Environmental and Utility Monitoring – Excursions Event Initiation and Investigation

SOP 22313 Rev. 03

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1.0 Purpose

The control of GMP utilities and environments requires periodic monitoring to assure that environments and utilities continue to meet the specifications that are appropriate for GMP manufacturing. This procedure describes how to document and investigate excursions from environmental and utility monitoring action and specification levels. Excursions to action levels (or three consecutive excursions to alert levels which is also an action level) or specifications must be detected, documented, communicated, and investigated. Product impact is evaluated and documented. Actions to the excursion are taken as needed to return the utility to its appropriate operating condition.

2.0 Scope

This procedure applies to employees who perform environmental and utility monitoring, those conducting the investigations and writing up the reports, and to BQA that has oversight of this procedure.

3.0 Authority and Responsibility

3.1 Environmental/Utility Monitoring Technicians are responsible for:

3.1.1 Detecting excursions to specifications and reacting to these events on becoming aware of an excursion.

3.1.2 Where results are available “real time” (for example, non-viable particulate counts, temperature, and humidity), immediately re-sampling for excursions to alert, action or specification levels.

3.1.3 Sending an e-mail notification of sampling results as specified in the SOPs that govern sampling.

3.1.4 Arranging for speciation of microbiological isolates involved in the excursion event.

3.1.5 Refer to SOPs listed in **section 6.0** for re-sampling of any excursion.

3.2 BQA Management is responsible for:

3.2.1 Assigning tracking numbers to excursion events (EM Events) and providing notification to PA EM Manager, BQA Auditing, BQA Engineering, BDP Engineering, Area Supervisor and Director, Technical Operations.

3.2.2 Putting areas/utilities out of service when monitoring results exceed established regulatory limits when continued use of the area/utility could adversely impact the quality of products being manufactured.

3.2.3 Closing the event and documenting conclusions at the close of an investigation.

3.3 Process Analytics technicians who collect the EM samples are responsible for assisting BQA by providing information regarding the collection of the sample(s).

3.4 Equipment Owners and Area Owners or their designee are responsible for assisting BQA, when needed, by providing resources and expertise to fully investigate the excursion event.

3.5 BDP Engineering is responsible for assisting BQA, when needed, by providing resources and expertise to fully investigate and correct the excursion event.

4.0 Guidance for Excursions to Environmental or Water Monitoring Levels, Limits, and Specifications

4.1 Initiation of Form 22313-01 for a Confirmed Event:

Document the initiation of an EM Event on Form 22313-01. One event may be used to document potentially related excursions. BQA is responsible for completing the information to describe the event.

4.1.1 Tracking Number Assignment. The tracking number follows the format “EM-YY-###”.

EM: indicates the tracking number is related to an environmental (or utility) monitoring excursion.

YY: is the last two digits of the year (for example 2022 would be “22”).

###: is a sequential number assigned to the event starting with 001 on Jan 1 of every year.

4.1.2 Compiling Sample Information: Following prompts on Form 22313-01, the information below will be compiled and documented on the form.

4.1.2.1 General information regarding the event (Room/Area, MEF#, equipment/utility name, Sampling Technician, QC Test Request numbers that correspond to the sample etc.)

4.1.2.2 Type of excursion:

- Action Level
- Regulatory Limit (or specification, when a regulatory limit has not been established).
- Repeated excursions (≥ 3 consecutive events) from an alert level.

- Repeated excursion (≥ 3 consecutive events) from a temperature or humidity specification (temperature and humidity are evaluated against a specification, not an Alert, Action or Regulatory Level.)

4.1.2.3 Identify any QC Test Request Number(s) associated with requests for speciation.

4.1.2.4 Indicate on the form that Tracking Number Assigned, Investigation Form Initiated, and Staff Notified By/Date. This refers to step 3.2.1 and is usually conveyed via email.

4.2 Compiling Data)

4.2.1 Activities/Comments: Activities that were taking place at the time of the excursion, including cleaning activites and any situation that could potentially lead to an excursion such as higher traffic due to any type of activity or specific situation. Area releases by Area Status Updates may also be included in this section.

4.2.2 Quality Engineering may utilize a questionnaire to gather information regarding conditions at the time of the sample(s) in question from the PA technician or from the area owner or staff working in the area at the time of the excursion.

4.2.3 Results of recent monitoring: Review recent monitoring data and draw (and document) conclusions. Look for trends, other recent excursions, etc.

