

GOOD DOCUMENTATION AND QUALITY MANAGEMENT PRINCIPLES



Vimal Sachdeva
**Technical Officer (Inspector), WHO Prequalification of
Medicines Programme**

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Why Good Documentation is essential?

- **An essential part of the quality assurance system and should exist for all aspects of GMP (reference: WHO GMP, Volume 2)**
- **Good documentation practice is an expected practice!**
- **Correct, complete, current, and consistent information effectively meet customer and stakeholder' requirements**
- **Helps to reduce observations raised on inadequate documentation practices.**



What constitutes Good Documentation?

- **Approve, review and update documents**
- **Changes & current revision status of documents identified**
- **Relevant versions of applicable documents available at points of use**
- **Documents remain legible and readily identifiable**
- **Documents of external origin identified and their distribution controlled**
- **Prevent unintended use of obsolete documents, and archiving.**



Observations on poor documentation practices

- Document error correction not signed/dated, and didn't include a reason for the correction
- Write-overs, multiple line-through and use of "White-out" or other masking device
- Sample sequence table and audit trail not documented (*if its not documented, it didn't happen*)
- SOP related to production, calibration, storage and maintenance not authorized by the QA head
- The delegation for the batch release, in case of absence of the QA manager, not recorded / documented
- Out-of-specification (OOS) procedure not detailed enough; flow chart and /or check-list not available.



How are mistakes corrected?

- **Draw a single line through the error**
- **Make the correction next to the error**
- **Write an explanation for the error**
- **Sign and date the correction.**



Some tips on Good Documentation Practices

- **Records should be completed at time of activity or when any action is taken**
- **Superseded documents should be retained for a specific period of time**
- **Records should be retained for at least one year after the expiry date of the finished product**
- **Concise, legible, accurate and traceable**
- **Picture is worth a thousand words**
- **Clear examples**
- **Don't assume knowledge.**



Quality Management

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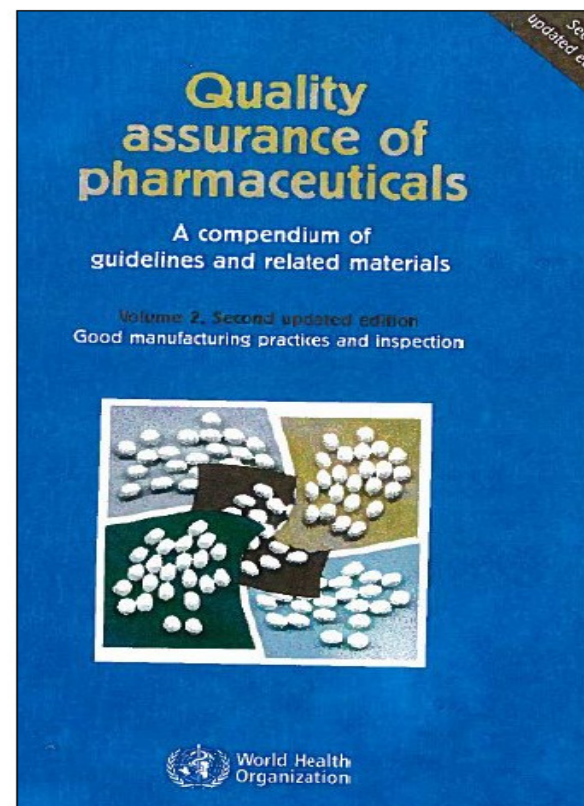


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What is Quality Management

- An appropriate infrastructure or "quality system", encompassing the organizational structure, procedures, processes and resources;
- Systematic actions necessary to ensure adequate confidence that a product (or service) will satisfy given requirements for quality. The totality of these actions is termed "quality assurance".



Quality Management



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Considerations for Quality Management

To incorporate an approach to doing business that stresses *building in quality* through techniques such as:

- design controls, continuous improvement, auditing, management review and risk management.

To incorporate a robust quality system encompassing good documentation practices, including but not limited to:

- handling of complaints, recalls, change controls, deviation controls, vendors qualifications using appropriate risk management tools.



