# ●Concept of Process Validation

BSI Group (Thailand) Ltd.

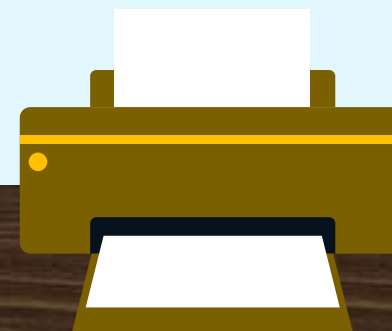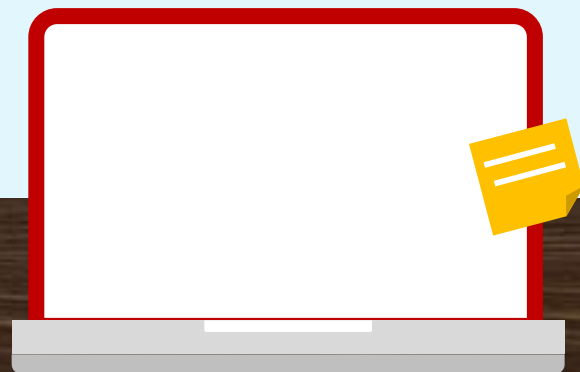Be able to apply your knowledge to your business to ensure you produce compliance products

Improve your understanding of process validation

Be confident your devices meet regulatory, quality and safety standards

Encourage professional development and knowledge sharing

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# Agenda

Concepts and rationale of process validation

Gain awareness of ISO 13485:2016 expectations and IMDRF guidance (previously GHTF)
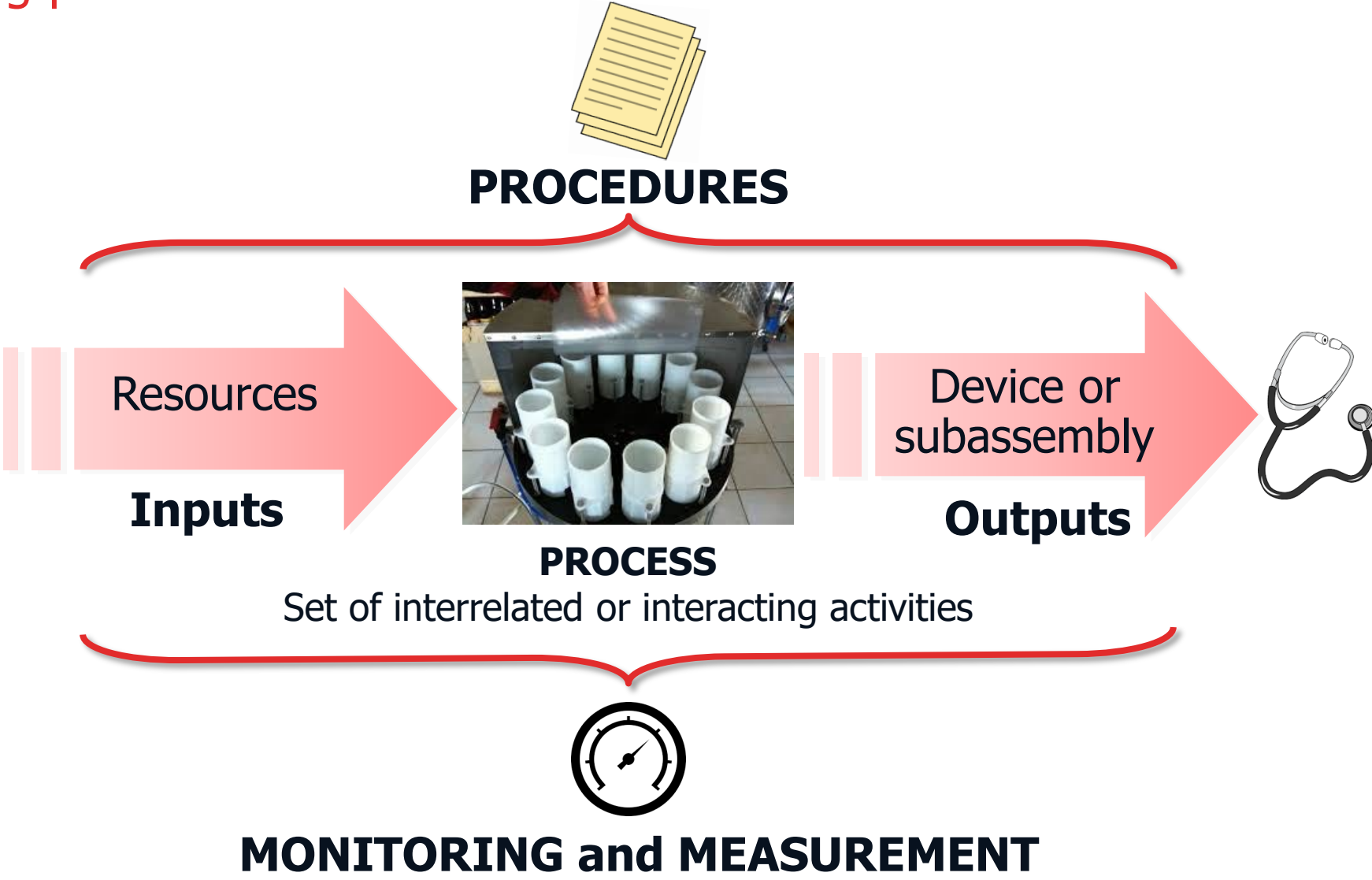
Importance of process validation

