Process Validation Overview

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Objectives

- Understand how present your process validation to an Inspector or Auditor:
  - Explain process validation as an element of medical device manufacturing
  - Describe the regulatory requirements from QSR and ISO 13485:2016
  - Explain what Investigators and Auditors look for using the QSIT and MDSAP Audit Models
  - Implementing the process validation system

Topics

- The QSR Requirements
  - The Preamble
- The ISO 13485:2016 Requirements
  - The Handbook
- GHTF Guidance Document
- The Validation Paradigm
- The Validate Phase
  - When to Validate
  - Goal of Validation
  - validation Paradigm – IQ, OQ, & PQ
- The Perform Phase
- The Revalidate Phase
- Data Analysis
- Summary
- Questions

The QSR Requirements

Definition

- §820(z)(1) *Process validation* means establishing by objective evidence that a process consistently produces a result or product meeting its predetermined specifications.

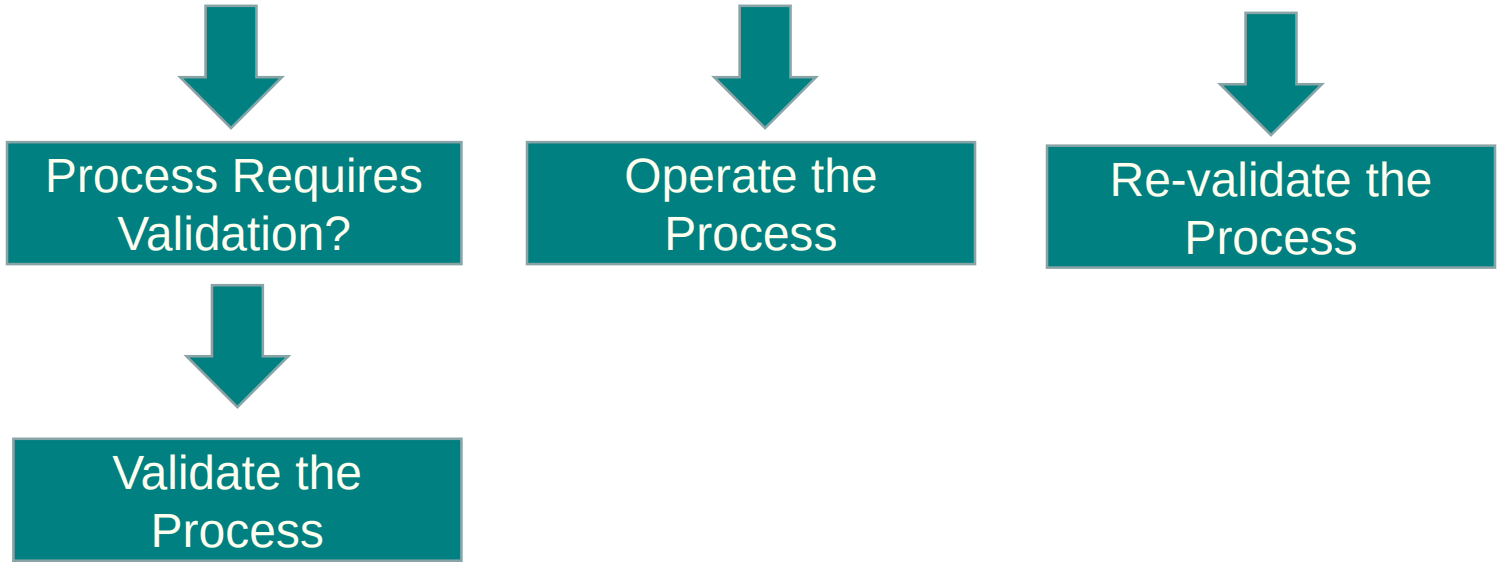
- Parsing the definition
  - Objective evidence means documentation of the results
  - Constituently produces a product means that the process output is consistent over time
  - Predetermined specification means knowing, in advance, the output the process should produce

Production and Process Changes

- §820.70(b) Production and process changes
- Each manufacturer shall establish and maintain procedures for changes to a specification, method, process, or procedure. Such changes shall be verified or where appropriate validated according to §820.75, before implementation and these activities shall be documented. Changes shall be approved in accordance with §820.40.

- Linkage
  - A change under §820.70(b) that affects a validated process leads to §820.75(c)

Process Validation System



Validate the Process

- §820.75(a) Where the results of a process cannot be fully verified by subsequent inspection and test, the process shall be validated with a high degree of assurance and approved according to established procedures. The validation activities and results, including the date and signature of the individual(s) approving the validation and where appropriate the major equipment validated, shall be documented.

- Major Points:
  - Fully verified process results
  - Subsequent inspection and test
  - High degree of assurance

Operate the Process

- §820.75(b) Each manufacturer shall establish and maintain procedures for monitoring and control of process parameters for validated processes to ensure that the specified requirements continue to be met.
  - (1) Each manufacturer shall ensure that validated processes are performed by qualified individual(s).
  - (2) For validated processes, the monitoring and control methods and data, the date performed, and, where appropriate, the individual(s) performing the process or the major equipment used shall be documented.

- Major Points:
  - Process parameters
  - Qualified individuals
  - Quality records

Revalidate

- §820.75(c) When changes or process deviations occur, the manufacturer shall review and evaluate the process and perform revalidation where appropriate. These activities shall be documented.

- Major Points:
  - Process changes
  - Process deviations
  - Review and evaluate
  - Perform revalidation where appropriate

Considerations from the QSR Preamble

Preamble

- Several comments stated the term “fully verified” was unclear and should be deleted.
  - The new §820.75, entitled “Process validation”, is consistent with ISO 9001:1994, section 4.9, including the terminology “fully verified”. FDA does not believe this terminology is unclear since it has been used in ISO 9001:1987 and 1994 and explained in several guidance documents.
- ISO 9001:1994, 4.9
  - Where the results of processes cannot be fully verified by subsequent inspection and testing of the product and where, for example, processing deficiencies may become apparent only after the product is in use, the processes shall be carried out by qualified operators and/or shall require continuous monitoring and control of process parameters to ensure that the specified requirements are met. The requirements for any qualification of process operations, including associated equipment and personnel (see 4.18), shall be specified.

Preamble

- FDA also added that “where appropriate, the major equipment validated” must be documented. Depending on the process that is validated, it may be necessary to document the person performing the process or the equipment or both in order to have adequate controls on the process.

Preamble

- §820.75(a) relates to the initial validation of the process.
- §820.75(b) applies to the performance of a process after the process has been validated.
- FDA deleted the [phrase continuous monitoring]" because the agency concurs that monitoring can be accomplished at a determined interval and frequency depending on the type of validated process being monitored and controlled. FDA notes that the interval and frequency should be periodically evaluated for adequacy, especially during any evaluation or revalidation that occurs in accordance with the requirements in new §820.75(c).

Preamble

- §820.75(b)(1) … , requires that validated processes be performed by qualified individuals. FDA notes that §820.75(b)(1) is similar to the requirements under §820.25 Personnel but emphasizes that validated processes must not only be performed by personnel with the necessary education, background, training, and experience for their general jobs but must be performed by <u>personnel qualified for those particular functions</u>.

Preamble

- §820.75(b)(2) … contains the amended documentation requirements for validated processes, to include the monitoring and control methods and data. FDA notes that it is always “appropriate” to document the equipment used in the process where the manufacturer uses different equipment on different manufacturing lines. To investigate a problem with the device, the manufacturer will need to know which equipment was used, since the problem could be with the equipment itself. The same holds true for the individual performing the process.

ISO 13485:2016 Requirements

Definitions

- *Sterile barrier system* means a minimum package that prevents ingress of microorganisms and allows aseptic presentation of the product at the point of use [3.19]

- *Sterile medical device* means a medical device intended to meet the requirements for sterility [3.20]

Validate the Process

- 7.5.6
- The organization shall validate any processes for production and service provision where the resulting output cannot be or is not verified by subsequent monitoring or measurement and, as a consequence, deficiencies become apparent only after the product is in use or the service has been delivered.
- Validation shall demonstrate the ability of these processes to achieve planned results consistently.

- Major Points:
  - Output cannot be verified
  - Output is not verified
  - Subsequent monitoring or measurement
  - Achieve planned results consistently

Process Validation Procedures

- 7.5.6
- The organization shall document procedures for validation of processes, including:
  a) defined criteria for review and approval of the processes
  b) equipment qualification and qualification of personnel
  c) use of specific methods, procedures, and acceptance criteria
  d) as appropriate, statistical techniques with rationale for sample sizes
  e) requirements for records
  f) revalidation, including criteria for revalidation
  g) approval of changes to the processes

Sterilization and Sterile Barriers

- 7.5.7
- The organization shall document procedures for the validation of processes for sterilization and sterile barrier systems.

- Processes for sterilization and sterile barrier systems shall be validated prior to implementation and following product or process changes, as appropriate.

- Records of the results and, conclusion of validation and necessary actions from the validation shall be maintained.