Deviation control

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What is a deviation?

- **A departure from standard practices or specifications resulting in non-conforming material / or processes, with potential to impact on product quality, safety, efficacy or data integrity.**
- **Planned and unplanned deviation**
- **Different levels of deviation: critical, major, minor**

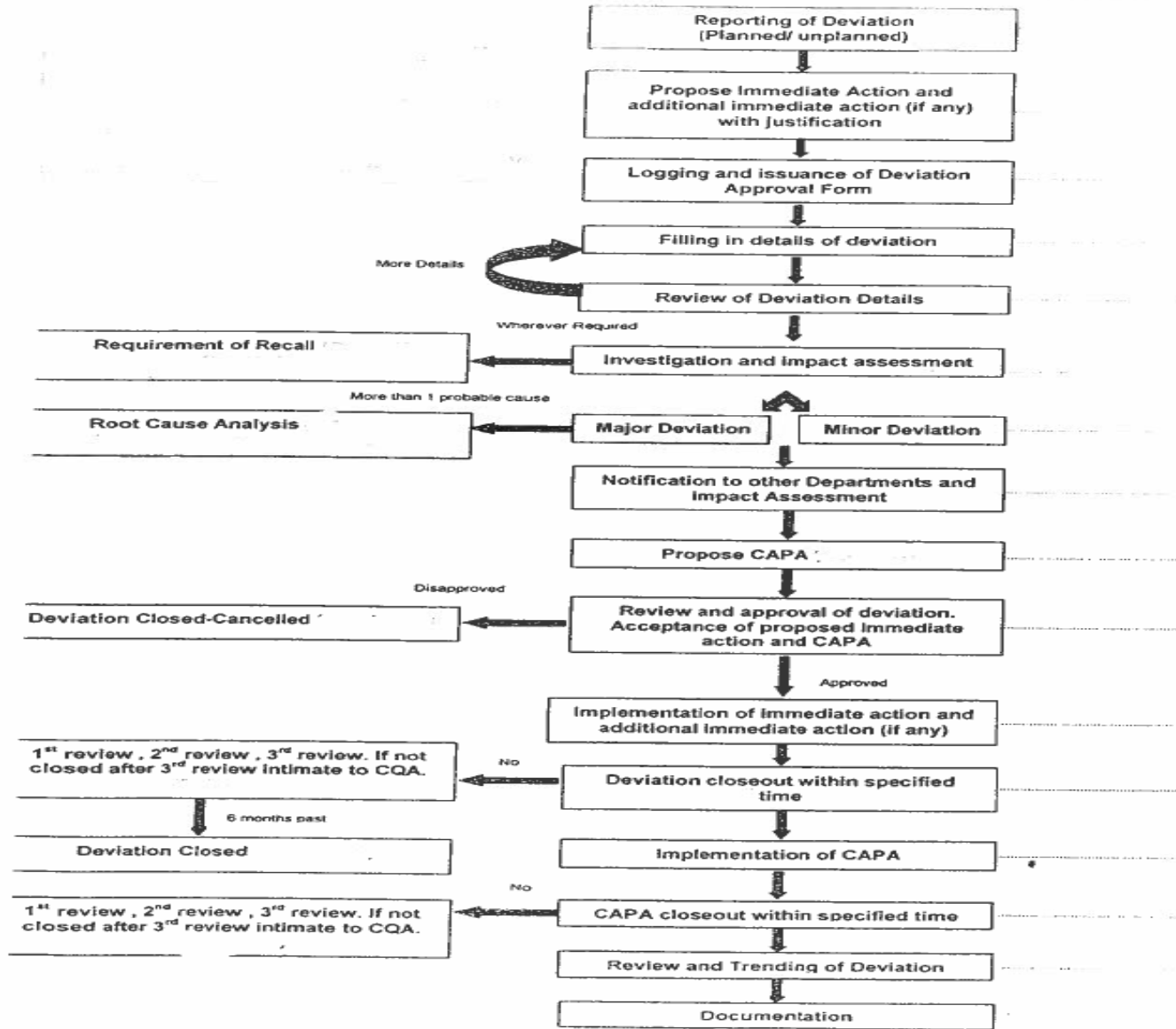


How to manage deviations?

