TITLE: Investigating and Reporting Discrepancies and Performing CA/PA

SOP Number: D-GLO-PRO-013 Revision Number: 0

Effective Date: 09 Aug 2015

Author: _____ Date: _____

Reviewer: _____ Date: _____

QA Approval: _____ Date: _____

A. OBJECTIVE

1. To outline the procedure utilized to report and track incidences, for investigating and reporting discrepancies and for performing Corrective and Preventive Actions (CA/PA).

B. APPLICABILITY

This procedure is to be followed by The University of Iowa Dezii Translational Vision Research Group (DTVR) personnel under the guidance of their supervisor.

C. REFERENCES

F-D-GLO-PRO-006 Investigation and Corrective Action-Preventive Action Report Form
F-D-QC-PRO-001 Laboratory Investigation form
F-D-GLO-PRO-007 Preventive Action Report Form
F-D-GLO-PRO-042 CAPA Progress Report
D-GLO-PRO-016 Deviations to Approved Processes

D. PROCEDURE: INCIDENTS

1. An incident is a random event that does not trigger an investigation or it may be an event that is a breach of an alert limit. QA will be notified within 24 hours of the occurrence of the incident. Incidents will be reported when:

1.1. Environmental Monitoring results exceed alert limits, but do not trigger an investigation.

1.2. Manufacturing, facility, or laboratory equipment breaks down or does not function properly during conditions of use and needs to be repaired and the incident is not captured in an investigation report (see Section E below) or deviation form (F-D-GLO-PRO-039). For example, the AKTA Pure HPLC pump begins to leak during use.

1.3. During the performance of an analytical test method when system suitability fails at the start of a test or during a test or similar equipment or method related issues arise.

1.4. At start-up, failure of a piece of equipment to operate properly (e.g., lack of power transmission in western blot transfer cassette due to broken wire).

1.5. If the quantity or description of samples received by the laboratory or materials delivered to production do not match the information provided on the test sheet, shipping paperwork, or material requisition.

1.6. Out of date or unreleased materials are found in storage.

1.7. A cleaning verification swabbing failure occurs.

1.8. The Quality Manager or designate deems an incident report should be prepared. This listing is not intended to be exhaustive. When in doubt ask the Quality Manager, or designate, if preparation of an incident report is appropriate.

2. Each incident report shall be assigned an individual number by QA and recorded in the Incident Report Log (F-D-QA-PRO-019). The Incident Report Log will contain: the name of equipment, method, material, or product concerned; an identifying number for the equipment, method, material, or product, where appropriate; a short description of the incident; the incident number; the name of the individual reporting the incident; the date the incident occurred; and the date the incident report was filed.

3. Incidents shall be reported on form F-D-GLO-PRO-029 unless some other form is required to be completed for the incident that includes the incident report number on it (e.g. an environmental monitoring excursion). In that case the requirements of the alternate form take precedence to what is required by this SOP.

4. Each incident report header will state the name of equipment, method, material, or product concerned; an identifying number for the equipment, method, material, or product, where appropriate; the individual reporting the incident; the date of the incident and the incident number.

5. The body of the report will contain detailed description of the incident; the root cause of the incidence if possible, the potential impact of the incident on any product or material or method; any actions planned based on the incident; any other lots affected by the incident.

6. Once the incident report is finished, the individual reporting the incident will sign and date the form. The Functional Director will review the form and verify that any actions planned are appropriate. If necessary, corrective actions may be performed and should be documented on form F-D-GLO-PRO-042. Once the Functional Director is satisfied with the incident report the Functional Director will sign and date the form and submit to Quality Assurance.

7. The Quality Assurance Officer or designate will review the form and indicate if a deviation report or investigation report is required in addition to the incident report. Typically these will not be necessary. If the form does not contain enough detail it will be returned to the Functional Director for revision. Once the Quality Assurance Officer or designate is satisfied with the incident report the Quality Assurance Officer or designate will sign and date the form and file in the incident report file.

8. All incident reports should be completed within 10 working days of when the incident occurs. If the incident report cannot be completed within 20 working days, then an interim report will be issued to QA to be filed with the incident report file.

9. Quality Assurance will review the Incident Report Log and Incident Reports on a monthly basis to determine if any adverse trends are evident. Where trends are detected recommendations will be provided where procedure changes, training, or the like may be necessary to decrease the rate of incidence occurrence. A report will be given to the Director of DTVR and each department director.

E. PROCEDURE: DISCREPANCIES

1. An investigation will be conducted when discrepancies that are considered breach of cGMP, contradictions of commitments made in regulatory submissions or institutional SOPs and formal documents, or any discrepancy that may affect the safety, identity, quality, and/or purity of the

materials produced are discovered. QA will be notified within 24 hours of the occurrence of the discrepancy and the investigation will commence within 24 hours of the occurrence of the discrepancy. The following are examples of discrepancies warranting investigations:

1.1 Specified yield limits are not met (form F-D-GLO-PRO-006).

1.2 Directions in a batch record or SOP are not followed correctly (form F-D-GLO-PRO-006).

1.3 A batch or one of its components fails to meet specifications (form F-D-GLO-PRO-006 or F-D-QC-PRO-001).

1.4 An action limit defined in an SOP is exceeded and that SOP requires an investigation (form F-D-GLO-PRO-006).

1.5 Investigations will be performed when out of specification results are found during equipment, system, or facilities calibration, monitoring, validation, and qualification (form F-D-GLO-PRO-006).

