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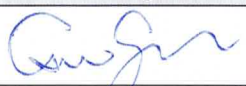
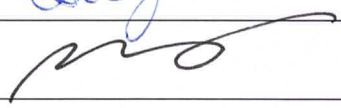
| **Owner** | **Sijin Guo** | **15Dec2025** |  |
| **Operation Management** | **Baozhong Zhao** | **15Dec2025** |  |
| **Quality Assurance** | **Xibo Li** | **15Dec2025** |  |

**Changes from previous version:**

| Section | Summary of Changes | Change Control Number |
|---|---|---|
| ALL | 1. New document | |

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| **Owner** | **Sijin Guo** | **15Dec2025** | |
| **Operation Management** | **Baozhong Zhao** | **15Dec2025** | |
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1. PURPOSE

The purpose of this procedure is to provide requirements for the initiation, classification, investigation, and closure of Deviation Investigation Reports.

2. SCOPE

This procedure applies to all deviations generated by Synoligo that are related to the receipt, storage, manufacture, testing and release of molecular diagnostic products.

3. INTERNAL REFERENCES

| Document ID | Title |
|---|---|
| QUA004 | Quality Policy |
| QUA010 | Corrective Action and Preventative Action Policy |
| QUA017 | Root Cause Analysis |

4. qEXTERNAL REFERENCES

| Document ID | Title |
|---|---|
| 21 CFR Part 820 | Medical Device; Current Good Manufacturing Practice (cGMP) Final Rule; Quality System Regulation, Food and Drug Administration, Federal Register |
| 21 CFR Part 210 | Current Good Manufacturing Practice in Manufacturing, Processing, Packaging, or Holding of Drugs; General |
| 21 CFR Part 211 | Current Good Manufacturing Practice for Finished Pharmaceuticals |
| ISO 9001 | Quality management systems -Requirements, International Organization for Standardization |
| ISO 13485 | Medical devices – Quality management systems – Requirements for regulatory purposes, International Organization for Standardization |
| ISO/IEC 17025:2017 | General Requirements for the Competence of Testing and Calibration Laboratories |
| ICH Q7 | Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients |

5. RESPONSIBILITIES

| Job Function and/or Department | Responsibility |
|---|---|
| QA | • Provides oversight of the deviation process and guides the lead investigator to ensure timely completion of investigations.<br>• Issues deviation numbers and tracks the deviation to closure. May reject or cancel the deviation based on initial assessment.<br>• Confirms initial deviation classification. Note that Major and Critical deviations require communication to senior management and client.<br>• Reviews investigation report, and performs final deviation classification and closure.<br>• Notifies senior management of any potential impact to previously released/distributed product batches or any changes to the material status.<br>• Issues CAPA numbers, reviews, and closes CAPA and CAPA Effectiveness Checks<br>• Notifies management of any changes to the material status.<br>• Trends and reports on deviation process status.<br>• Evaluates and approves proposed addendum, extension requests, and records.<br>• Responsible in verifying quarantine material or products that have been identified as potentially impacted by the deviation are labelled and segregated as needed. |
| Subject Matter Experts (SME) | • Individuals that support investigation by providing documented assessments |

| | |
|---|---|
| | related to deviations, as requested by the investigator and/or QA as needed.<br>• Validation assessments: Performed by the investigator with assistance as needed from Process Development and/or QA to review the requirements and recommend conclusions. QA is responsible for verifying these requirements and approve the recommended conclusions.<br>• Stability assessments: Stability Assessment Reports relating to deviations, as requested by the investigator and/or QA.<br>• Customer agreements: Performed by the investigator with assistance as needed from Process Development to review the requirements and recommend conclusions. QA is responsible to |

6. DEFINITION

| Term | Definition |
|---|---|
| CAPA | **Corrective Action** – Action taken to prevent **recurrence**.<br>Definition: Measures implemented to eliminate the cause(s) of a detected deviation, nonconformity, defect, or other undesirable situation. The corrective action should ensure the issue does not recur.<br>**Preventive Action** – Action taken to prevent **occurrence**.<br>Definition: Measures implemented to eliminate the cause(s) of a potential deviation, nonconformity, defect, or other undesirable situation. Preventive action should ensure the issue does not occur in the first place.<br>**CAPA Effectiveness Check** – An assessment conducted to verify whether the documented root cause has been eliminated and whether appropriate monitoring mechanisms are in place to sustain effectiveness |
| Cause | **Cause (General Definition)**<br>The reason an incident or deviation occurred. If eliminated or modified, the deviation would not have happened.<br>**Causal Factor**<br>A state or condition that, if eliminated, would have either prevented the occurrence or reduced its severity.<br>**Contributing Cause**<br>A factor that worsened the situation or accelerated its occurrence, but by itself was not sufficient to cause the deviation.<br>**Probable Cause**<br>The most basic cause of a deviation that can reasonably be determined to be causal.<br>**Root Cause**<br>A fundamental, system-related cause that underlies the deviation. Addressing the root cause is essential to prevent recurrence. |
| Correction | Action taken immediately to correct a detected deviation. A correction is an immediate solution such as repair or rework. Correction are also known as remedial or containment actions and are typically one-time fixes that may or may not prevent recurrence. |
| Dates | Date Observed: Date the deviation was observed/confirmed.<br>Date Occurred: Actual date the deviation happened.<br>Date Reported: Date deviation was reported to Quality Assurance. |