Considerations from the ISO 13485:2016 Handbook

Handbook

- Process validation includes the development of a plan, the staged conduct of a number of evaluations of a particular process and the collection and interpretation of recorded data. These activities can be considered to fall into a model consisting of four phases:
  - review and approval of equipment specifications
  - initial qualification of the equipment used and provision of necessary services — also known as installation qualification (IQ)
  - demonstration that the process will produce acceptable results and establishment of limits (worst case) of the process parameters — also known as operational qualification (OQ)
  - establishment of long-term process stability — also known as performance qualification (PQ)

Handbook

- Planning of process validation should include, but not be limited to, the following considerations:
  - accuracy and variability of the process parameters, including the settings of the equipment used
  - skill, capability, and knowledge of operators needed to conform to quality requirements
  - adequacy of control of all process parameters, including environmental parameters
  - qualification of processes and equipment, as appropriate
  - acceptance criteria and the process for handling process performance that does not meet these criteria
  - circumstances that require process revalidation
  - handling changes to the process

Handbook

- The need for revalidation should be evaluated and documented. This evaluation should include historical results from quality indicators, product changes, process changes, changes in external requirements (regulations or standards) and other such circumstances.

- Revalidation might not be as extensive as the initial validation if the situation does not require that all aspects of the original validation be repeated. Some elements of OQ or PQ could need to be repeated, for example, depending on the effect of the new equipment.

Handbook

- Sterilization processes, including aseptic processes, are processes that cannot be verified by inspection and testing of the medical device. Therefore, these processes need to be performed in accordance with documented procedures, validated before use, and closely controlled and monitored.

- Process validation of sterile barrier systems demonstrates reproducibility, control, and capability of the process to consistently producing sterile barrier systems meeting the established specifications. … It is equally important to validate sterile barrier systems to demonstrate that stability requirements are met over the entire shelf life and sterile barrier integrity is maintained through the hazards of the specified transportation, distribution, and handling.

GHTF Guidance Document

GHTF

- The Global harmonization Task Force (GHTF) had a mission to harmonize medical device regulations
- They were organized into Study Groups to publish guidance documents
  - Study Group 3 covers Quality Systems
- The International Medical Device Regulators Forum (IMDRF) replaced the GHTF
  - The GHTF guidance documents are available on the IMDRF website
- The IMDRF website is www.imdrf.org

Guidance

- The guidance is GHTF/SG3/N99-10:2004 Quality Management Systems - Process Validation Guidance
- You can download it at no change
- FDA-CDRH doesn’t have a process validation guidance document
  - FDA Investigators train on this document

The Guidance

- The GHTF guidance, as published has
  - The main text
  - Annex B on statistical techniques
  - Annex B illustrating an example

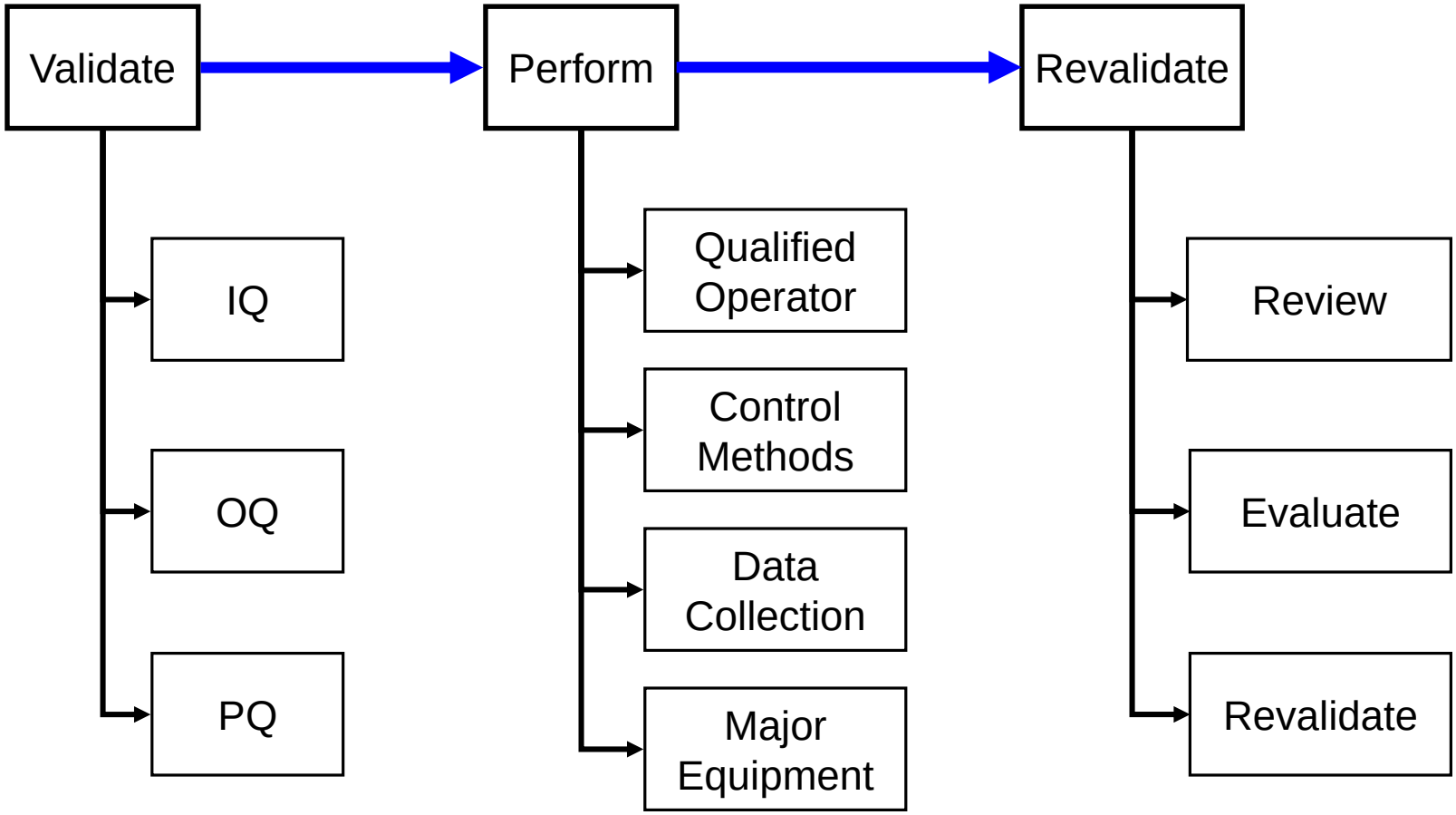
- I reformulated the guidance
  - The main text remains unchanged
  - Annex B corrects some typos and clarifies the text
  - Annex C corrects some typos and eliminates sterility considerations

Process Validation Paradigm

Process Validation Paradigm

- The common paradigm divides process validation into three phases.
  - Validate the process when necessary
  - Perform the validated process
  - Revalidate the process when necessary

Process Validation Phases



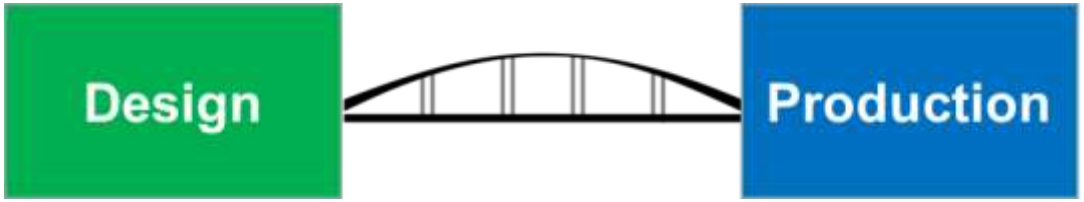
The Validate Phase

The Validate Phase

- Context
  - The validate phase is part of design transfer, which is the bridge between design and production
- Trigger
  - Design transfer identifies a process whose output cannot be fully verified by subsequent inspection and test
- Result
  - Process validated with a high degree of assurance
  - Validation approved according to established procedures
  - Documented validation activities and results
  - Approval with signature and date
- Method
  - There are no prescribed methods
  - IQ, OQ, and PQ provide a common paradigm

Validate – Context

- Conduct the validate phase as part of Design Transfer
- Design Transfer converts the product requirements, developed as design outputs, into production process specifications



- The design outputs are reviewed, approved, and documented in the Design History File (DHF)

- Production process specifications are reviewed, approved, placed under document control, and documented in the Device Master Record (DMR)

Regulatory Requirements

- §820.30(h) Design transfer
- Each manufacturer shall establish and maintain procedures to ensure that the device design is correctly translated into production specifications.

- 7.3.8 Design and development transfer
- The organization shall document procedures for transfer of design and development outputs to manufacturing. These procedures shall ensure that design and development outputs are verified as suitable for manufacturing before becoming final production specifications and that production capability can meet product requirements.
- Results and conclusions of the transfer shall be recorded (see 4.2.5).

