investigation to determine the root cause and to assess quality impact to other products should be completed and documented on *COMM-QA-*



*042 FRM4 Deviation and Investigation Report.* If no definitive root cause can be identified, the most probable root cause(s) should be discussed in the report. In certain cases, specific tools may be needed to assist with clearly identifying root cause.

8.4.6.1 Refer to *COMM-QA-042 JA3 Root Cause Analysis Job Aid* for additional details, expectations, and guidance on root cause analysis. Formal Root Cause Analysis tools, such as “5 Whys” and Fishbone Analysis are acceptable techniques to determine and ensure thorough root cause analysis determination.

8.4.6.2 In scenarios where root cause is not readily identifiable, is undetermined, or is determined to be “a failure to follow SOP”: documentation of the formal Root Cause Analysis tool/exercise utilized to determine this root cause is required within *COMM-QA-042 FRM4 Deviation and Investigation Report*. In this situation, minimally a specific tool for the root cause analysis must be named (ex. “5 Whys”) and described, if the root cause is to remain as “Failure to follow SOP”.

8.4.7 Any events related to an external contracted vendor, service provider, or test laboratory should refer to *COMM-QA-042 JA4 Vendor Event Job Aid*.

## 8.5 Planned Deviations

8.5.1 Planned deviations are acceptable in scenarios with a short timeline to implement a transitory or temporary change due to an unforeseen event or requirement.

8.5.1.1 Planned deviations are not allowed for changes known to be permanent at the time of submission and that should be immediately captured through the change control process, *COMM-QA-019 Change Control*.

8.5.2 Refer to *COMM-QA-042 Appendix A* for instructions on completing a planned deviation.

8.5.3 Refer to *COMM-QA-077 Risk Assessment Procedure* for assistance on evaluating and determining how to assess risk to facilitate completion of a risk assessment that is captured within *COMM-QA-042 FRM4 Deviation and Investigation Report*.

8.5.3.1 Additionally, during the risk assessment, any program risk report(s) conducted per *COMM-QA-080 Quality Risk Management* should be reviewed/consulted to ensure that no updates are necessary.

8.5.4 Refer to procedure *COMM-QA-076 Corrective and Preventive Actions* for additional information and instructions on completing a CAPA. If a CAPA is implemented, please ensure that the corrective and/or preventive actions are noted in the designated CAPA section of *COMM-QA-042 FRM4 Deviation and Investigation Report*. Details and the

effectiveness check will be documented and monitored per *COMM-QA-076 Corrective and Preventive Actions*.

8.5.4.1 If a CAPA is warranted, a specific plan for the implementation, monitoring, and follow-up (effectiveness checks) will be drafted for approval using *COMM-QA-076 FRM1 CAPA Report*.

8.5.4.2 If a CAPA is implemented, ensure the corrective and/or preventive actions are noted in the designated CAPA section of *COMM-QA-042 FRM4 Deviation and Investigation Report*. Details and the effectiveness check will be documented and monitored per *COMM-QA-076 Corrective and Preventive Actions*.

8.5.5 Approval by the Supervisor/Manager, Medical/Program Director or designated physician, and QSU should be documented prior to implementing the planned deviation from policy, process, or procedure.

8.5.6 An electronic version of the planned deviation is maintained in the MasterControl system, and a reference to the approved planned deviation report is added within the associated file, such as product files or batch records, as applicable.

## 8.6 Documentation of Unique Product Identifiers Affected

8.6.1 In typical situations, all affected unique product identifiers are included in *COMM-QA-042 FRM4 Deviation and Investigation Report* and are used to identify products related to an event.

8.6.1.1 For planned deviations, it may be necessary to open a supplemental deviation to document associated ISBTs if they are not known at the time of report approval. Refer to section 8.9.3 of this procedure.

8.6.2 For atypical situations, QSU can utilize bracketed date ranges included in the Title/Problem Statement of *COMM-QA-042 FRM4 Deviation and Investigation Report* to identify products associated with an event in the case that no ISBTs are included.

## 8.7 Review Process

8.7.1 As part of the review process, QSU completes an assessment on all submitted deviations/investigations to determine the necessity for Biological Product Deviation Reporting (BPDR) as well as any external reporting to outside vendors/sponsors per applicable quality agreement. QSU also designates an event code.

8.7.2 QSU assesses step routing for completeness and accuracy and modifies steps as necessary to ensure thorough review.

8.7.3 Review and approval routes include, at a minimum, the following roles:

8.7.3.1 Initiator

8.7.3.2 Medical/Program Director

## 8.7.3.3 QSU Representative.

- 8.7.4 Reviewers may reject any route step during the review and approval process to ensure consistent and accurate documentation.
- 8.7.5 QSU will ensure any associated lots and batch records units are removed from quarantine, if applicable, upon resolution of a deviation.
- 8.7.6 If, during the review process, it is determined that the deviation/investigation report is no longer necessary, QSU must be consulted, and a path for aborting the event in MasterControl can be determined.