- **Regulatory requirement to capture all sorts of deviations evolves in order to maintain the continuous improvement of processes and systems**
- **All batch production deviations (planned or unintended) covering all manufacturing facilities, equipments, operations, distribution, procedures, systems and record keeping should be reported and investigated for corrective and preventative action (CAPA)**
- **Deviation should be documented when there is a deviation from methods or controls in manufacturing documents, material control documents, and/or standard operating procedures.**



FLOW CHART FOR HANDLING OF DEVIATION



Considerations for Deviation Management

- **Develop policy on deviation**
- **Determine approach i.e. differentiation among various deviations**
- **Tracking of deviation**
- **Trending of deviation**
- **Create database (software based or manual system) to assist in tracking and trending of deviations.**



Change control

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Change control

Change: any modification to product, document, process, equipment, instrument, system, facility etc.

Change control: procedure reviews, verifies, regulates, manages, approves and controls changes made to the existing operating system or facility or process or procedure or document or product of any combination

The key principles of change control are understanding and documenting:

- What was done, why, when, where, by whom, how and
- Results, including the impact of changes to other processes.



How to manage change control

Written procedures should be established and maintained to control changes for:

- **Processes, Facilities, Utilities**
- **Methods, Validation, Computer systems**
- **Training and training materials**
- **Regulatory filings and Quality systems**

Changes should be justified and documented.

All changes that have the potential to impact the quality, safety and efficacy should be evaluated, reviewed and approved.

