• What can we learn from deviations?

• Why is it important to determine the root cause of deviations?

• How can we implement an effective CAPA?
ICH Q10 PQS

Pharmaceutical Development → Technology Transfer → Commercial Manufacturing → Product Discontinuation

Investigational products

GMP

Management Responsibilities

Process Performance & Product Quality Monitoring System
Corrective Action / Preventive Action (CA/PA) System
Change Management System
Management Review

PQS elements

Enablers

Knowledge Management
Quality Risk Management
State of control CONSISTENCY

Monitoring process performance
(quality management indicators & trend analysis)

Monitoring product quality
(product quality review or PQR)

Change management system

Internal & External Audit system

Corrective action and preventive action (CAPA) system

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• Deviation: departure from an approved instruction or established standard (WHO TRS 957, 2010. Annex 2).

• There should be formal procedures to report, investigate and approve deviations.

• Deviations should be evaluated considering the likelihood of the risk to the product/patient.

• Develop a policy on deviation management

• Determine a classification approach i.e. differentiation among various types of deviations

• Track deviations and analyze trends

• Database (software based or manual system) to assist in tracking and trending of deviations.
• Deviations should be investigated to understand if there is a serious impact in product quality

• Decision making process to follow any CAPA or batch release/rejection

• Investigation and its conclusions should be documented.

• Investigation of critical or major deviations should extend to other batches that may have been associated with the specific failure or deviation.
“...collect information, analyze information, identify and investigate product and quality issues, and take appropriate and effective corrective and/or preventive action to prevent recurrence of a problem.”

The heart of an effective quality management system

(key quality system element)

Corrective action: action taken to eliminate the cause(s) of a non-conformity, defect, or other undesirable situation to prevent re-occurrence.

Preventive action: action taken to eliminate the cause of a potential nonconformity, defect, or other undesirable situation in order to prevent occurrence.
Preventive & corrective action

**Corrective action example**

- Investigate to determine the root cause of a packaging problem and take appropriate action to ensure that this problem does not re-occur.

**Preventive action examples**

- Trending of environmental monitoring indicates that the cleanroom is drifting toward alert limit.

- Investigation indicates that a small tear in a HEPA filter is the root cause of the drift.

- Replace the HEPA filter

- Verify/validate that the process meets specification.
Elements of a sound CAPA program
(check list)

Documented procedure
- Inputs (data sources)
- Method for analyzing inputs
- Method for prioritizing
- Investigation (determine root cause)

Identify solutions (corrective or preventive)
- Verification or validation
- Impact assessment (risk analysis), where appropriate
- Corrective action plan
- Implement and Monitor
- Effectiveness verification
- Management review
Root cause analysis -
What do you think about the following situation:

“To address this mistake we must use root-cause analysis. I’ll begin by saying it’s not my fault.”
Root cause analysis

Root cause analysis tools:

- The “5 Whys”

- Cause and effect diagrams (also called an Ishikawa diagram or fish bone diagram).

- QRM tools (e.g. Fault tree analysis or FTA).
Quality data sources that should feed into CAPA
Internal data sources feeding into CAPA

- Deviations & Nonconformances
- Internal Audits
- 3rd Party Audits
- Supplier Evaluations
- Inspection & Test
- Process Monitoring
- Equipment Monitoring
- Design Controls
- Change Control
- Material Review Board
- Management Review

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External data sources feeding into CAPA

CA/PA System

Complaints & Adverse Events
Tissue Recovery Organizations
Distribution Partners
Product Returns
Suppliers
Recalls
Legal Claims
Management Review

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5 step CAPA approach

- Identify
- Implement
- Review
- Verify
- Analysis

Auditor road map

- Is there objective evidence of action taken to prevent recurrence?
- Were quality data sources identified and analyzed?
- Was root cause identified?
- Were the actions effective, verified or validated?
- Was it controlled that the actions didn’t adversely affect the product?
- Was CAPA information submitted for management review?
Summary

• Deviation management must assure prompt action, be based on quality investigations when required, and not to be repeated if CAPA is effective.

• Proper CAPA assures an effective learning process and prevents reoccurrence of deviations.