## 8.8 Tracking and Trending

- 8.8.1 QSU generates DEV reports on a regular basis to facilitate tracking and trending, dashboards, management review, and also to support lookbacks for similar deviations during investigations.
- 8.8.2 Using this source data, QSU generates trending data (e.g., type and frequency of event) and provides this in quarterly reports to applicable Supervisor/Managers, Project Coordinator, and Medical/Program Directors.

8.8.2.1 Within each Deviation/Investigation report, QSU assigns an event code and deviation category that most closely reflect the root cause and category of issue. To facilitate tracking and trending, deviations and investigations are trended by the event code for each specific event on a quarterly basis, which is summarized and presented in quarterly reports and/or summaries signed by management. Additionally, within this quarterly trending, QA will review all events with the specific goal of identifying commonalities that may not be captured solely by event coding.

8.8.2.2 For reference, examples of quarterly trending data generated by QSU include, but are not limited to:

- Quarterly reports
- Deviation reports and dashboards
- Management review

8.8.2.3 In addition to event coding, deviations are trended on a quarterly basis to identify relationships/trends that are not solely identified by event coding alone. This may include, but is not limited to, analyzing root causes by type, open/closure rates and time to completion, and identifying repeat deviation types across systems/products/processes that are recurring, but not always specific to one system.

8.8.2.4 When investigating deviations, specifically related to the probability risk score, initiators should review the trending data described above to determine whether similar deviations have been noted in the previous 2 years of data

provided. For bracketing purposes, the search should review 2 years of deviation data from the date of discovery.

- 8.8.2.5 If a repeat deviation is noted on review of the previous 2 years of deviation data, within COMM-QA-042 FRM4 *Deviations and Investigation Report*, the report must include investigation into any perceived trend, including whether previous actions intended to address root cause were effective. Any CAPAs, if required, must address the effectiveness of previous corrective actions in relation to repeat deviations.

## 8.9 Maintenance of Records

- 8.9.1 *COMM-QA-042 FRM4 Deviation and Investigation Report*, and associated forms are maintained in MasterControl and are accessible for printing and review. Reports may be generated by Document Control Operations (DCO) or QSU upon request.
- 8.9.2 For events impacting or potentially affecting product, during review, QSU will verify that *COMM-QA-042 FRM4 Deviation and Investigation Report* is referenced appropriately within the associated file/batch record to alert file reviewers of the event.
- 8.9.3 In the event *COMM-QA-042 FRM4 Deviation and Investigation Report* is found to need additional documentation after closure; e.g., missing data such as ISBT product identifiers, relevant attachments, or other pertinent information, an additional report may be opened as a supplement to the initial report.
- 8.9.3.1 The title of the report should be populated as “Supplement to (insert Deviation and Investigation number)”.
- 8.9.4 All records are maintained according to the associated Program’s procedure(s) for Records Management or Records Retention.

## 9 RELATED DOCUMENTS/FORMS

- 9.1 CCBB-QA-011 Licensed Biological Product Deviations (BPD)
- 9.2 CCBB-QA-020 Handling Out of Specifications and Unexpected Results
- 9.3 CCBB-QA-026 Postmarketing Receipt of Adverse Experiences
- 9.4 CCBB-QA-032 Tracking and Traceability of Cord Blood Units
- 9.5 COMM-QA-042 FRM4 Deviation and Investigation Report
- 9.6 COMM-QA-042 JA3 Root Cause Analysis Job Aid
- 9.7 COMM-QA-042 JA4 Vendor Event Job Aid
- 9.8 COMM-QA-075 Management Review and Responsibility
- 9.9 COMM-QA-076 Corrective and Preventive Actions
- 9.10 COMM-QA-077 Risk Assessment Procedure
- 9.11 COMM-QA-080 Quality Risk Management

- 9.12 GMP-QA-003 Non-Conforming Products and Out of Specifications Results
- 9.13 GMP-QA-005 Evaluation of Complaints and Adverse Experiences
- 9.14 GMP-QA-016 Out of Specification Investigations for RETHYMIC
- 9.15 STCL-DIST-006 FRM2 Adverse Event Reporting Form
- 9.16 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 Cellular Therapy; 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**

<b>Revision No.</b>	<b>Author</b>	<b>Description of Change(s)</b>
18	Austin Rudisill	<ul style="list-style-type: none"><li>• Updated to add new requirement for deviation lookbacks, and instructions on how this information is incorporated into deviation reports.</li></ul>

## Appendix A

### Instructions for completing COMM-QA-042 FRM4 *Deviation and Investigation Report*:

- Complete the Deviation/Investigation Report, filling in all required information.
- Record N/A in any section that does not apply.