| | |
|---|---|
| Deviation | A deviation is a departure from an established standard or approved instruction, or noncompliance with a governing body's regulation or requirement. It may also be an unexpected observation requiring impact assessment.<br>Planned Deviation<br>A deviation that has been pre-approved by Quality Assurance. It applies to a specified time period or number of batches.<br>Unplanned Deviation<br>An unexpected event occurring at any stage of manufacturing, packaging, testing, holding, or storage of product.<br>Categories include:<br>• Critical Deviations<br>Deviations that represent a potential adverse health risk, a potential regulatory enforcement action, and/or a significant violation of the marketing or manufacturing license.<br>• Major Deviations<br>Deviations that represent significant local or systemic GMP (Good Manufacturing Practice) or quality-related deficiencies/failures with a potential impact on final product quality. This includes the combination of minor deficiencies which indicate system failures<br>• Minor Deviations<br>Deviations from established procedures without impact on final product quality |

7. Deviation Observation and Initiation

7.1. Notification of Deviation

7.1.1. All employees, upon observing a deviation (or upon receipt of a vendor deviation notification), must immediately notify:

- The department Supervisor/Manager in the area where the deviation occurred or was observed.
- Quality Assurance (QA).

7.1.2. Examples of deviations include:

- Protocols and procedures (e.g., Batch Record, SOP, Validation Protocol) not followed.
- Maintenance or calibration schedule not followed.
- Failure to meet customer quality requirements.
- Persistent or repeated recordkeeping failures.
- Audit observations reviewed by QA to determine if a deviation should be captured in the Deviation Management System.
- Non-Reportable events: do not need to be entered into the Deviation Management System. Deviations opened and downgraded to Non-Reportable after evaluation may be closed as events.

7.2. Immediate Action

7.2.1. Employees must identify immediate actions required to secure the system or process to prevent further deviations.

7.2.2. Justification must be provided to continue processing, if applicable.

7.3. Deviation Report Initiation

7.3.1. The observer, initiator, or Supervisor/Manager must:

- Enter all mandatory information into the Deviation Report.

- Collect all pertinent information and perform an initial assessment for submission to QA.

7.3.2. This may include:

- Relevant data.
- Initial cause determination.
- Product segregation.
- Justification for any deviations opened after the allowed reporting period.

7.4. Executive Summary

7.4.1. Include brief statements summarizing:

- The problem.
- Cause.
- Remedial actions.
- Impact**.**

7.4.2. Do not include full deviation descriptions, references, or specific details.

7.5. Deviation Description

7.5.1. The deviation description must address:

- WHEN: Date and time of occurrence.
- WHERE: Location and process step.
- WHO: Process group/title of the observer (employee names must not be included).
- WHAT: Description of the discrepant state versus the expected state.
- Identify product, component, or equipment.
- State what went wrong.
- State which requirement, specification, or limit was not met.
- Reference relevant documents (SOP, Batch Record, specifications, limits, etc.).
- HOW: Describe how the incident deviated from the approved process.

7.6. Initial Risk Classification

7.6.1. The investigator, in collaboration with QA, performs an initial risk classification based on impact/consequence:

- Product Quality/Conformance Risk.
- Compliance Risk.
- Containment Risk.

7.7. QA Confirmation

7.7.1. QA confirms the initial classification prior to the investigator's full investigation.

7.7.2. Classification may change during the course of the investigation if the risk assessment changes.

Table 1: Deviation Classification

| Classification | Criteria |
|---|---|
| Critical | Impact to released/distributed product/devices. Potential adverse health risk. Significant violation of the marketing/manufacturing license. High compliance impact or potential health authority action. |
| Major | Moderate compliance impact that cannot be corrected immediately. Reprocessing/rework required. Major GMP or quality-related deficiencies/failures. Potential impact to Safety, Identity, Strength, Quality, Purity, or Efficacy. Potential impact to other batches or in-process batch. Potential impact to process/equipment robustness. |

| Classification | Criteria |
|---|---|
| Minor | Possible GMP violation but minor in nature. Departure from procedure with no impact to Safety, Identity, Strength, Quality, Purity, or Efficacy. Process parameter excursion previously assessed as non-impactful. Pre-release raw material deviations without potential to affect product, process, or facility. |

7.8. Deviation Report Numbering

7.8.1. QA reviews the initiated deviations log to verify Deviation Report numbers.

7.9. Escalation of Major and Critical Deviations

7.9.1. For major and critical deviations with potential impact on the quality of distributed product:

- Escalate without undue delay to senior Quality Management.