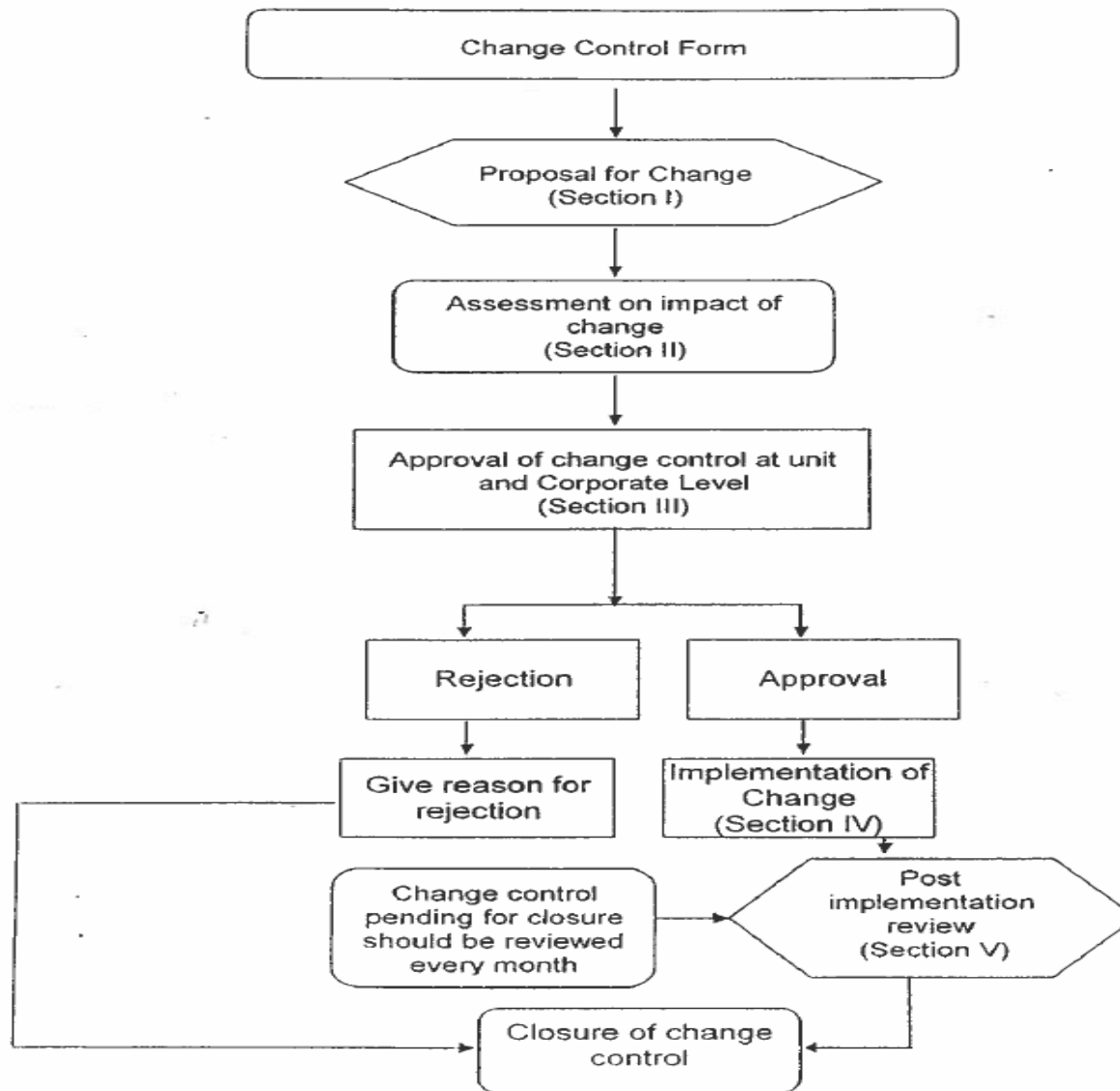


Change request form

Form ID:	Change ID:	Item ID:
Item Location:		
Change Initiator:	<i>Enter name.</i>	<i>Date of request.</i>
Description of Change:	<i>Enter a summary and a reason for the change and the business benefit.</i>	
Change Priority:	High <input type="radio"/>	Medium <input type="radio"/> Low <input type="radio"/>
Latest Acceptable Date:	<i>Only necessary if the change is time critical.</i>	
Impact Assessment:	<i>Describe the technical impact, on the individual item and on the entire network, typically done by the validation group.</i>	
Risk Assessment:	Risk: Likelihood: Severity: Recovery:	
Test Plan: (Validation Group)	<i>Describe test efforts.</i>	
Regulatory Notification Required:	Yes <input type="radio"/>	No <input type="radio"/> (Done by QA)
Change Approval:	Accepted <input type="radio"/>	Rejected <input type="radio"/> Comments or reasons for rejection:
Signatures: Laboratory Mgt. QA Mgt.	Name:	Signature: Date:



Flow chart of Change control



Considerations for Change control

According to the nature and extent of the changes, and the effects these changes may have on processes & products:

- Realistic and based on the risk (critical, major and minor) associated with each change
- SOP on change control should provide as many examples / scenario as possible for the various changes
- Impact assessment following implementation of each change
- Approval from the respective regulatory authority on the changes which has direct impact on the quality, safety and efficacy
- Tracking to manage all types of changes
- Periodic review should be done on all changes taken place.



Conditions to Change control

- **Revalidation**
- **Requalification**
- **Increased testing**
- **Stability analysis**
- **Document change**
- **Regulatory action / variation application.**