Validate Phase – When to Validate

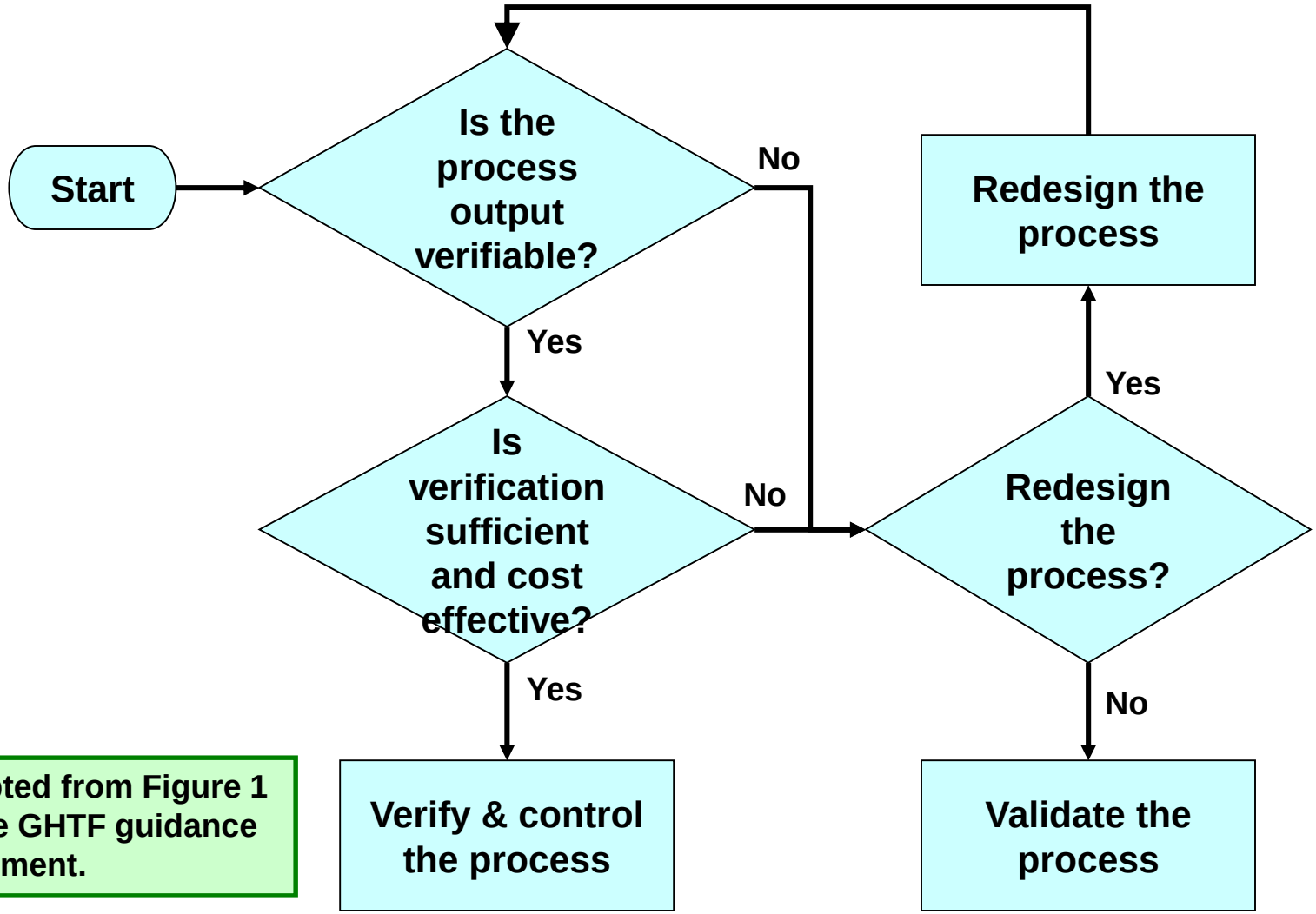
Fully Verify

- The phrase has some ambiguity
  - Consider the specifications are on a drawing with 27 features. Five of the features are classified as Critical to Quality, CTQ

- Which of the following satisfies “fully verify”
  - Check 100% of the features on 100% of the pieces made
  - Check 100% of the features on a sample of the pieces made
  - Check 100% of the CQTs on 100% of the pieces made
  - Check 100% of the CQTs on a sample of the pieces made

- I vote for 100% of the CQTs on 100% of the pieces made
  - I’ve had FDA investigators tell me it is 100% of the features on 100% of the pieces

When to Validate



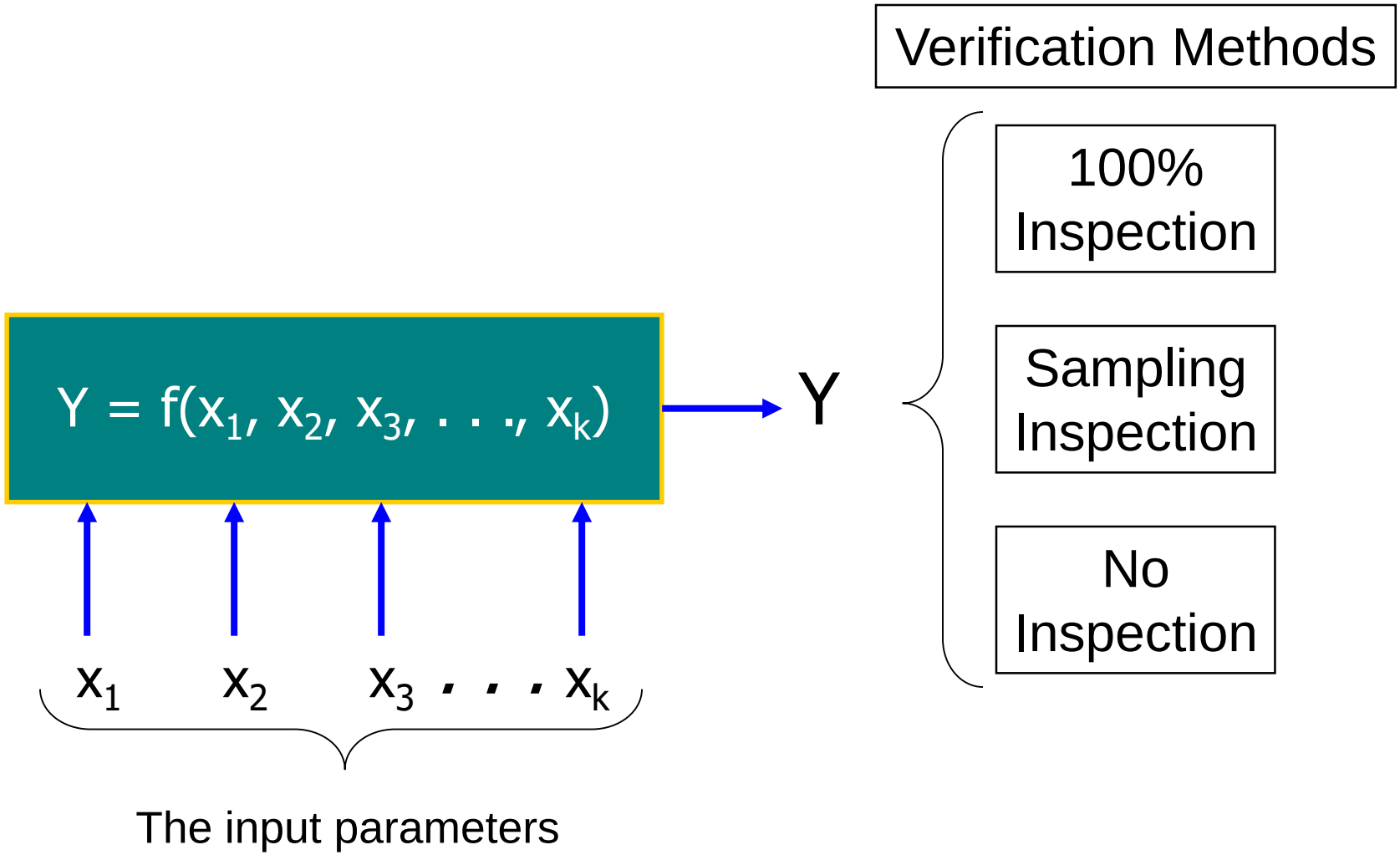
Adapted from Figure 1 in the GHTF guidance document.

The Decision Process

- Make a process map of the production process
  - Include product verification steps

- Analyze each product verification step to determine:
  - Whether or not the process can be fully verified by subsequent inspection and test [QSR]
  - Whether or not the resulting output can be verified by subsequent monitoring or measurement [ISO 13458:2016]
  - Whether or not the product verification is cost effective [GHTF Guidance]