8. Deviation Investigation

Note:

- This procedure provides general guidance for investigations.
- Minor deviations may not require a full root cause investigation.

8.1. Guidelines for Major/Critical Deviation Report

8.1.1. Process Overview/Background

8.1.1.1. Provide a brief overview of the process area/system where the deviation occurred to give context to the investigation.

8.1.2. Root Cause Investigation

8.1.2.1. Refer to QUA017.

8.1.2.2. Document the cause analysis tool used in the Deviation Report (DR).

8.1.2.3. Discuss root cause analysis with appropriate headings.

8.1.2.4. Cite data reviewed, possible causes considered (with inclusion/exclusion rationale), and conclusions.

8.1.3. Impact Assessments

8.1.3.1. Include assessment of all identified risks.

8.1.3.2. Assessments for License, Validation, Stability, BPD, and Safety may be exempt if criteria are met.

8.1.3.3. If criteria are not met, provide explanation or attach SME assessment.

8.1.3.4. Sub-assessments (if applicable):

- License Assessment
- Validation Assessment
- Stability Assessment
- Distributed Product Assessment

8.1.4. Escalation

8.1.4.1. If investigation determines potential impact on distributed product quality, escalate without undue delay to senior Quality Management.

8.1.5. BPD Assessment

8.1.5.1. For deviations impacting distributed product (including trend investigations), perform a BPD assessment.

8.1.5.2. Include the Distributed Product Assessment form in the DR record.

8.1.6. Timelines

8.1.6.1. Distributed Product Assessments must be completed before Day 30 of the DR.

8.1.6.2. Any delay must be escalated to appropriate personnel.

8.1.7. Safety Assessments

8.1.7.1. Document Safety Assessments in the DR record, if deemed necessary.

8.1.7.2. Pharmacovigilance Assessments may also be documented, if required.

8.2. Guidelines for Minor Deviation Report

8.2.1. Investigator Responsibilities

8.2.1.1. Identify and document assessment and cause directly in the record.

8.2.1.2. Root Cause Field:

- Cause Summary (identify cause if available, or state if not identified).
- Background (as needed).
- CAPA(s)/Corrections (if applicable).
- Historical Review.

8.2.1.3. Assessment Field:

- Deviation Risk (Product Quality Risk, Compliance Risk, Containment Risk).
- Impact Assessment.
- Include sufficient supporting documentation to justify minor-level classification.

8.3. Handling Out of Specification (OOS) Test Results

8.3.1. Scope

8.3.1.1. Applies to all deviations for OOS test results of product.

8.3.2. Batch Disposition

8.3.2.1. All product batches with confirmed OOS results are rejected and not released.

8.3.3. Exceptions

8.3.3.1. If a non-conforming batch can be made acceptable after correction but cannot be completed immediately:

- Deviation may remain open until correction is made, OR
- Deviation may be closed with disposition to accept, subject to corrective terms or client approval.

8.4. Impact Assessment/Cause Investigation Guidelines

8.4.1. Risk-Based Impact Assessment (RBIA)

8.4.1.1. For unknown/complex impact assessments (Major/Critical), RBIA may be performed.

8.4.1.2. RBIA determines immediate/long-term impact on affected batch(es), equipment, and/or facilities.

8.4.1.3. RBIA assists in product disposition decisions.

8.4.2. SME Data and Documentation

8.4.2.1. Document SME data and interview information as it becomes available.

8.4.2.2. Include signed memos and supporting documentation in the deviation record.

8.4.2.3. Transcribed/processed data must be verified.

8.4.2.4. E-signature confirms authenticity of attached documents.

8.4.2.5. SME Memo Requirements:

- One signature: If data is from controlled/validated source (e.g., validated software, approved study)

and conclusions are within SME's role/experience.

- Two signatures: Required if data is from uncontrolled/unvalidated source, or at discretion of SME/QA management.

8.4.3. Additional Testing/Evaluation

8.4.3.1. Additional tests may be required for cause investigation or impact assessment.

8.4.3.2. An Investigation Plan must be signed by Operational Management and QA Management.

8.4.3.3. Attach signed protocol, execution documents, training records, and supporting documentation to the deviation record.