Quality Risk Management

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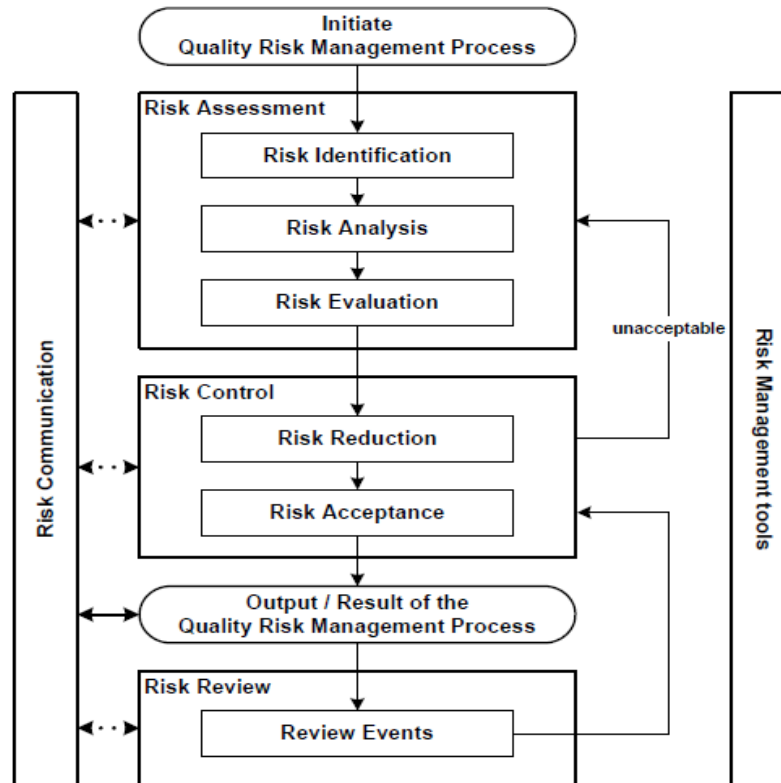
Quality Risk Management

The main risk management process includes:

- Risk assessment
- Risk control
- Risk review
- Risk communication



Overview of a typical quality management process



Ref: ICH Q9



Considerations for Quality Risk Management

No guidance documents specifying what documents and records must be kept by an organization.

Our expectations are to scrutinize processes, products, materials, vendors, equipment, facilities, distribution systems using appropriate risk management tools. Following documents and records should at least be available to support a risk management program:

- policies
- procedures
- analysis-specific plans
- records and reports.



Considerations for Quality Risk Management-2

Evaluation of the risk to quality should be based on:

- **Scientific knowledge and**
- **Ultimately link to the protection of the patient**

The level of effort, formality and documentation should be commensurate with the level of risk.

Note: WHO Guideline on Quality Risk Management



Product Quality Review

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What is Product Quality Review (PQR)

"Regular evaluations of the quality of pharmaceutical products should be conducted with the objective of verifying the consistency of the process and ensuring its continuous improvement (WHO GMP 1.2/I)".

"Regular quality reviews of APIs should be conducted with the objective of verifying the consistency of the process. Such reviews should normally be conducted and documented annually and should include at least a review of.... (WHO GMP for APIs 2.5)".

The EU PQR requires a greater number of items and areas for review as compared with the US product annual review (PAR).

Note: A detail section on PQR (similar to the EU GMP) has been included in the revised Annex 3, WHO GMP Guide.