Verification Approaches



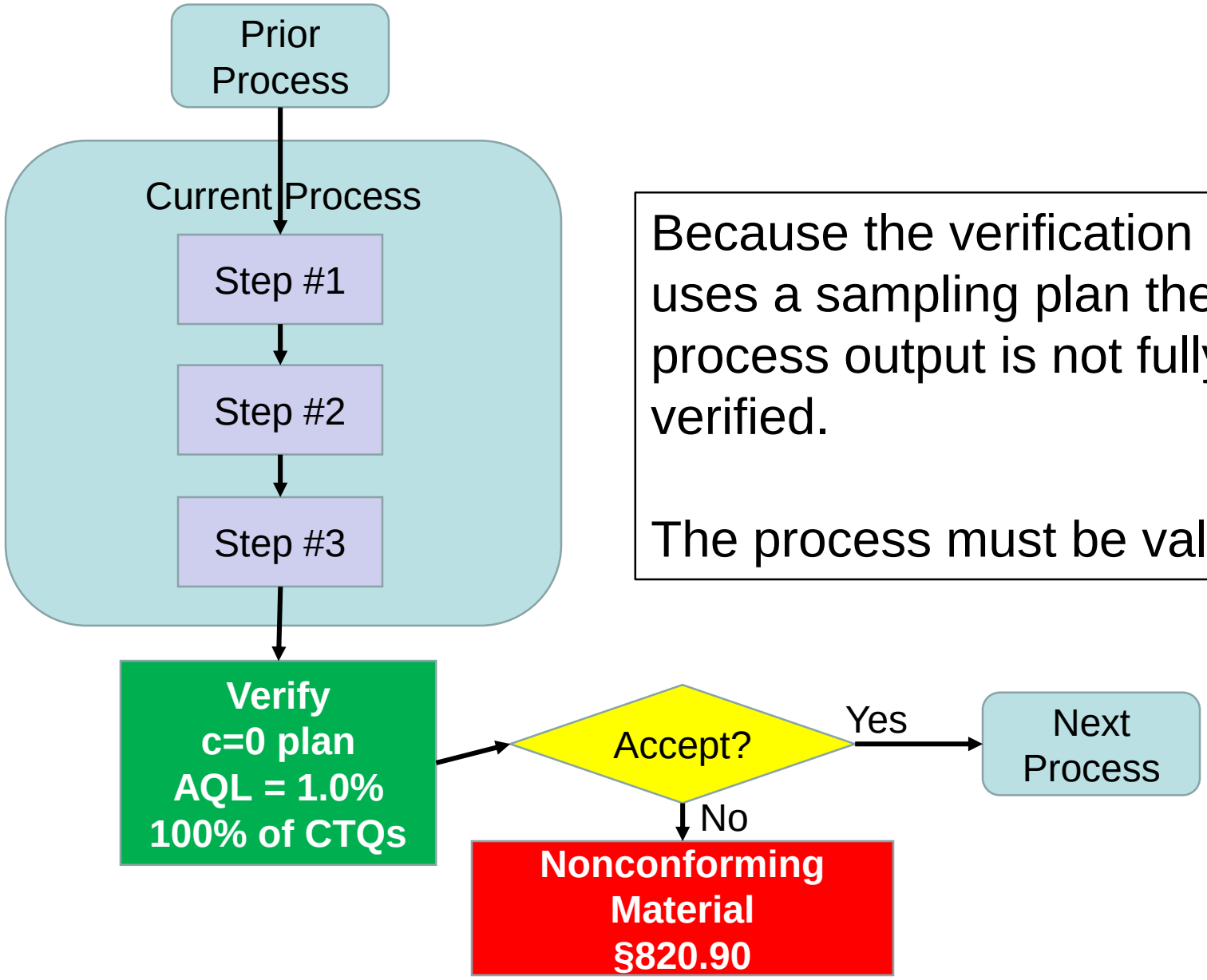
When to Validate

	Can Fully Verify Process Output	Cannot Fully Verify Process Output
Verification by Sampling Inspection	Process Validation Required	Process Validation Required
Verification by 100% Inspection	Process Validation Not Required	N/A

Regulatory Requirements

- Quality System Regulation
  - Where the results of a process cannot be fully verified by subsequent inspection and test, the process shall be validated … [21 CFR §820.75(a)]

- ISO 13485:2016
  - [V]alidate any processes for production and service provision where the resulting output cannot be verified by subsequent monitoring or measurement [Clause 7.5.6]



Because the verification step uses a sampling plan the process output is not fully verified.

The process must be validated.

Warning Letter
Hammill Manufacturing Co.
July 6, 2009

- Failure to validate a process whose results cannot be fully verified by subsequent inspection and test, and approve the validation according to established procedures, as required by 21 CFR §820.75(a).
- For example, you have not validated:
  - the static ultrasonic cleaning and passivation process, or
  - the tumbling, cleaning and passivation process, nor
  - have you validated the following machines used in the manufacture of medical devices:
    - CNC 771 machine,
    - CNC grinding machine,
    - CNC [redacted] machine,
    - CNC turning machine,
    - CNC milling machine,
    - robotic polishing machine, and
    - the [redacted] machine.

Warning Letter
Hammill Manufacturing Co.
July 6, 2009

- We have reviewed your response, which lists several other manufacturing processes (for example, your CNC processes and polishing) that you state do not need validation because you perform in-process and final inspection/tests. We have concluded that your response is inadequate because you are not testing every device to assure it meets specifications, and the results are not fully verified.

- All of these processes must be validated to ensure the specifications are consistently met or you must test all devices.

Hammill argues that it does perform inspection and testing

The FDA argues that Hammill must test every device or validate the process

Conclusion
FDA expects 100% inspection
or
a validated process

Acceptance Sampling

- The production process and the verification step combine to assure that only conforming material goes to the next process
- 100% inspection makes a conforming/nonconforming decision on each item produced
- Acceptance sampling makes an accept/reject decision on a lot, not the individual item
  - An accepted lot could have nonconforming items in the portion of the lot that wasn't in the sample and, consequently, go to the next process
  - There are sampling methods that don't rely on lots

Quality Plan

- §820.20(d) Quality planning
- Each manufacturer shall establish a quality plan which defines the quality practices, resources, and activities relevant to devices that are designed and manufactured. The manufacturer shall establish how the requirements for quality will be met.

- In the quality plan, for each verification step, document the process validation decision and the rationale for the decision.

Validate Phase – Goal of Validation

Regulatory Requirements

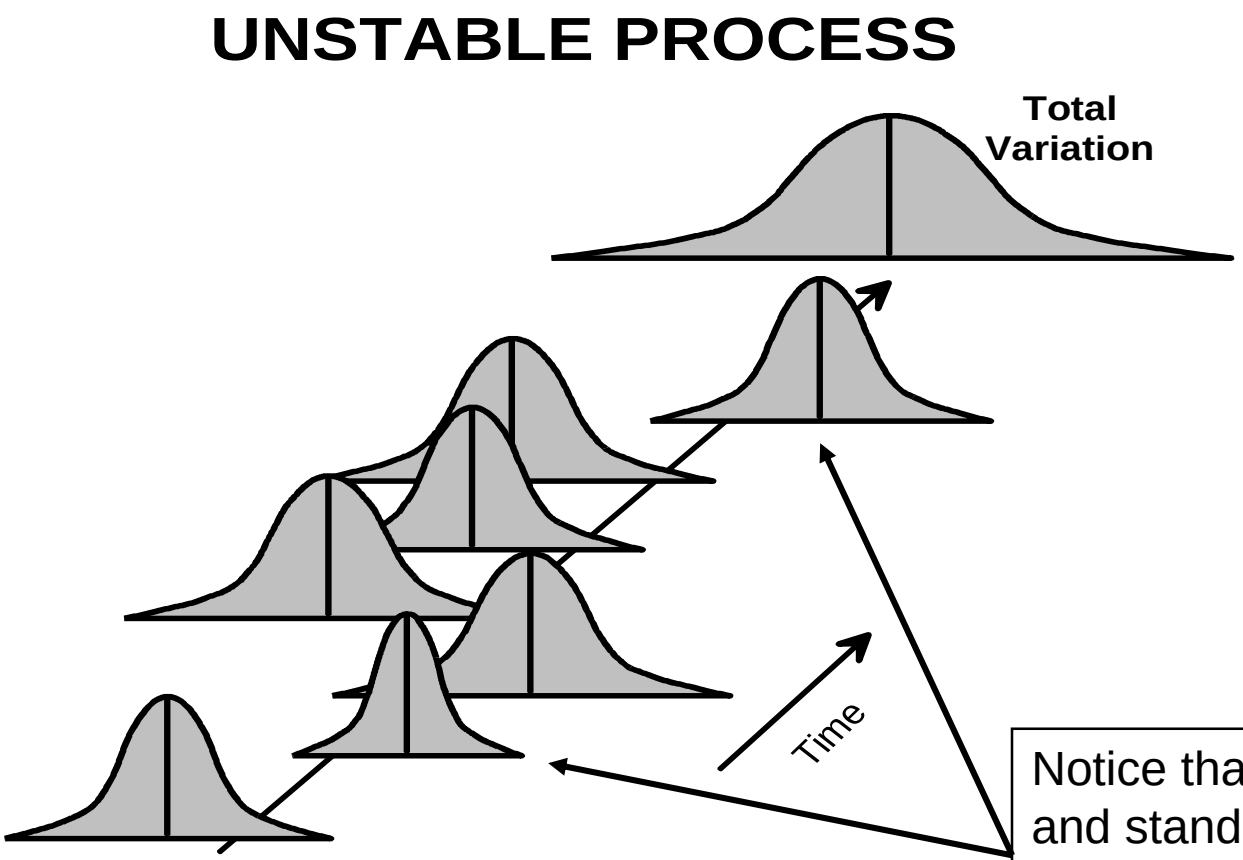
- Quality System Regulation
  - [T]he process shall be validated with a high degree of assurance … [§820.75(a)]

- ISO 13485:2016
  - Validation shall demonstrate the ability of these processes to achieve planned results consistently. [Clause 7.5.6]

Assurance

- What does process validation assure?
  - The process produces conforming product
- What constitutes a high degree of assurance?
  - The process consistently achieves the required level of performance
- Process capability indices can provide assurance information
  - A high degree of assurance means a $C_{pk} \geq 1.33$

