Procedure: Managing Deviations

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| Document information, authorship and approvals | | | |
| Author signs to confirm technical content | | | |
| Prepared by: | Job title: | Signature: | Date: |
| Subject matter expert reviewer signs to confirm technical content | | | |
| Reviewed by: | Job title: | Signature: | Date: |
| Quality representative signs to confirm document complies with quality management system | | | |
| Authorised by: | Job title: | Signature: | Date: |

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# Purpose

The purpose of this procedure is to describe the requirements for managing all Good Manufacturing Practice (GMP) deviations at [Company].

# Scope

The scope of this procedure includes all deviations with the potential to impact product quality of GMP products, processes and systems, including (but not limited to):

* Non-conforming starting materials, manufactured interim or finished products, Quality Control (QC) or stability testing, or any other deviation from approved specifications, criteria or requirements
* Deviating from a Quality Management System (QMS) procedure, test method, specification, limit/criteria or manufacturing instruction or using an unauthorised or uncontrolled document not managed by the QMS
* Deviating from mandatory regulations or standards (as applicable)
* Any other deviation within the facility or associated with services, computer systems or environmental monitoring
* When an adverse trend has occurred
* Planned deviations from a QMS procedure, test method, specification or manufacturing instruction.

Excluded from this procedure are:

* business, administrative or facility deviations not covered by the QMS and/or that are not GMP
* managing corrective and preventative actions (CAPA). **[Refer to QP809 –Corrective and Preventative Actions]**

# Responsibilities

Amend to reflect the organisational structure.

|  |  |
| --- | --- |
| Role | Responsibility |
| Quality Manager (or delegate) | * Provide Quality oversight for all deviations. * Ensures impacted batches are not released during investigation and approves final batch disposition. * Assign deviation criticality. * Management of the deviation quality system. |
| Department Managers (Deviation Owner) | * Facilitates deviation investigation. * Notifies Quality Department of deviation, impacted batches/product or initial containment actions. * Ensures deviation corrective actions and any preventative actions are completed. |
| All staff | * Immediately notifies the Department Manager when a deviation is first detected * May be required to be a team member for a deviation investigation team |

# Procedure

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| **Important:** | * Impacted batch(es) **must not** be released until the deviation is closed out and batch disposition assessed. * All actions, conclusions and recommendations must be documented on **FP805-1 – Deviation Report** as the investigation progresses. |

The following steps are required for all GMP deviations:

## Identifying a deviation

All staff are responsible for immediately notifying the Department Manager when a deviation is detected. If staff are unsure if an unusual event or circumstance is a true deviation, the staff member must notify the Department Manager.

The Department Manager confirms whether the event or result is a true deviation. Deviation types include:

* Non-conforming material/product, result or data
* Deviation from a QMS procedure/document
* Deviation from mandatory regulations
* Deviation within facility/services/environment
* Adverse trend detected
* Planned deviation
* Unknown - to be determined (status must be updated once the deviation type is known).

The Department Manager determines if any immediate actions are required and consults with the Quality Manager if required. When immediate actions are required, the Department Manager notifies the Quality Manager of the proposed actions.

## Documenting a deviation and initiating containment

When a non-conformance is identified:

* FP805-1*:* Deviation *Report* is initiated by the staff member who identified the problem in conjunction with the Department Manager. The report must be filled out as directed with all details of the non-conformance being recorded.
* The initiated deviation report is given to the Quality Manager who will log the non-conformance and issue a unique deviation number.
* The affected material is appropriately labelled, including the relevant deviation number, and assigned a Quarantine status pending investigation and a decision regarding the actions to be taken.
* The Quality Manager ensures impacted batches are placed on hold and cannot be released. The deviation may be escalated to executive management at this stage if required.

Local procedures must be in place for these activities.

Deviations must be raised in a timely manner in accordance with local procedures (generally 24 hours).

