



Root Cause Analysis in Pharma

***A Practical Guide to Investigations, Deviations,
Nonconformities, CAPA, and Continuous Improvement***

***Featuring Real-World Examples, RCA Methods, Case Studies,
Templates, and Practical Exercises***



www.henvorasolutions.com

info@henvorasolutions.com

What is a Nonconformity (NC)? 4

 Types of Nonconformities 5

 Nonconformity Classification 6

 Practical Example 7

What is a Deviation? 9

 Initial Assessment 11

 Deviation and Investigation 11

What is Root Cause Analysis (RCA)? 13

What is a CAPA? 17

Corrective Action versus Preventive Action 17

Why Are CAPAs Important? 18

 The Quality Event Journey 22

Regulatory Expectations 28

 Investigation Lifecycle 30

 Human Error versus System Failures 35

 Selecting the Right RCA Method 37

 Method Comparison 40

The 5 Whys Method 41

 The 5 Whys Method 42

 The Fishbone (Ishikawa) Method 44

Pharmaceutical Example 48

 Final QA Closure Statement 68

 Investigation Flow Summary 68

Weak versus Strong CAPAs 71



CAPA Effectiveness.....	72
Technical Investigation Writing.....	74
From Compliance to Continuous Improvement	78
Henvora Solutions	79

What is a Nonconformity (NC)?

A Nonconformity (NC) is one of the most fundamental concepts within pharmaceutical quality management. Every pharmaceutical organization strives to manufacture products according to approved procedures, specifications, regulations, and quality standards. When an activity, process, product, document, or system fails to meet one of these requirements, a Nonconformity occurs.

Simply stated:

A Nonconformity is a failure to meet a specified requirement.

The requirement may originate from:

- GMP regulations
- Internal procedures
- Approved specifications
- Validation requirements
- Customer requirements
- Regulatory commitments
- Quality standards

Nonconformities can occur in any department and at any stage of the pharmaceutical product lifecycle.

Why Are Nonconformities Important?

Nonconformities are not simply mistakes that need to be documented. They are opportunities to identify weaknesses within processes and quality systems before they affect product quality or patient safety.

An unmanaged Nonconformity may result in:

- Product defects
- Batch rejection

- Regulatory observations
- Recalls
- Patient harm
- Loss of customer confidence

For this reason, every identified Nonconformity should be evaluated, documented, and addressed appropriately.

Types of Nonconformities

Nonconformities may be identified in many areas of pharmaceutical operations.

Manufacturing

Examples:

- Incorrect equipment settings
- Incomplete batch record entries
- Failure to follow an SOP
- Missing line clearance

Quality Control

Examples:

- Out-of-specification (OOS) results
- Incorrect sample preparation
- Unapproved analytical method use
- Missing laboratory records

Validation

Examples:

- Protocol deviations
- Incomplete testing
- Failed acceptance criteria
- Missing qualification documentation

Engineering

Examples:

- Preventive maintenance not completed

- Calibration overdue
- Equipment alarms ignored
- Unapproved equipment modifications

Documentation

Examples:

- Missing signatures
- Incorrect document version
- Data entry errors
- Uncontrolled copies

Nonconformity versus Deviation

Many professionals confuse Nonconformities and Deviations.

A Nonconformity is the broader concept.

A Deviation is a specific type of Nonconformity involving a departure from an approved procedure, instruction, specification, or process.

Example

A batch record contains a missing operator signature.

This is a Nonconformity because documentation requirements were not met.

An operator skips a required cleaning step described in an SOP.

This is both a Nonconformity and a Deviation because an approved procedure was not followed.

Nonconformity Classification

Organizations often classify Nonconformities according to risk.

Minor

Little or no impact on product quality or patient safety.

Example:

- Typographical error in a controlled document.

Major

Potential impact on quality, compliance, or process performance.

Example:

- Incomplete equipment cleaning documentation.

Critical

Actual or potential impact on patient safety, product quality, or regulatory compliance.

Example:

- Release of product that does not meet specifications.

Classification determines the level of investigation required.

The Nonconformity Process

A typical NC process includes:

1. Identification
2. Documentation
3. Initial Assessment
4. Risk Evaluation
5. Investigation
6. Root Cause Analysis
7. CAPA Implementation
8. Effectiveness Verification
9. QA Closure

Every step contributes to continuous improvement and regulatory compliance.

Practical Example

Scenario

During batch review, QA discovers that an operator signed a manufacturing step one day after the activity was performed.

Question

Is this a Nonconformity?

Answer

Yes.

The documentation was not completed contemporaneously, which violates Good Documentation Practices and ALCOA+ principles.

Further assessment is required to determine:

- Product impact
- Data integrity impact
- Need for investigation
- Corrective actions

Practical Exercise

Read the following situations and determine whether a Nonconformity exists.

Situation 1

An operator uses an expired calibration sticker.

Situation 2

A laboratory analyst records results on scrap paper before entering them into the official worksheet.

Situation 3

A controlled SOP contains a spelling mistake but the instruction remains clear.

For each situation:

- Is a Nonconformity present?
- Why?
- How would you classify it?
- Would an investigation be required?

Discuss your answers before reviewing the proposed solution.

Not every Nonconformity is a Deviation, but every Deviation is a Nonconformity.

What is a Deviation?

In a pharmaceutical environment, processes are performed according to approved procedures, specifications, instructions, and validated methods. When an activity does not occur as planned or does not follow an approved requirement, a Deviation may occur.

A Deviation is one of the most frequently reported quality events within pharmaceutical operations and often serves as the starting point for an investigation.

Simply stated:

A Deviation is an unplanned departure from an approved process, procedure, specification, instruction, or expected outcome.

Not every Deviation will impact product quality, but every Deviation should be assessed to determine potential risks and the need for further investigation.

Why Are Deviations Important?

Deviation management is a critical component of pharmaceutical quality oversight.

Effective management of Deviations helps organizations:

- Detect process weaknesses
- Identify risks to product quality
- Prevent recurrence of issues
- Improve process understanding
- Demonstrate GMP compliance
- Support continuous improvement