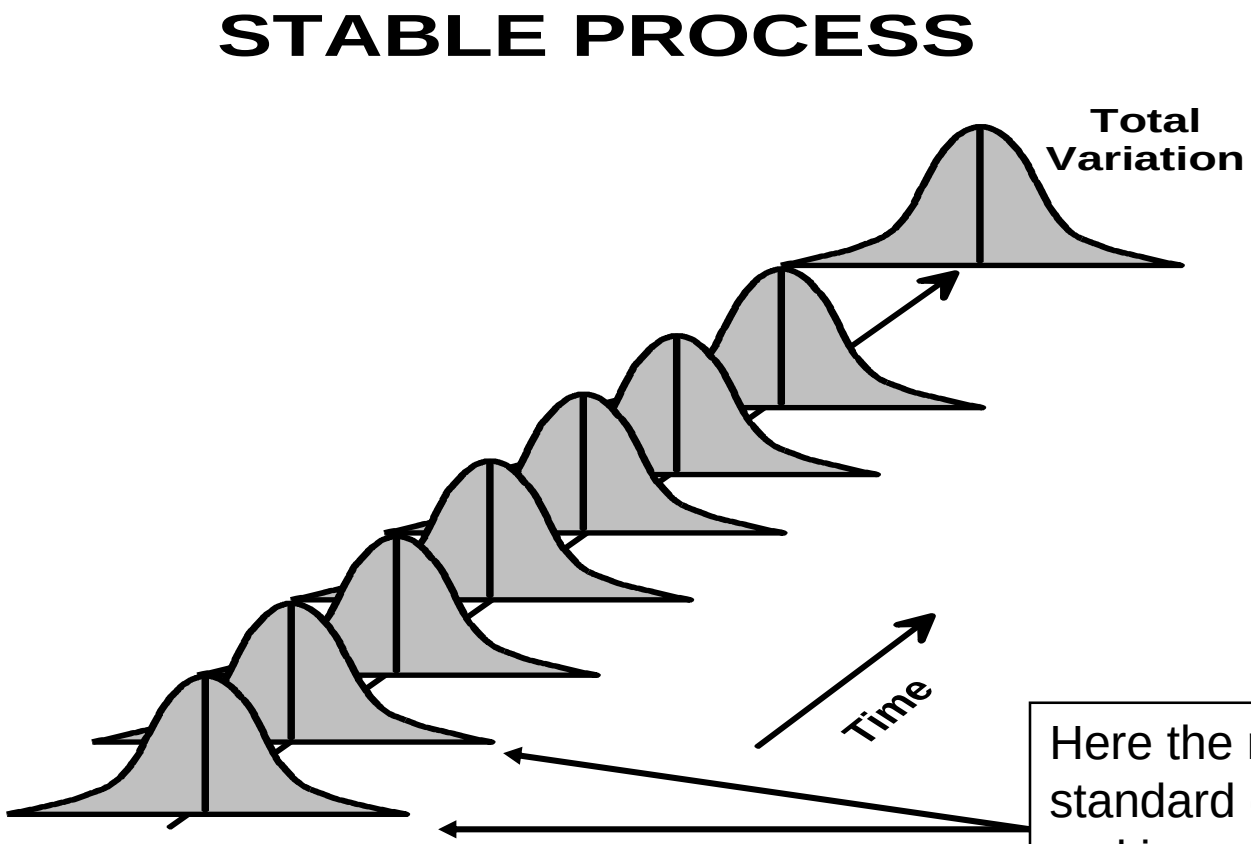
Unstable Process



The total variation is high. This is what your customer sees!

Notice that the mean and standard deviation are changing by large amounts

Stable Process

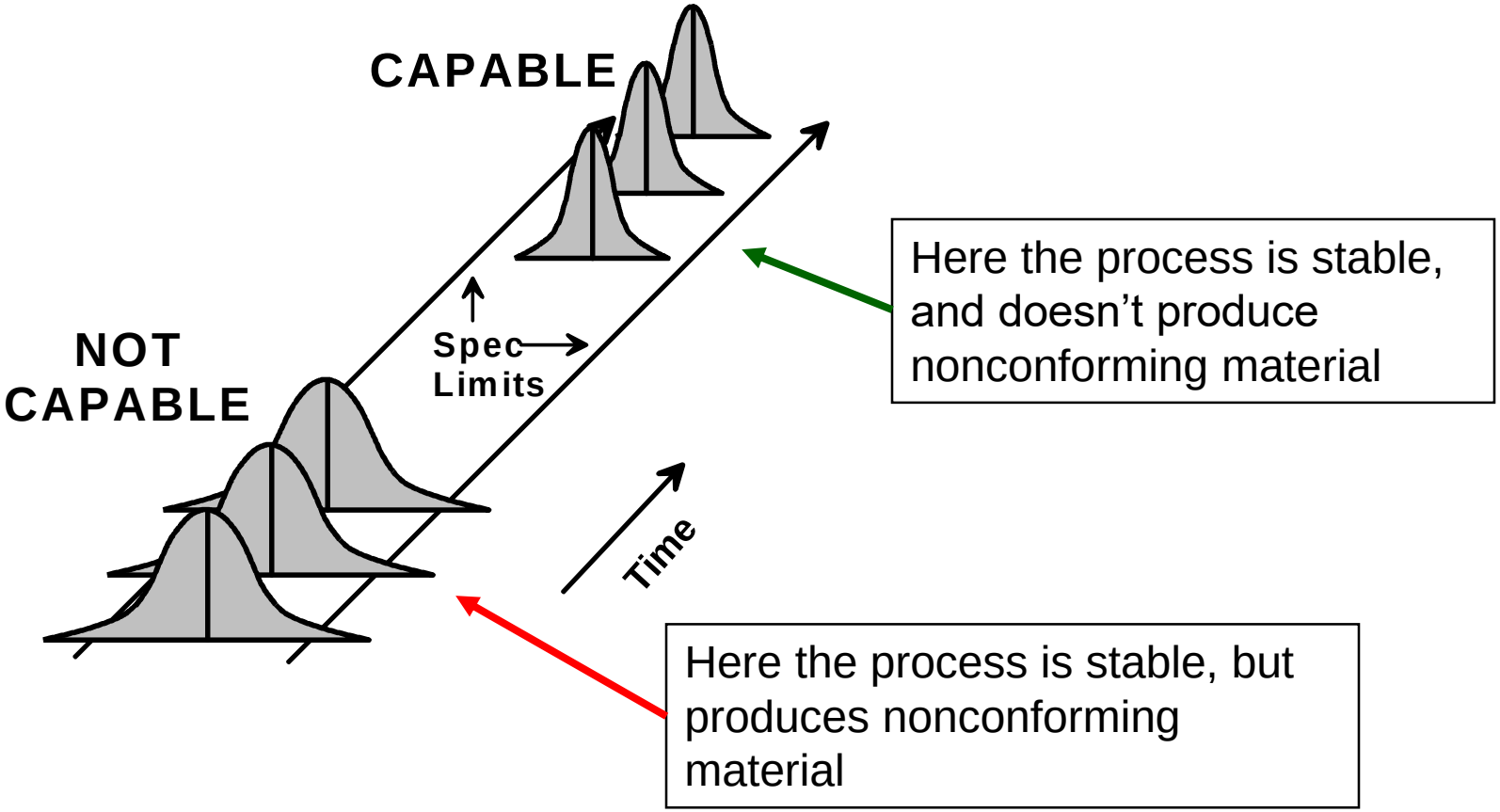


The total variation is smaller. Your customer sees more consistent product.

Here the mean and standard deviation are making much smaller changes

Process Capability

PROCESS CAPABILITY



Process Capability

- There are two common measures of process capability
  - C_p compares the process width and the specification width.
  - C_{pk} includes a factor that considers process centering.

C_p Calculation

- Notation
  - USL means Upper Specification Limit
  - LSL means Lower Specification Limit
  - σ means the process standard deviation
  - ^ means an estimate

$$\hat{C}_p = \frac{USL - LSL}{6\hat{\sigma}}$$

C_{pk} Calculation

- Notation
  - USL means Upper Specification Limit
  - LSL means Lower Specification Limit
  - μ means the process mean
  - σ means the process standard deviation
  - ^ means an estimate

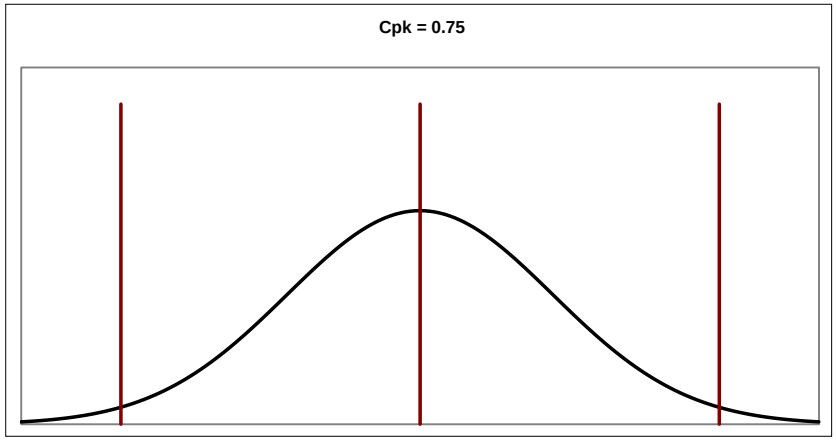
$$\hat{C}_{pk} = \min\left(\frac{\text{USL - }\hat{\mu}}{3\hat{\sigma}}, \frac{\hat{\mu} - LSL}{3\hat{\sigma}}\right)$$