Data Field	Instructions
Deviation/Investigation Number	Event number is auto-populated by MasterControl.
Initiated By	This field is auto-populated by MasterControl to indicate which user initiated the Deviation/Investigation Report.
Date Initiated	This field is auto-populated by MasterControl to indicate what date the Deviation/Investigation Report was initiated.
<b>Tab 1: General Information</b>	
Program	Select applicable program in which the event occurred.
Project Affected/Impacted (Select All that Apply)	Select applicable product(s)/project(s) impacted by this event.
Date Discovered	Enter the date the issue being investigated/documentated was discovered.
Date(s) Affected	Document the time period in which the Deviation/Investigation may have affected product by selecting the data range in the fields provided. For situations where only one date is impacted, please list the same date in both fillable fields in MasterControl. <i>Note: For planned deviation, enter time period for which the planned deviation is needed. If a specific date range does not apply, enter N/A.</i>
Title	Enter a title that clearly identifies what the Deviation/Investigation Report is about.
Supply/Reagent	Enter name and lot number of supply reagent, if applicable.
Equipment	Enter name and serial number of equipment, if applicable.
<b>Tab 2: Problem Statement and Containment</b>	
Problem Statement	Clearly describe the situation. Identify the problem being addressed at the start of the narrative. If applicable, state the requirement/procedure not met and describe the deviation from the requirement. State the date the event occurred. Include a description of how and when the event was identified.  <i>Note: If deviation is planned, include justification for action.</i>
Containment Actions	Detail all containment (immediate) actions taken, in chronological order to resolve the problem. Include dates completed. Examples: Stop of shipment/supply, Destruction of Product or Product Recall, Suspend production process.  <b>Note:</b> Action(s) taken to address the root cause of a problem or to prevent initial occurrence of a problem is not typically a containment/immediate action. This is a CAPA (ex. additional training or changes to procedures, processes or systems.)  <i>If deviation is planned, specify:</i> <i>What the action(s) will be</i> <i>Who will do it</i> <i>When it will be done</i>

Data Field	Instructions
<b>Tab 3: Investigation and Root Cause</b>	
Investigation (Identifying Root Cause)	<p>Define the scope of the event in greater detail and include applicable dates on which events/actions occurred. If investigation is conducted over time, update/refine the investigation as new information is discovered. Include:</p> <ul style="list-style-type: none"> <li>○ Information that was gathered, reviewed and/or evaluated</li> <li>○ Applicable dates/date ranges and an explanation of each</li> <li>○ Results of the reviews/evaluations of the information</li> <li>○ Summary of information gathered to help identify root cause(s) and/or contributing factors</li> <li>○ Consideration if the event may have impact to product, other processes, documents, samples, results, etc. If other programs/departments will be impacted, notify the department/management, as appropriate.</li> <li>○ If the report was initiated &gt; 3 business days after the date of discovery, written rationale for the delay is required.</li> <li>○ If the report remains open &gt; 30 days after the date of discovery, written rationale for the delay is required.</li> <li>○ As a best practice, it is recommended to include both the <b>SOP</b> and <b>Step Number</b> from which the Deviation occurred</li> </ul> <p><i>Note: Planned deviations by nature may contain fewer investigation components/details. N/A may be allowable if certain details are present.</i></p>
Root Cause (Statement of Detailed Root Cause)	<p>Statement of Root Cause identified during investigation.</p> <p>Please ensure that this is a statement of the root cause of the issue and not solely a re-statement of what happened.</p> <p>If needed, utilize root cause analysis tool (some details below), such as “5 Whys”.</p> <p><i>Note: If deviation is planned, please still include a root cause.</i></p>
Root Cause Analyst Tool Attached?	<p>In scenarios where root cause is not readily identifiable, is undetermined, or is determined to be “a failure to follow SOP”: documentation of the formal Root Cause Analysis tool/exercise utilized to determine this root cause is required and should be in the event or attached. In this situation, minimally a specific tool for the root cause analysis must be named (ex. “5 Whys”) and described, if the root cause is to remain as “Failure to follow SOP”. Other tools could include brainstorming, fishbone analysis, or FMEA, among others.</p>
<b>Tab 4: Deviation Information and Reporting</b>	
Deviation Identification	<p>Complete this section to document, by listing SOP numbers, if any deviation from SOP was identified. As a best practice, please list the SOP Step/Section number that was deviated from in the Investigation. This section is also used to differentiate between planned and unplanned deviations.</p>
Report(s) associated with this Deviation/Investigation	<p>Enter any report number(s) associated with this Deviation/Investigation (other Deviation(s), Adverse Events, complaint(s), validations, OOS, risk assessment report)</p>
External Reporting	<p>This section is completed to document the determination if additional regulatory or other external reporting such as to a vendor or sponsor may be required per the applicable quality agreement. If notification is required prior to event closure, then documentation, such as email, FAX etc., should, ideally, be attached to the document in the Attachments section. This section is to be populated by author/initiator if known at time of report and/or QSU at time of review.</p>
<b>Tab 5: Risk Assessment and Rationale</b>	