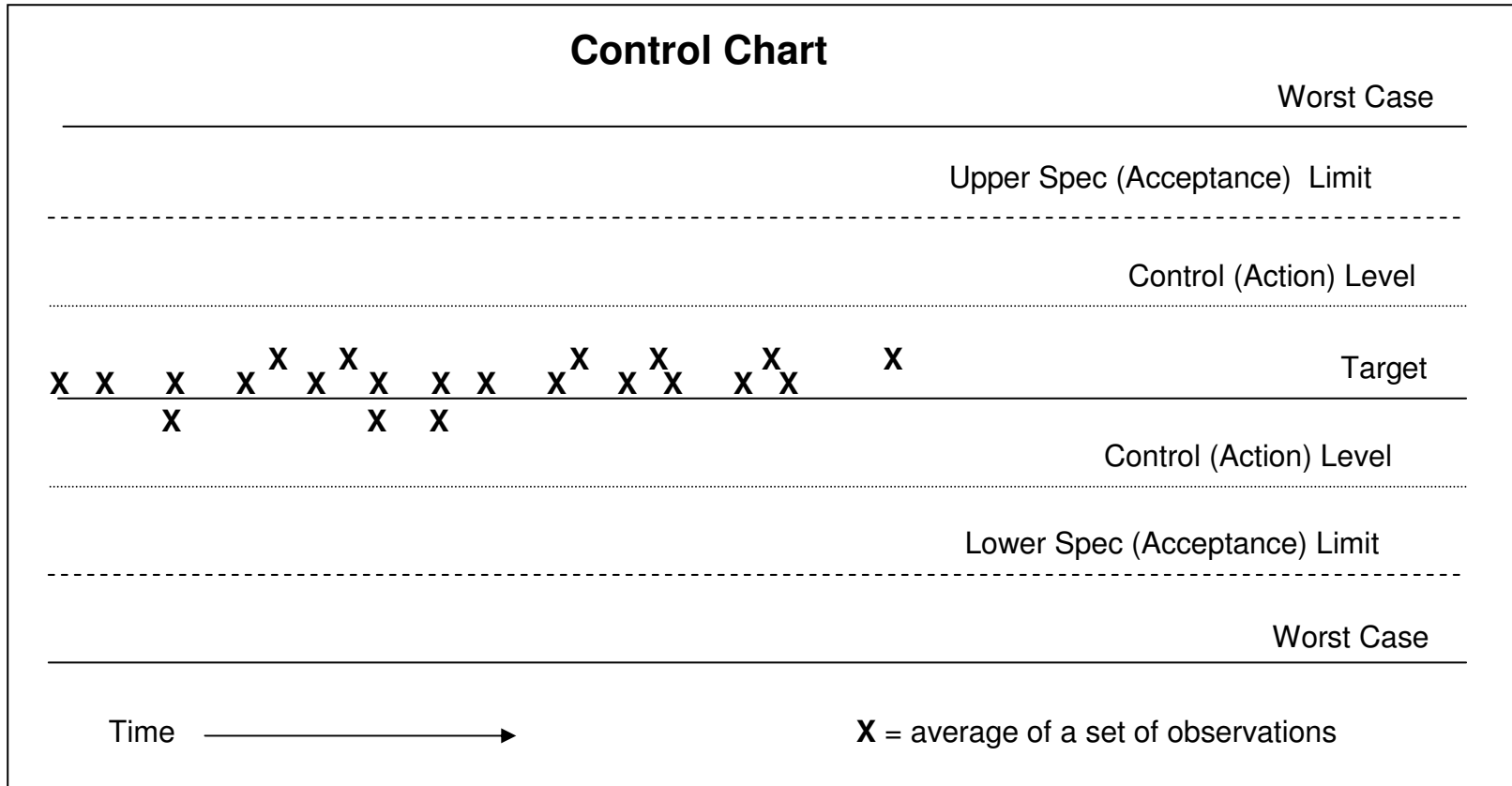


Considerations for PQR

- The PQR should be written in a common language (e.g. English) which must be understood by all the parties involved.
- The procedure for performing a typical product review involves the review, analysis, and trending of historical data (i.e., data generated in the past 12 months).
- Data generated from the batch or product should be trended using appropriate statistical techniques (control charts, process capability study) to determine if the process is in control/capable and any need to make changes.
- Based on the review, an assessment be made whether corrective and preventive action (CAPA) or any revalidation be undertaken, and the same should be completed in a timely and effective manner.