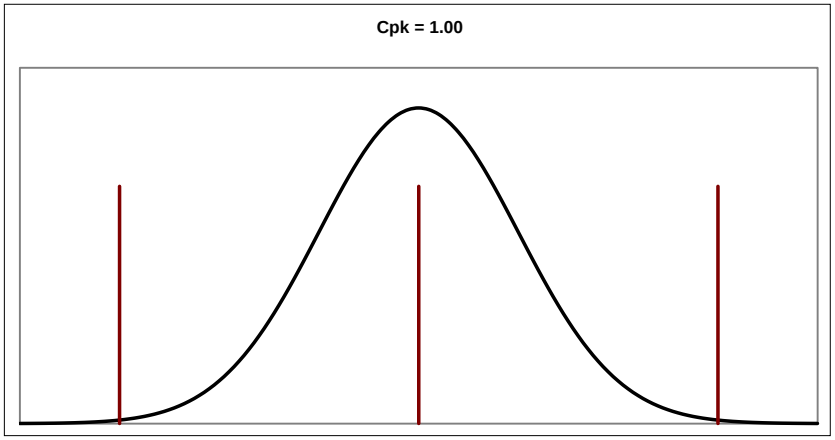
Capability Study

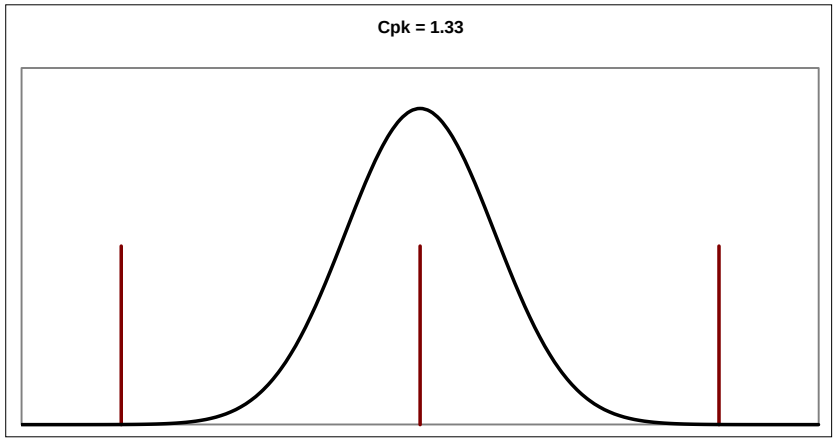
- Determine the capability of a process
  - Measure the process characteristics
  - Compare them with the design specification
  - Calculate C_p and C_{pk}

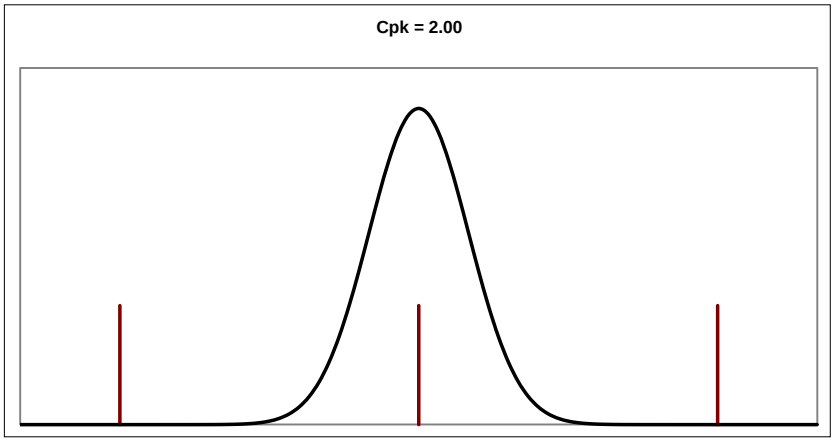
- A $C_{pk} \geq 1.33$ or better allows for natural process variability

C_{pk} Graphical Examples - Centered

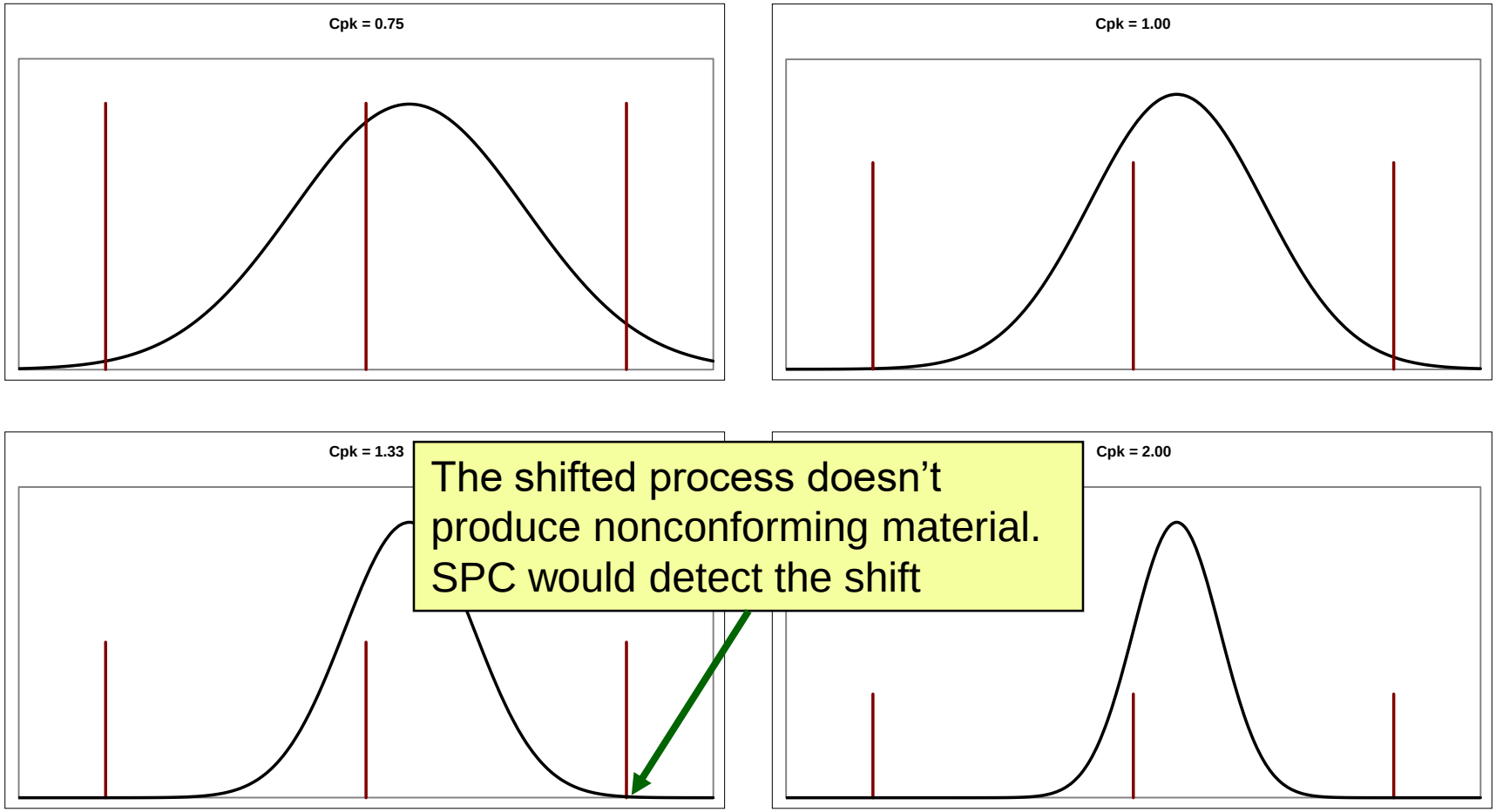








C_{pk} Graphical Examples – A Process Shift



The shifted process doesn't produce nonconforming material. SPC would detect the shift

Validate Phase – Methods for Validation – Installation Qualification

Installation Qualification (IQ)

- IQ ensure correct production equipment installation. Important IQ considerations are:
  - Equipment design features (*i.e.,* materials of construction cleanability, *etc*.)
  - Installation conditions (wiring, utilities, functionality, *etc*.)
  - Calibration, preventative maintenance, cleaning schedules
  - Safety features
  - Supplier documentation, prints, drawings, and manuals
  - Software documentation
  - Spare parts list
  - Environmental conditions (clean room requirements, temperature, or humidity)

Source: GHTF Guidance Document

Installation Qualification

- *Installation qualification* (IQ) means establishing by objective evidence that all key aspects of the process equipment and ancillary system installation adhere to the manufacturer's approved specification and that the recommendations of the supplier of the equipment are suitably considered. [GHTF/SG3/N99-10:2004, 2.1]

- IQ ensures the production equipment and any supporting equipment are correctly installed and functioning correctly
  - This also means systems are in place for maintenance and calibration to ensure the equipment continues to function

Use the Regulations

- IQ usually doesn’t involve statistical methods. However, ensure you meet the regulatory requirements

- QSR
  - §820.70(g) Equipment
  - §820.70(c) Environmental control
  - §820.70(i) Automated processes
  - §820.72 Inspection, measuring, and test equipment

- ISO 13485:2016
  - Clauses that align with the QSR sections

- OSHA
  - 29 CFR §1910.212 Machine Guarding
  - 29 CFR §1910.147 Lock out – Tag out

Validate Phase – Methods for Validation – Operational Qualification

Operational Qualification (OQ)

- In this phase, the process parameters should be challenged to assure that they will result in a product that meets all defined requirements under all anticipated conditions of manufacturing, i.e., worst case testing. During routine production and process control, it is desirable to measure process parameters and/or product characteristics to allow for the adjustment of the manufacturing process at various action level(s) and maintain a state of control. These action levels should be evaluated, established and documented during process validation to determine the robustness of the process and ability to avoid approaching “worst case conditions”.

