Template Provided By:

Cancer Imaging Program

National Cancer Institute

Standard Operating Procedure

GEN-M120

Documentation of Manufacturing Variances

1. **Purpose:** To provide procedures for the documentation of manufacturing events where the actual production processes inadvertently vary from those as they are written in either of the following: Standard Operating Procedures, the compounding records, the Specification Sheets, Forms, and/or the Master Production and Master Batch Records.

2. **Scope:** To provide written procedures for the documentation of any inadvertent process/manufacturing variance that may occur at the *site of manufacture* radiopharmaceutical.

3. **Responsibilities:**
   3.1. *Site of Manufacture & Sponsor*: To follow this procedure as written and to ensure that all results, control information, and raw data are documented as specified in dedicated Quality Control Laboratory Notebooks and recorded on the appropriate testing forms. Document the manufacturing variance on the manufacturing variance report form, MVR-001, as appropriate.

4. **References**
   USP 28 ‹821› Radioactivity
   USP 28 ‹823› Radiopharmaceuticals For Positron Emission Tomography—Compounding
   FDA Draft Guidance PET Drug Products—Current Good Manufacturing Practice (CGMP)—September 2005 (CDER)

5. **Forms**
   - **Form MVR-001**, Manufacturing Variance Report Form

SOP**: GEN-M120** Date: _____

Printed Name	Signature	Date
Author:		
Regulatory Approval:		

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6. Policies

Technical Equipment Failure is a variance attributed to the mechanical failure of the equipment not caused by improper usage or operation.

Operator Error is a variance that can be attributed to either, a rare but occasional inadvertent human error, or to improper training on a certain procedure or process that could have been avoided with proper training.

Quality Error is a variance that can be attributed to the sub-standard quality of any reagent, supply, or solution used in a QC test, or manufacturing process, that was not identified prior to its use.

7. Materials and Equipment

N/A

8. PROCEDURES

Variances for Master Batch & Compounding Records

Assign the variance a number by first entering the document control number followed by a dash, a "v," and then a sequential number, 0001, 0002, 0003, etc. Each variance should have its own unique number.

Record the variance number on the **Manufacturing Variance Report Form, MVR-001**.

Reference the variance number in the record at the step in which the variance occurred. Initial and date the reference.

On the variance report form, **MVR-001**, record the date the variance occurred, and whether the variance was a result of a technical equipment failure, operator error, or quality error.

Document in detail, the immediate events subsequent to when the variance occurred, and any relevant details that could potentially impact the product's quality, purity, or potency. Include and capture any relevant control information, measurements, signatures, etc. on the **MVR-001 Form**.

Document the corrective actions taken in response to this manufacturing variance on the **MVR-001 Form**, and the status of the product (if applicable) in relation to this incident.

Sign and date the variance report.

Make a copy of the completed Variance report form.

Place the original completed Variance report form with the Master Batch Record or the Compounding Record.

Submit the copy of the completed Variance report form to the *Sponsor's* Regulatory Affairs Administrator *via* facsimile.

Variances for SOPs and Forms

Assign the variance a number by first entering the document control number, followed by a dash, followed by the location code, and then the six digit date, e.g. X063004, subsequently followed by a "v" and a sequential number 0001, 0002, etc.

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Record the variance number on the **Manufacturing Variance Report Form, MVR-001**.

On the variance report form, **MVR-001**, record the date the variance occurred, and whether the variance was a result of a technical equipment failure, operator error, or quality error.

Document in detail, the immediate events subsequent to when the variance occurred, and any relevant details that could potentially impact the product's quality, purity, or potency. Include and capture any relevant control information, measurements, signatures, etc. on the **MVR-001 Form**.

Document the corrective actions taken in response to this manufacturing variance on the **MVR-001 Form**, and the status of the product (if applicable) in relation to this incident.

Sign and date the variance report.

Make a copy of the completed Variance report form.

Place the originals of the completed Variance report forms of the other control documents in separate storage retention files for tracking purposes.

Submit the copy of the completed Variance report form to the *Sponsor's* Regulatory Affairs Administrator *via* facsimile.

24-Hour Reporting of Variances

If the variance causes the batch to be aborted or if it has any other significant impact on the batch of final product it must be reported *via* telephone within 24-hours to the *Sponsor's* Regulatory Affairs Administrator. (Please note that this is in addition to submitting the variance form, **MVR-001**.)

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