Example of control chart



Example of control chart-2

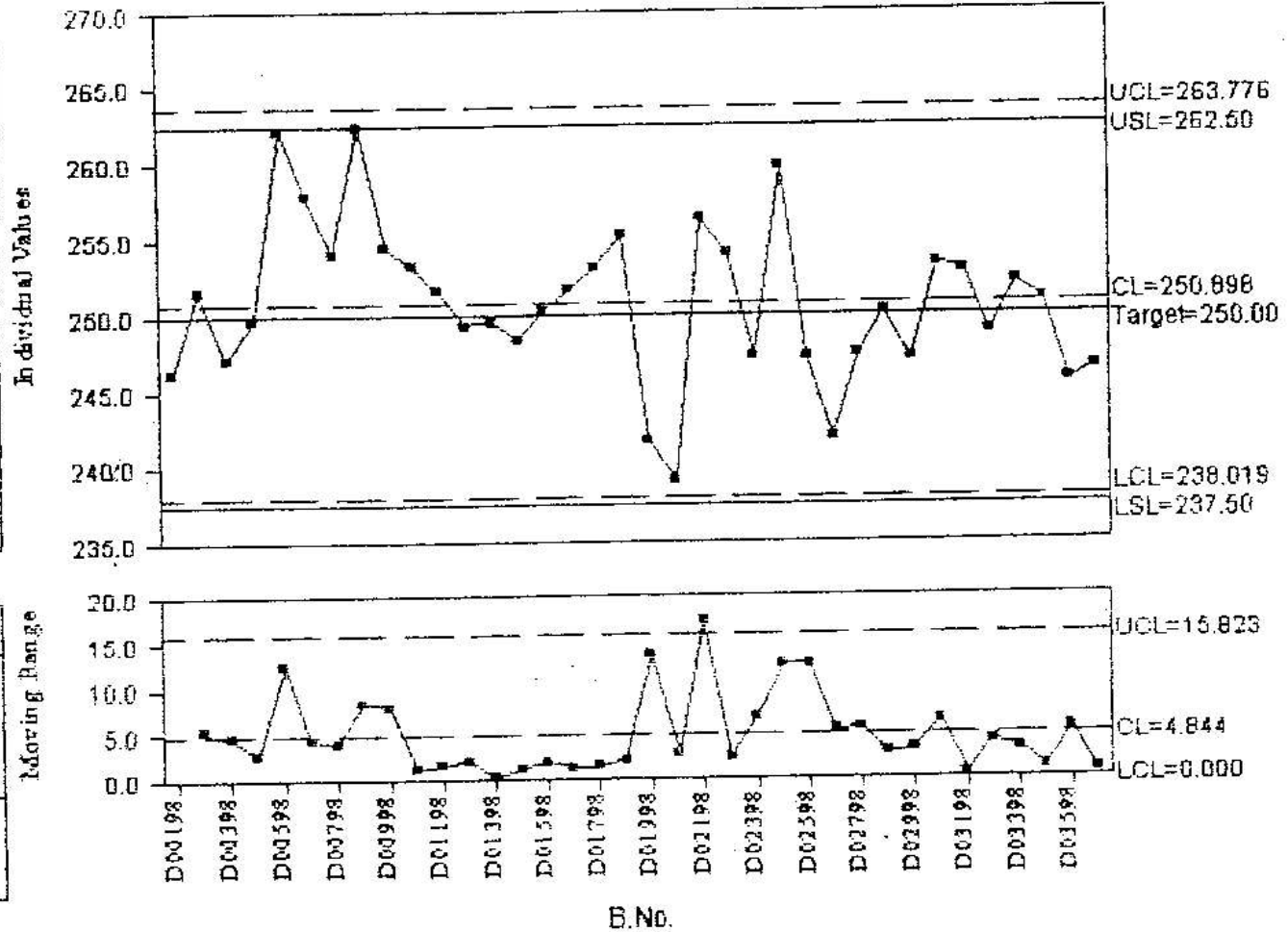
Process Statistics

Total:	36
Rows:	All
Std Dev:	5.227
CpM:	0.950
CpK:	0.901
Est % out SL (Cap):	0.43
Act % out of SL:	0.00
Dist:	Normal
<hr/>	
X-Bar:	250.898
Est Sigma:	4.293
Sigma Type:	Est
MR-Bar:	4.844

Chart Point

Label:	
X	
X UCL:	
X CL:	
X LCL:	
<hr/>	
MR:	

Assay



Process Capability

Capability Value (C_P or C_{PK})	Translate into
< 1.00	Process is not capable
1.00 to 1.33	Product is barely manufacturable
1.34 to 3.00	Process is a good one
>3.00	Process is excellent