Source: GHTF Guidance Document

Operational Qualification (OQ)

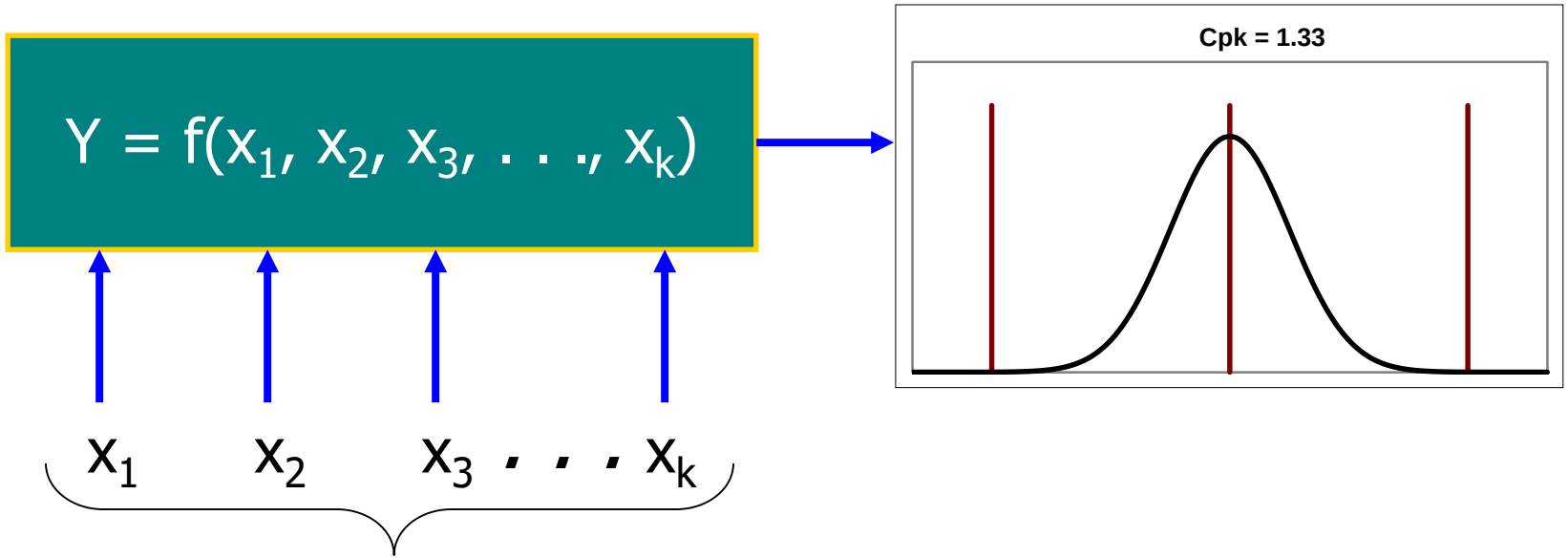
- *Operational qualification* (OQ) means establishing by objective evidence process control limits and action levels which result in product that meets all predetermined requirements. [GHTF/SG3/N99-10:2004, 2.2]

- OQ determines the process input parameters that assure the resulting product is conforming, *i.e.,* meets all of its predetermined requirements.

Operational Qualification (OQ)

- OQ establishes process control limits and action levels
  - *Process control limits* are specification limits on the process parameters
  - *Action levels* are values that trigger action on the process parameter to prevent it from exceeding the process control limits

The Process Model



What <u>input parameters</u> create the desired output, $C_{pk} \geq 1.33$?

Input Parameters

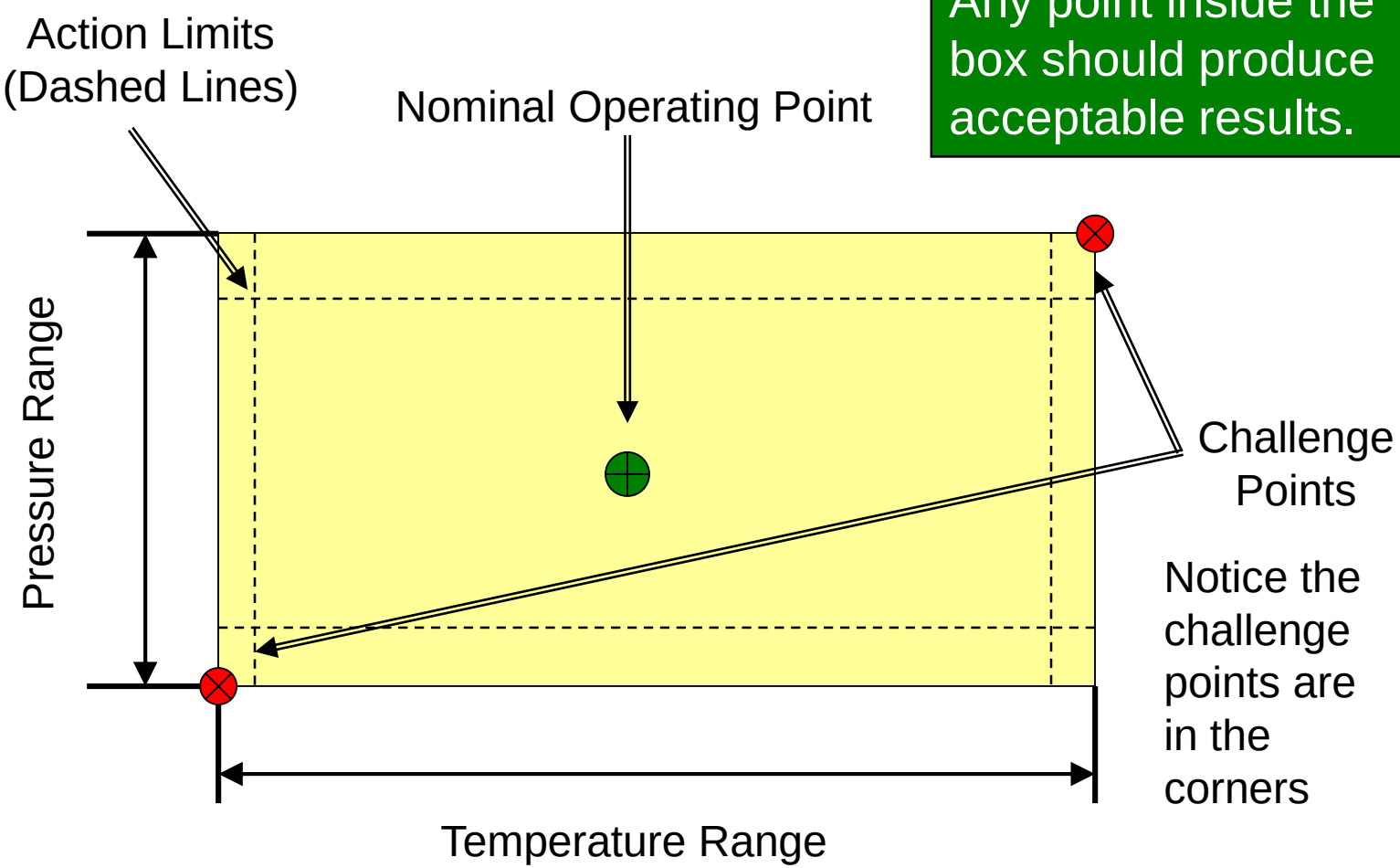
- Assume our process has two input parameters:
  - Temperature (x_1)
  - Pressure (x_2)

- What range of x_1 & x_2 provide an output with a $C_{pk} \geq 1.33$?

- Because the process inputs may affect each other, consider parameter interaction!

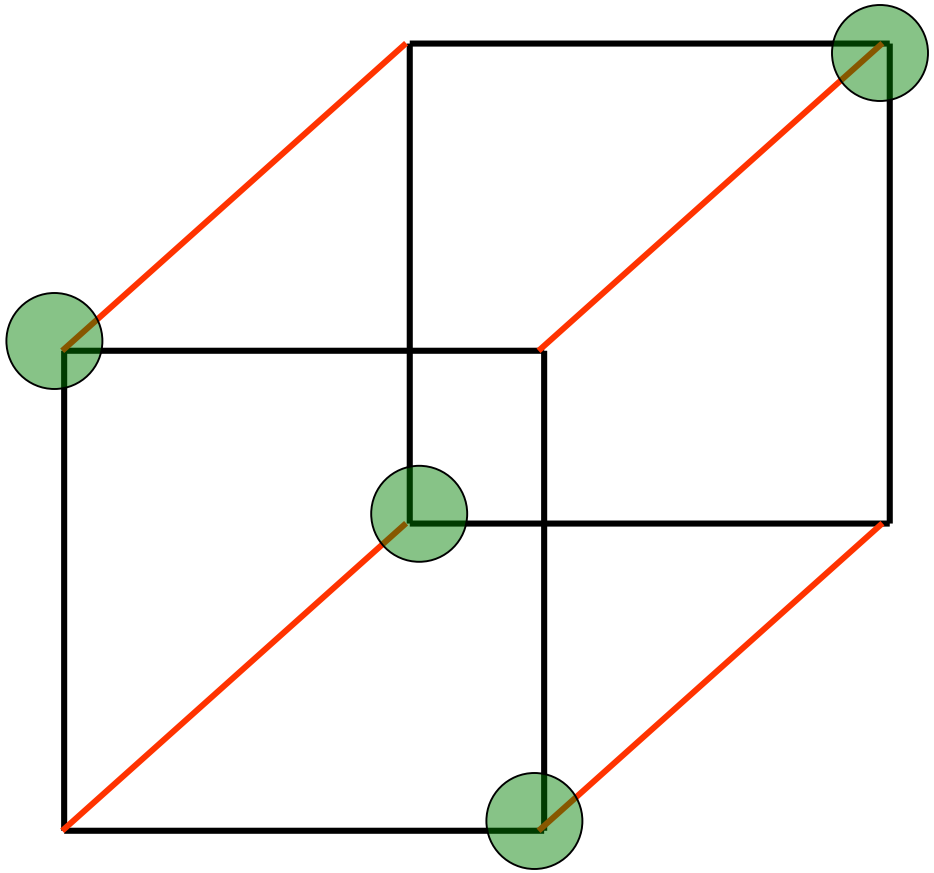
Operating Points

Any point inside the box should produce acceptable results.