## Assign the criticality level of the deviation

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| --- | --- |
| **Important:** | * An initial risk assessment is required to assign the deviation level and must be completed and reviewed by the Quality Department within three (3) working days of the date the deviation is logged. [Note: 3 days is suggested as an industry guideline] * When assessing the risk, emphasis should be on identifying the immediate impacts of the deviation on product attributes, product formulation and process/system performance rather than identifying the final consequences or harm (determined during impact assessment). |

The initial risk assessment is used to quickly assign the:

* overall risk to product quality and patient safety,
* level of effort required for the deviation investigation, and
* requirement for escalation to senior management.

This initial risk assessment is not intended to be a detailed analysis of all hazards or potential risks as this is captured during the investigation (ref. Section 4.4).

As part of the initial risk assessment for the deviation, the Quality Manager (or delegate) must assign one of the following deviation criticality levels:

* Minor
* Major
* Critical

The deviation level is based on risk class (low, medium, high) and existing controls. Refer to *Appendix 1 - Level of deviations* for guidance on assigning risk class and deviation level.

If the deviation has not impacted on product quality or patient safety in any way then record a comment on *Form FP805-1: Deviation Report* justifying why the deviation has no impact.

## Investigating the deviation

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| --- | --- |
| **Important:** | * The deviation investigation must be completed within 30 days of the date the deviation is logged. [Note: 30 days is suggested as an industry guideline and may be varied with deviation criticality dependent on company policy] * All aspects of the investigation must be documented according to GMP requirements. |

The deviation investigation should be completed at a level commensurate with the deviation criticality level (based on risk class). Critical deviations will necessarily require a more comprehensive investigation using the appropriate QRM tools than a minor deviation and similarly result in a more thorough and wide-ranging set of corrective actions.

Consideration must also be given as to whether the deviation constitutes a trend against previous related events.

A change to the assigned deviation criticality level, as other information becomes available during the investigation, may be appropriate subject to Quality Manager approval. Justification for changing the deviation level must be based on a risk assessment and be approved by the Quality Manager.

The investigation may include:

* Interviewing staff involved in the deviation
* Consulting with site subject matter experts (SMEs)
* Discussing the investigation with appropriate Quality and Department Managers

### Information to be reviewed

Sources of information may include (but are not limited to):

|  |  |
| --- | --- |
| * Batch records * Validation and calibration records * Maintenance and usage logs * Associated procedures * Stability data * Regulatory dossiers and specifications * Training records of associated staff * Interviews with associated staff * QC test results for raw materials and final products * QC test methods | * Trending data (product, equipment, room, personnel, QC results, environmental monitoring) * Environmental monitoring (viable and non-viable) * Supplier history (raw materials, containers, primary packaging) * Cleaning records * Published scientific data * Regulations, standards, compendia * Risk assessments |

### Root cause analysis

Root cause analysis (RCA) must be completed for all critical deviations and may be completed for major or minor deviations at the discretion of the Quality Manager. Investigation tools for determining root cause can include (but is not limited to):

* FMEA / Risk Assessment
* 5 Whys
* Fishbone analysis/Cause and Effect
* ‘Plan, Do, Check, Act’ (PDCA)

Refer to PE 009-11, Annex 20, Appendix 1 for suggested QRM tools available for deviation investigation activities.

### Impact assessment

Determine the impact of the deviation and provide recommendations for the impacted batch(es). Provide:

* justification for adding batches to, or removing batches from, the deviation investigation
* justification for the disposition of each batch
* justification on how risks will be mitigated
* supplier name, lot number, material name, material grade (for raw materials, components, packaging) and any supplier-related recommendations.

### Propose corrections and corrective actions

There are two types of actions that may be required as a result of a deviation (refer to the **Definitions** section of this procedure):

* Corrections - address or correct the outcome of the deviation.
* Corrective actions – are permanent solutions that must address the root cause of the deviation, typically via the CAPA system, and include an effectiveness check to confirm corrective actions have had the intended impact.