4.2.3.1 Data should have sufficient replicates to discern trends.

4.2.3.2 Data may be presented in text format, but tables and graphs offer improved readability for multiple data points.

4.2.3.3 Adjacent spaces or sampling locations and complimentary test results (in addition to tests which were elevated) should be included as required for the investigation.

4.3 Event Action and Follow-up (BQA)

4.3.1 Potential product impact is evaluated and documented. Input from area owner/user may be included.

4.3.1.1 Severity of Impact is rated as “Minor,” “Major,” or “Critical.”

- Minor: An event that WILL OBVIOUSLY NOT cause a product to fail established final product test specifications or general product expectations for proper labeling lack of particulates, sterility assurance, etc. (This would apply to sampling locations outside of processing areas and samples that were taken when there was no active GMP processing.)

- Major: An event that could POSSIBLY cause a product to fail established final product test specifications or general

expectations but that may still allow the product to be used as intended with an approved corrective action.

- Critical: An event that is LIKELY to cause a product to fail established final product test specifications or general expectations and that makes the product unfit for its intended use.

4.3.2 The event is investigated to determine potential cause(s) and root cause (if possible) of the event. Conclusions are documented. In cases where the cause is not directly determinable, detail causes that were ruled out and the means by which they were eliminated. A conclusion may include several possible causes with rationale. The depth of investigation should be proportional to the severity of impact with more severe excursions receiving increased attention.

4.3.3 If the excursion was determined to have been caused by equipment failure, an engineering event is initiated (see ***SOP 21526, Engineering Event Management***).

4.3.4 Action(s) that have been taken or are proposed to address the immediate excursions and reduce the likelihood of future excursions are described. Attach or cross-reference any applicable Work Orders.

4.3.4.1 If an engineering change or if a breach to the system is required as part of actions, an engineering event is required (see ***SOP 21526, Engineering Event Management***).

4.3.5 Results of Subsequent Resampling

4.3.5.1 Document the results of subsequent resampling. This data may be included in the DATA section.

4.3.5.2 The number of data replicates may depend on the nature of the Actions such that the more involved the Actions, the more data that may be needed to verify effectiveness.

4.3.6 Review and Approvals

4.3.6.1 The Event Action and Follow-up are reviewed and approved by the Equipment Owner, and BQA Engineering. These signatures are required every time.

4.4 **In addition, the Event Action and Follow Up may be reviewed and approved by the Equipment Owner if this individual is unique from the area owner and the event is due to equipment failure of the equipment requires and EE. This should be marked NA if not used.** BQA Review/Closure of Event (BQA Engineering)

4.4.1 BQA Engineering documents when any Action(s) have been acceptably executed and documented.

4.4.2 Microbial isolate identification is recorded (if applicable). Any relevant details regarding the organism such as source, pathogenicity, prevalence of recovery in the facility, or special characteristics like the ability to live in wet or low nutrient areas should be included.

4.4.3 The cause of the event is coded for trending purposes as “man,” “materials,” “methods,” “machines,” or “environments.”

4.4.4 The BQA Engineering signature indicates that the event has been satisfactorily closed.

4.5 ATTACHMENTS

4.5.1 This is a checklist of applicable attachments to include with the report form. Typical de

4.5.2 All reports shall include the original QC Test Request. The original test request(s) is the original QCTR with elevated value(s) triggering the EM Event.

4.5.3 A map to identify the location of the sample provides context and clarity to those less familiar with the utility or room layout is suggested. This can alternatively be included in the body of the report. This would not be applicable for a stand along water system or similar with only a single sample point.

4.5.4 The speciation QCTR provides the identification of identified isolates.

5.0 Documentation

Form 22313-01 including the associated attachments will be filed in a binder labeled with the year of the event indicated. Binders are maintained in the Document Control Room. (If the report is signed electronically, a paper copy is not required.) Digital drafts and attachments are maintained in the EM Excursions Events folder, a subfolder of QAOnly. An approved digital copy may also be maintained.

6.0 References and Related Documents

SOP 22314	*Monitoring of Compressed Gas Systems*
SOP 22315	*Environmental Monitoring in BDP GMP Areas at the ATRF*
SOP 22316	*Water Monitoring in BDP GMP Areas at the ATRF*
SOP 21526	*Engineering Event Management and Status Placarding*
SOP 22335	*ATR B2 Cell Therapy Suite Environmental Monitoring*
Form 22313-01	*Excursion Event Initiation and Investigation*

7.0 Change Summary