Notice the challenge points are in the corners

A 2 Level 3 Factor Experiment



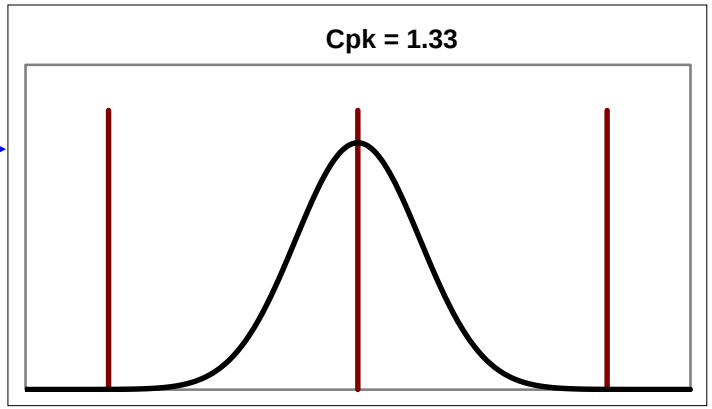
A full factorial experiment tests all $2^3 = 8$ corners

A half-fraction factorial experiment tests $\frac{1}{2}(2^3) = 4$ corners

Each corner tested has acceptable results: $C_{pk} \geq 1.33$

The Process Model

$$Y = f(x_1, x_2, x_3, \ldots, x_k)$$



Cpk ≥ 1.33

$x_1 \quad x_2 \quad x_3 \ldots x_k$

The input parameters →

$$a_1 \le x_1 \le b_1$$
$$a_2 \le x_2 \le b_2$$
$$a_3 \le x_3 \le b_3$$
$$\ldots$$
$$a_k \le x_k \le b_k$$

→ define the parameter space

The corners define the potential challenge points

Validate Phase – Methods for Validation – Performance Qualification

Performance Qualification (PQ)

- In this phase the key objective is to demonstrate the process will consistently produce acceptable product under normal operating conditions.
- The GHTF guidance has a discussion of methods for process stability.

- PQ considerations include:
  - Actual product and process parameters and procedures established in OQ
  - Acceptability of the product
  - Assurance of process capability as established in OQ
  - Process repeatability, long term process stability

Source: GHTF Guidance Document

Performance Qualification (PQ)

- *Performance qualification* (PQ) means establishing by objective evidence that the process, under anticipated conditions, consistently produces a product which meets all predetermined requirements. [GHTF/SG3/N99-10:2004, 2.3]

- PQ demonstrates that the process does consistently produce conforming product under normal operating conditions.

Performance Qualification (PQ)

- Operate the process using the conditions that will be encountered during actual manufacturing.
- Include the range of conditions as defined by the various action levels established as part of OQ.
- Repeat the conditions enough times to assure the meaningful and consistent results.

Perform Phase

The Perform Phase

- Context
  - The perform phase is part of production, which makes the product
- Trigger
  - The validated process is run following a demand signal that identifies the need for the product. The documentation might be a work order, production order, *etc*.
- Result
  - Product produced by the validated process
  - Records demonstrating that the process operated correctly
- Method
  - Procedures to monitor and control the process parameters
  - Qualified operators
  - Records of the process operation

Production – Qualified Operators

- Only qualified individuals perform validated processes

- Establish an operator qualification program for each validated process
  - Base qualification on the dimensions of competency: education, background, training, and experience [§820.25(a)]
  - Add additional qualification factors specific to the process

- One method uses a four step process:
  - Train the operator on the procedure
  - Have the operator observe someone perform the process
  - Have the operator perform the process while being observed
  - Have the operator “solo”

Production – Control

- There are two requirements to control validated process procedures
  - Documented instructions, standard operating procedures (SOPs), and methods that define and control the manner of production [§820.70(a)(1)]
  - Monitoring and control of process inputs to ensure that the specified requirements continue to be met [§820.75(b)]
- The two requirements are usually met by one SOP or Work Instruction.
  - Be sure the process includes the nominal value for each process input, the process control limits, action levels, monitoring methods, and monitoring frequency

Production – Data Collection

- Each production run using a validated process generates data in the form of records
  - The monitoring and control methods (could be a reference to the SOP)
  - The data
    - It will be the values of the input parameters during the production run
    - It should include any occurrences when a parameter went outside an action level and the value after adjustment

Production – Major Equipment

- Document the major equipment used to perform the validated process
- The identity of the major equipment, in the records, creates a link to the production lots
  - This information can be particularly valuable for problem investigation, corrective action implementation, *etc*.
- While required, a good practice documents the calibration status and the maintenance status of the major equipment
  - Don’t use the equipment for a validated process if the calibration or the preventive maintenance is past due!

The Revalidate Phase

The Revalidate Phase

- Context
  - The revalidate phase is part of production
- Trigger
  - The are two different triggers:
    - A process or product change
    - A process or product deviation
- Result
  - A document review and evaluation of the process
  - A documented revalidation when necessary
- Method
  - Evaluate any process or product changes to determine the impact on the current validation
  - Evaluate any deviations to determine if there was a problem associated with the validated process

Revalidate – Changes

- Process changes could include:
  - A new member of the device family
  - A new piece of major equipment
  - A new method or equipment for monitoring input parameters

Revalidate – Deviations

- Process deviations could include failure to operate the process correctly, or an input parameter that went outside a process control limit
  - Part of the investigation should evaluate the interval and frequency of process parameter monitoring. If the interval is too long or the frequency too low, the parameter could go outside the limit

- Product deviations could include a product that doesn't meet requirements detected as part of a sampling plan or shipped and the subject of a complaint
  - Evaluate the role of the validated process in the nonconforming product
  - Using the production records, determine if there were any process deviations

Revalidate – Review

- Look at all of the information related to the change or deviation

- For deviations, pay particular to the production process records:
  - Monitoring methods
  - Monitoring frequency
  - Monitoring data, especially related to action levels

- For changes, pay particular attention to:
  - Production process settings (nominal) and process control limits
  - Monitoring methods
  - Changed or upgraded equipment

Revalidate – Evaluate

- Using the information collected in the review, evaluate the need to revalidate the process and the scope of the revalidation.
- Regardless of the evaluation results, document the basis for the decision and record the name of the person making the decision and the date
- The evaluation could lead to changes that don't require revalidation, such as a revised frequency for parameter monitoring or a change in the action levels
- If there are sampling plans associated with performing the validated process, review them as well. See §820.250(b).

Revalidate – Revalidate

- For revalidation, the evaluation should also provide a scope.

- For example:
  - A change that adds a new member of a device family would probably not require a rerun of the IQ

  - If the new member requires a different input parameter setting, then a partial OQ is probably warranted, i.e., the setting for existing members of the family won't change

- Perform the revalidation, based on the scope, using an appropriate protocol and preparing a report of the results

Data Analysis

Data Analysis

- §820.100(a)(1) requires the manufacturer to analyze processes and work operations, using appropriate statistical methodology, to identify quality problems.

- Because process validation generates a lot of data, especially related to process input parameters and their values, there are opportunities for analysis.

Data Analysis – Methods

- §820.75(b)(2) requires the manufacturer to record the "control methods and data"

- Often, the data is in a table or a printout from a monitoring instrument
  - Convert it to a run chart
  - Apply time series analysis to determine trends or cycles in the data
  - Apply "standards given" SPC methods to determine that the input parameter is "in control"

Data Analysis – Methods

- §820.75(b)(2) requires the manufacturer to record the “control methods and data”

- Part of the process control could include sampling
  - For each item in the sample, record the production time on the same time scale as the input production parameters
  - Record the value of the CTQs for the product, even if they are converted to attributes for sampling
  - Apply scatter charts to identify the relationship between input parameter values and product CQT values
  - Apply regression techniques to help understand the relationship between input parameter values and product CQT values
    - Excel provides many regression methods including linear, higher order polynomials, *etc*.

Summary

Summary

- Regulatory requirements require validated processes
  - Quality System Regulation
  - ISO 13485:2016

- Validate processes where the verification uses sampling
  - The verification is destructive
  - The verification could have used 100%, but used sampling instead

Summary

- Describe the process using the statistical model
  - Incorporate your verification methods into the model

- Process output should capable, $C_{pk} \geq 1.33$

- Control process input parameters
  - Explore the parameter space with designed experiments
  - Challenge the process at the worst points
  - Establish warning limits for the process inputs

- Validated processes are often high risk
  - Integrate complaint investigation, Risk Management, and process validation

Summary

- Perform the process as determined by the validation
  - Use qualified operators
  - Document the control methods
  - Keep records of process inputs and analyze them

- When changes or deviations occur:
  - Evaluate them for the need to revalidate
  - Document the decision
  - Revalidate as necessary

QUESTIONS