The investigation and proposed corrections and/or corrective actions are forwarded to the Quality Manager for review and approval. These actions may be managed within the scope of the deviation itself or may be transferred into a CAPA system, change control, training or similar Quality system for action.

### Non-conforming product

If the deviation is in relation to non-conforming product there are a number of different scenarios. The non-conforming product may be:

#### Reprocessed or reworked

To address the quality deficiency identified in the deviation, non-conforming product may be reprocessed by recrystallisation, washing and/or refiltering, as agreed with the Quality Manager or as written in the manufacturing instructions. Reprocessing of product is carried out in accordance with Procedure QP716: Reprocessing of Drug Products and API.

Any reprocessing operation carried out on a batch must be documented in the batch record. The reprocessed product is then tested to determine if they meet the required specification and are assigned a new batch number.

#### Accepted

Non-conforming product may be accepted after consultation with the customer. In this case, the Quality Manager must document the justification, the correspondence and the final decision to approve the product.

#### Rejected

Non-conforming product that is not fit for sale is destroyed. Appropriate State and National environmental / waste handling regulations are followed where required.

#### Re-assigned

Non-conforming product may be considered unfit for sale but may be kept for the use of R&D for experimental purposes. In this case, the batch must be labelled and moved to a suitable R&D store.

#### Returned

All materials returned from customers are handled in accordance with Procedure QP808: Customer Complaints. If non-conforming product is detected after dispatch, follow Procedure QP807: Product Recall.

Local procedures should be in place for these activities. In the event reprocessing or reworking is to occur, this must be performed under an approved rework document. Each activity must have the appropriate level of approval including the Quality Manager or delegate and make reference to the relevant deviation report.

## Closing the deviation and finalising batch disposition

Once the corrections and/or corrective actions have been implemented, *Form FP805-1: Deviation Report* and all associated documentation (included as attachments) are forwarded to the Quality Manager for review and closeout.

The Quality Manager confirms the following stages before closing out the deviation:

| Stage | Description |
| --- | --- |
|  | The investigation has been completed to an appropriate quality standard and there is confidence in the identified root cause. |
|  | The risk class of the deviation is still appropriate – the risk class and/or deviation level may need to be reclassified if the investigation indicates that this is appropriate. |
|  | The recommendation for batch(es) disposition is appropriate. |
|  | Batch(es) disposition is scheduled and completed by QA. |
|  | Any CAPA or change control has been initiated and reflects the requirements of the deviation investigation. Include reference in *Form FP805-1: Deviation Report.* |
|  | All inspection rejects held for investigation purposes have been disposed of appropriately and integral samples returned to the appropriate storage area. |
|  | Retention sample reviews have been completed and retention samples returned to the retention storage area. |

When all aspects of the investigation are complete and meet GMP standards, the Quality Manager closes out the deviation by:

* Signing final approval of *FP805-1: Deviation Report*
* Closing the deviation record in appropriate register.

## Planned deviations

A planned deviation is when a legitimate deviation from what is described in a controlled document is required. Use *FP805-1: Deviation Report* to document a planned deviation. A planned deviation is different from a change control because the change is not permanent.

The planned deviation must be pre-approved by the Quality Manager before implementing the planned action.

Planned deviations must:

* be the exception and not routine
* refer to a temporary change only
* only be required for an individual batch/event.

All other changes must be captured using the change control system; refer to *Procedure* *QP703: Change Control*.

## Deviation extensions or cancellations

The Department Manager may request the deviation to be either:

* Cancelled – when the investigation is no longer required (e.g. the event is found to not be a deviation)
* Extended – when the deviation has legitimately taken longer than planned or unforeseen circumstances have delayed the implementation. Poor planning is not a legitimate reason for extension.

Justification for either cancellation or extension must be documented on the original *FP805-1: Deviation Report*. The Quality Manager reviews the extension or cancellation and approves/rejects the request as appropriate.