2. An investigation will not be performed when deviations or addendums are made to the processing of a batch using a non-validated process (See SOP D-GLO-PRO-016 Deviations to Approved Processes), or if an error is made in the recording of data into the record.

3. If the discrepancy or specification failure is not due to laboratory error, the following will occur:

3.1 Each investigation report (form F-D-GLO-PRO-006) shall be assigned an individual number at the start of the investigation and recorded in the Investigation Report Log. Quality Assurance will issue an investigation number to the department personnel initiating the report. The Investigation Report Log will contain the name and unique identifier of the product the investigation concerns, an investigation number, a description of the nature of the investigation, the name of the individual conducting the investigation, the corrective actions planned and the completed dates for corrective actions.

3.2 The header of each investigation report will state the following: the item being investigated and unique ID number of the product(s) being investigated, the date the discrepancy occurred, the date of the report and all the names of the individuals involved in the investigation, and the report number.

3.3 The director of the function/department where the discrepancy was identified will be notified as well as the director of any function/department affected by the discrepancy.

3.4. The following defines the classifications of discrepancies found. If a critical finding is observed, the department director, Quality, and the DTVR Director shall be notified immediately. The patient (if applicable) shall be notified as soon as possible (within 2 business days) for all critical and major discrepancies.

3.4.1 Critical - Any discrepancy that may affect the safety, identity, quality, and/or purity of the materials produced.

3.4.2. Major - Any discrepancies that are considered a serious breach of cGMP or contradictions of commitments made in regulatory submissions or institutional SOPs and formal documents.

3.4.3. Minor - Any discrepancies that are isolated breaches of GMP of a relatively minor nature.

3.5 The report will state the following:

3.5.1 A description of the discrepancy – detail who reported the discrepancy, when the discrepancy occurred, and the result of the discrepancy.

3.5.2 The investigative process - describe in full detail how the investigation was performed, who was contacted, dates and times of contacts and fact finding.

3.5.3 The conclusion for the investigation – detail the root cause if found during the investigation or justification for no direct root cause.

3.5.4 Investigations will extend to other batches of the same HCT/P product and other HCT/P products that may have been associated with the specific failure or discrepancy. List any other lots that may be affected - include a discussion of how the assessment of the potential impact of the discrepancy or failure on other lots was conducted. If no other lots are affected, describe why.

3.5.5 When investigating a calibration or preventive maintenance out of specification result, one must investigate back to the last time the item was found to be in a state of calibration or validation.

4. Once the investigation is finished, then the project manager or department supervisor will determine any departmental Corrective Actions / Preventive Actions that are to be performed. If warranted, a CAPA Form F-D-GLO-PRO-042 will be initiated. The CAPA number is the same as the investigation or incidence number. The author of the investigation will document the start date of the CAPA on form F-D-GLO-PRO-042.

5. The finished investigation will be signed and dated by the author, and reviewed, signed and dated by the project manager or department supervisor.

6. The investigation with all of the supporting documentation will be turned into QA for review. QA will complete the product impact and product disposition sections of the investigation form.

7. When the CAPA is completed turn a filled out form F-D-GLO-PRO-042 and all supporting data into QA. QA will document the end date of the CAPA and if the CAPA was successful. The completed Form F-D-GLO-PRO-042 will be attached to the investigation report and a copy will be attached to any affected document. If necessary a copy will be sent to the appropriate client(s).

8. Issues that may cause QA to initiate a further CAPA to be started are as follows:

8.1 QA determines that the trending of investigations finds the potential of problems within a department or multiple departments.

8.2 QA determines that inputs from 3rd Party audits, government audits, and internal audits require additional preventive action.

8.3 QA determines that based on the trending of key sources such as environmental monitoring preventive action is necessary.

8.4 QA determines that the departmental corrective action is insufficient to prevent the recurrence of the issues.

8.5 QA will initiate a PA report (Form F-D-GLO-PRO-007) after review of the CAPA. The PA report will specify the actions necessary to prevent a reoccurrence of the problem and any time lines that must be met. The PA report will be signed by QA when it is completed, and all supporting information will be filed with the report.

9. All investigations of critical discrepancies will be completed within 15 calendar days of when the discrepancy is discovered. All investigations of major and minor discrepancies will be finished within 30 calendar days of when the discrepancy is discovered. If the investigation cannot be completed within the allotted time, then an interim report (a memo to file to justify the delay) will be issued to QA to be filed with the investigation report log.

10. The original investigation report will be placed in the appropriate batch file or document folder and a copy will be kept with the Investigation Log in QA.

11. Quality Assurance will review the Investigation Report Log, CAPA Report log, investigational reports, and PA reports on a monthly basis to determine if any adverse trends are evident. The effectiveness of any preventive and/or corrective action will be assessed. A report will be given to the Director of DTVR and each department manager.

F. HISTORY

Effective Date	Revision	Change
09 Aug 2015	0	Original document