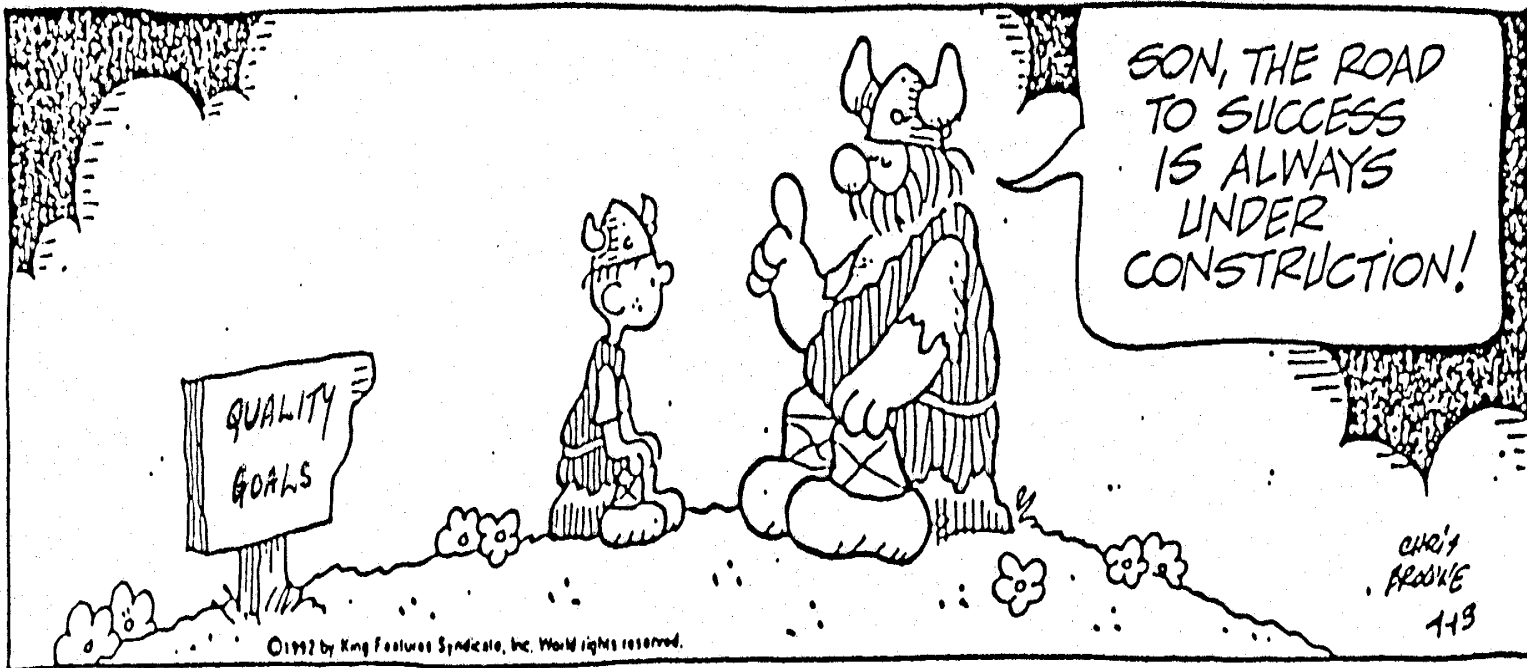
Ref: Establishing the Minimum Process Capability for a Drug-Product Manufacturing Process – Dr Paul King.



Summary

- **To make a firm commitment to medicines Quality, and Patient Safety and implementation of GMP**
- **To operate a robust quality management system**
- **Finally, companies should not work only to pre-qualify their pharmaceutical products, rather companies should operate their manufacturing facilities under quality system at all times.**





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Suggested reading

WHO, Quality Assurance of Pharmaceuticals, Vol 2, Second Edition

http://www.who.int/medicines/areas/quality_safety/quality_assurance/production/en/

OECD Principles of Good Laboratory Practices

http://www.oecd.org/document/63/0,3343,en_2649_34381_2346175_1_1_1_1,00.html

Risk Assessment and Risk Management – James L. Vesper

ICH, Q9 on QRM and Q10 on Quality System

<http://www.ich.org/home.html>



Thank you for your attention

sachdevav@who.int

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