8.4.3.4. Protocol must specify where conclusions will be documented (final DR or separate memo/report).

8.5. Final Deviation Classification and Product Disposition

8.5.1. After investigation, QA performs final classification in the DR based on product impact assessment.

8.5.2. Refer to Table 2 for guidance.

Table 2: Guideline for Final Classification

| Initial Classification | Deviation Impact Assessment | Final Classification | Batch Disposition* |
|---|---|---|---|
| Minor | N/A | Minor | N/A |
| Minor | No product impact | Minor | Accept batch |
| Minor | Potential product impact | Major*** | Reject batch (Full or Partial) |
| Major | No product impact | Minor | Accept batch |
| Major | Potential impact | Major*** | Reject batch (Full or Partial) |
| Critical | No product impact | Minor | Accept batch |
| Critical** | Potential impact (within control) | Major*** | Reject batch (Full or Partial) |
| Critical** | Potential impact (in the field) | Critical*** | Reject batch, field action |

* If applicable
** Immediately escalate to Senior Quality Management
*** Client notification required within three (3) days of decision

8.5.3. Customer Review

8.5.3.1. For deviations affecting batches with final classification of Major/Critical, deviation record must be reviewed and acknowledged by Customer (memo or signature).

8.5.4. OOS Batches

8.5.4.1. All confirmed Final Product OOS batches are rejected and not released to market.

8.5.5. Reprocessing/Reworking

8.5.5.1. No reprocessing/rework is allowed without a deviation.

8.5.5.2. Initiate a deviation for any potential reprocessing/rework step.

8.5.5.3. Investigation must assess license impact (including regulatory notifications).

8.5.6. Clarifications:

8.5.6.1. Continuation of a process step after in-process control/test shows incompleteness is considered part of normal process (if included in approved procedures).

8.5.6.2. Re-inspection is not considered rework or reprocessing.

8.6. Historical Review

8.6.1. Requirement

8.6.1.1. All deviations must include a Historical Review of similar/recurrent deviations.

8.6.1.2. If a trend is identified, investigation and action plan must address increased risk.

**Note:** Scope of Historical Review must be stated and justified (e.g., inclusion/exclusion of other areas/equipment).

8.6.2. Trend Evaluation

8.6.2.1. Evaluation timeframe: one year from date of observation to date report is submitted to QA.

8.6.2.2. Based on available data and past failures.

9. Corrective and Preventive Actions (CAPA)

9.1. Initiation of CAPA.

9.1.1. To prevent recurrence of problems, corrective actions (CA) and/or preventive actions (PA) may be initiated.

9.2. Justification for Non-Implementation

9.2.1. For critical, major, or trend deviations, if corrective or preventive actions are not taken, a justification must be provided. Example: A CAPA has already been initiated for a similar issue or the same issue.

9.3. Reference SOP

9.3.1. Guidelines for implementing and approving CAPA are described in QUA010.

10. Approvals

10.1. General Approval

10.1.1. All deviations require approval by Operational Management and Quality Assurance (QA).

10.2. Manufacturing Process Deviations

10.2.1. If the deviation is related to the manufacturing process, Process Development approval is also required.

11. Time Frames

11.1. Reporting

11.1.1. Deviations must be reported as soon as observed, but no later than three (3) business days after observation.

11.2. Customer Notification

11.2.1. Customers must be informed within three (3) calendar days, or as defined in the Technical Quality Agreement, upon report to QA regarding either a Major or Critical Deviation.

11.3. Investigation and Closure

11.3.1. All deviations must be investigated and closed within 30 calendar days from the date observed.

11.4. Submission of Final Report

11.4.1. To meet this timeline goal, the final report should be submitted to QA by day 25.

11.4.2. If a final report cannot be submitted, an Extension Request must be submitted by day 25 (or within 5 days of the new due date if previously extended).

11.5. Approval of Final Report

11.5.1. The final report must be completed and approved prior to the due date (day 30 or the new due date if previously extended).

11.6. Interim Reports

11.6.1. If applicable and justified, once an approved interim report is attached to the deviation, a new due date may be assigned.

12. Re-Opening a Deviation

12.1. Authorization

12.1.1. Deviation records may only be re-opened by QA Management/designate.

12.1.2. Proper justification for re-opening must be documented, including the change in justification.

12.2. Initial Qualification of a Supplier or Service Provider

12.2.1. The individual requesting a supplier to be added to the Approved Supplier List in order to place an order with that supplier must initiate Requesting New Supplier for the Qualification Process and send to Quality Assurance.

12.2.2. Quality Assurance must perform a DPL Check as part of the Supplier Qualification procedure. The new supplier must pass DPL Check for new suppliers.

12.2.2.1. If the DPL Check comes up as failed, send the report to DPL review team.

- If the DPL team advises us to proceed, attach the email communication as objective evidence. Proceed with supplier qualification.
- If the DPL team advises not to proceed, the supplier will not be qualified, and the notes will be added to the supplier file.