**Note**: Cancellation is not a means to not comply with GMP or other mandatory regulations.

## Trending deviation metrics

The Quality Manager should report to executive management the following metrics on a monthly basis and the trends for each metric over a rolling 12 month period:

* number of deviations opened each month
* number of deviations with ‘approved to implement’ corrections
* number of deviations closed each month
* number of minor/major/critical deviations raised each month
* number of deviations past the expected close-out date (expired or overdue deviations).

Include a breakdown of:

* deviations per department
* expired deviations per department.

Ongoing expired deviations should be escalated to executive management.

Appendices

Amend Appendices as required or delete.

# Appendix 1: Level of deviations

The table below provides some example risk classes and how they might translate into a deviation level.  
Deviation level is assigned from the risk class and the level of control.

| Risk Class | Severity | Probability of Occurrence | Examples | Controls | Deviation Level |
| --- | --- | --- | --- | --- | --- |
| Low | No impact on product quality, manufacturing efficiency and patient safety  (No impact) | No impact on other systems or processes | Damaged label of a dispensed material (material identification is known).  Different dilution series used to prepare the same sample concentration or dilution as required.  Sensor is out of calibration within the range of an independent, calibrated recording sensor. | Sufficient controls do not exist | Minor |
| Sufficient controls already exist | Minor |
| Medium | * May cause an atypical or out of trend (OOT) result for in-process, final product or process parameters, or * Minor, negative impact on manufacturing yield, or * Minor impact on patient safety (no long term detrimental effects)   (Indirect or direct impact) | * Impact limited to a single batch, or * Minor impacts on other processes or systems, or * Minor impacts on multiple batches (e.g. OOT), and * Does not cause a systematic error | Working standard used in batch release testing is not within specification.  Integrity test failure of a laminar flow workstation used to dispense raw materials.  Environmental monitoring failure at one point in Grade A or Grade B area on a non- product contact surface | Sufficient controls do not exist | Major |
| Sufficient controls already exist | Minor |
| High | * Major negative impact on product quality e.g. OOS in-process, final product or process parameter results, or * Major negative impact on manufacturing efficiency, or * Major (significant long term) negative impact on patient safety   (Indirect or direct impact) | * Serious impacts on a single batch, or * Serious impacts on other processes or systems, or * Systematic error, or * Reoccurred within three batches of same product or within two weeks of operations, or * Information on impact not available | Major HVAC system failures.  Major test method failure used to release multiple batches.  Processing delayed for more than the validated time.  Mix up of raw material codes used to manufacture a batch.  Post batch filter integrity test failure.  Grade A or Grade B environmental failures for a product contact surface. | Sufficient controls do not exist | Critical |
| Sufficient controls already exist | Major |

**Definitions**

Amend as required or delete.

| Term | Definition |
| --- | --- |
| Non-conformance | Material that does not meet or no longer meets the specification. |
| Product | Material purchased, manufactured or processed to fulfil customer or stock requirements. |
| Corrections | Address or correct the outcome of the deviation |
| Corrective actions | Permanent solutions that must address the root cause of a deviation, typically via the CAPA system, and include an effectiveness check to confirm corrective actions have had the intended impact |
|  | Insert terms/abbreviations and definitions for those used within the procedure. Do not include any terms or abbreviations not used within the procedure. |
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Document Information

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| Associated forms and procedures | |
| --- | --- |
| Doc. No. | Document Title |
| PE 009-11 | PIC/S Guide to Good Manufacturing Practice for Medicinal Products |
| QM001 | Quality Manual |
| QP703 | Change Control |
| QP716 | Reprocessing of Drug Products and API |
| QP807 | Product Recall |
| QP808 | Customer Complaints |
| FP805-1 | Deviation Report |

List all controlled procedural documents referenced in this document (for example, policies, procedures, forms, lists, work/operator instructions

| Associated records | |
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| Doc. No. | Document Title |
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List all other referenced records in this document. For example, regulatory documents, in-house controlled documents (such as batch record forms, reports, methods, protocols), compliance standards etc.

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