Data Field	Instructions
Risk Assessment	Reference SOP <i>COMM-QA-077 Risk Assessment Procedure</i> to assess risk on all three parameters (severity, probability, and detectability). An individual score should be assigned and detailed rationale provided for that assigned score. Risk assessments should be expanded to include potential, related outcomes that could occur in the future despite not having occurred in this specific event so that any potential preventive actions can be evaluated and captured appropriately as a CAPA. To accomplish this, a systemic view should be taken when looking at the event/issue to help determine if any changes can be made to facilitate reduced risk of a similar event occurring in the future. The final score will help assess if a CAPA is required due to risk. A CAPA may still be appropriate even if not required due to risk.
Combined Risk Assessment Score	Use the Risk Assessment Matrix to assign a numerical value for each risk parameter in the risk assessment. Multiply the scores to obtain the final, combined risk assessment score.
Risk Assessment Summary/Conclusion	<p>Use this field to populate a summary of the overall risk assessment if not sufficiently detailed in the individual parameter fields above; any additional information about the expanded risk assessment can also be described here.</p> <p>If one risk parameter is scored a 5 during the risk evaluation and no CAPA is launched, justification will be required and captured within this field, addressing specifically how the risk was evaluated to be at an acceptable level.</p> <p>Finally, this field may be utilized to describe any impact to risk assessment reports per <i>COMM-QA-080 Quality Risk Management</i> if not otherwise addressed in the event or risk documentation already provided.</p> <p>The field can be N/A if no additional details are needed.</p>
<b>Tab 6: CAPA</b>	
CAPA Number	Enter number of CAPA Report generated. Enter N/A if no CAPA.
Summary of CAPA	<p>Give an overview of CAPA(s) to be implemented in associated CAPA report (if applicable).</p> <p>As a best practice, please route any associated CAPA (first routing) concurrently with the corresponding Deviation/Investigation Report.</p>
<b>Tab 7: UPIs/Quarantine/Licensure</b>	
Unique Product Identifier(s) Affected [Lot Number/ISBT]	Add associated product identifier(s), as applicable, based on the investigation.
Was quarantine applied to product associated with this report?	Select radial button to indicate applicable quarantine of product and describe rationale.
If all specifications for licensure are met, is there any reason that product(s) cannot be released under the license due to this event?	<p>Select appropriate toggle to indicate any change to license status and describe rationale.</p> <p>Select N/A if the event solely involves a non-CCBB or licensed MC3 GMP product.</p>
<b>Tab 8: Event Coding and BPDR</b>	
QA Assessment (Completed by QSU)	QSU will reference program specific SOPs for BPDR assessment.
Event Code (Completed by QSU)	Select the event code from the data set that most closely matches the root cause.

Data Field	Instructions
Deviation Category	Select the deviation category from the data set that most closely matches the root cause.
<b>Tab 9: Attachments and Appendix</b>	
Attachment(s)	Use this function to attach all applicable documents.
Appendix from COMM-QA-042	The Appendix from COMM-QA-042 is attached for easy reference.

**Signature Manifest****Document Number:** COMM-QA-042**Revision:** 18**Title:** Deviations and Investigations**Effective Date:** 03 Apr 2024

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**COMM-QA-042 Deviations and Investigations****Author**

Name/Signature	Title	Date	Meaning/Reason
Austin Rudisill (ADR35)	Associate Director, Quality Assurance	13 Mar 2024, 01:37:23 PM	Approved

**Medical Director**

Name/Signature	Title	Date	Meaning/Reason
Joanne Kurtzberg (KURTZ001)		13 Mar 2024, 02:22:33 PM	Approved

**Quality**

Name/Signature	Title	Date	Meaning/Reason
Frank Rider (FNR5)	GMP, Quality Assurance Associate II	20 Mar 2024, 08:24:01 AM	Approved

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