Situations where a process requires validation

Installation, operational and performance qualification
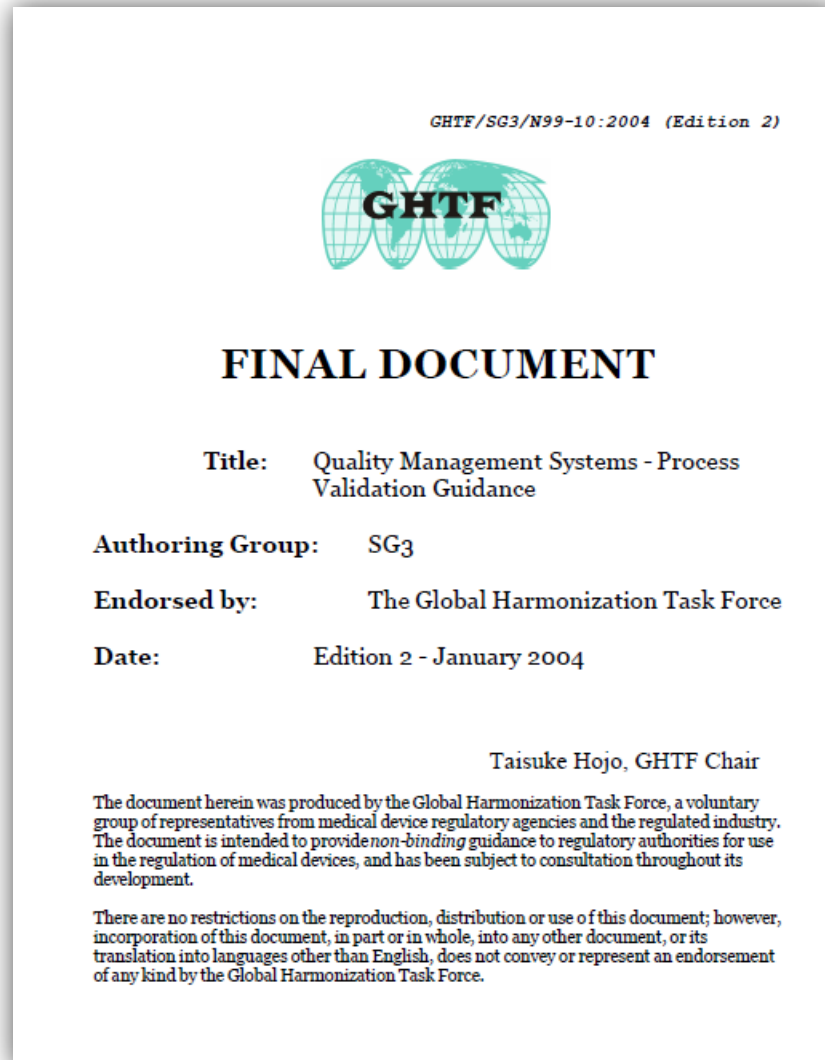
Maintain a state of validation

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# Process validation
## Overview

**PROCEDURES**

Resources

Inputs

Device or subassembly

Outputs

**PROCESS**
Set of interrelated or interacting activities

**MONITORING and MEASUREMENT**

# What is process validation?

GHTF/SG3/N99-10:2004 (Edition 2)

**GHTF**

## FINAL DOCUMENT

**Title:** Quality Management Systems - Process Validation Guidance

**Authoring Group:** SG3

**Endorsed by:** The Global Harmonization Task Force

**Date:** Edition 2 - January 2004

Taisuke Hojo, GHTF Chair

The document herein was produced by the Global Harmonization Task Force, a voluntary group of representatives from medical device regulatory agencies and the regulated industry. The document is intended to provide *non-binding* guidance to regulatory authorities for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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Defined as:

'establishing by <u>objective evidence</u> that a process <u>consistently</u> produces a result or product meeting its <u>predetermined requirements</u>'.

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# Why is process validation important?

It assures that a product can be manufactured consistently using processes that are capable of manufacturing the product

What could happen if processes are not validated?

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# Why validate?

Regulatory/legal requirement

Enhance quality

Eliminate scrap

Reduce cost

Increase customer satisfaction

Process control

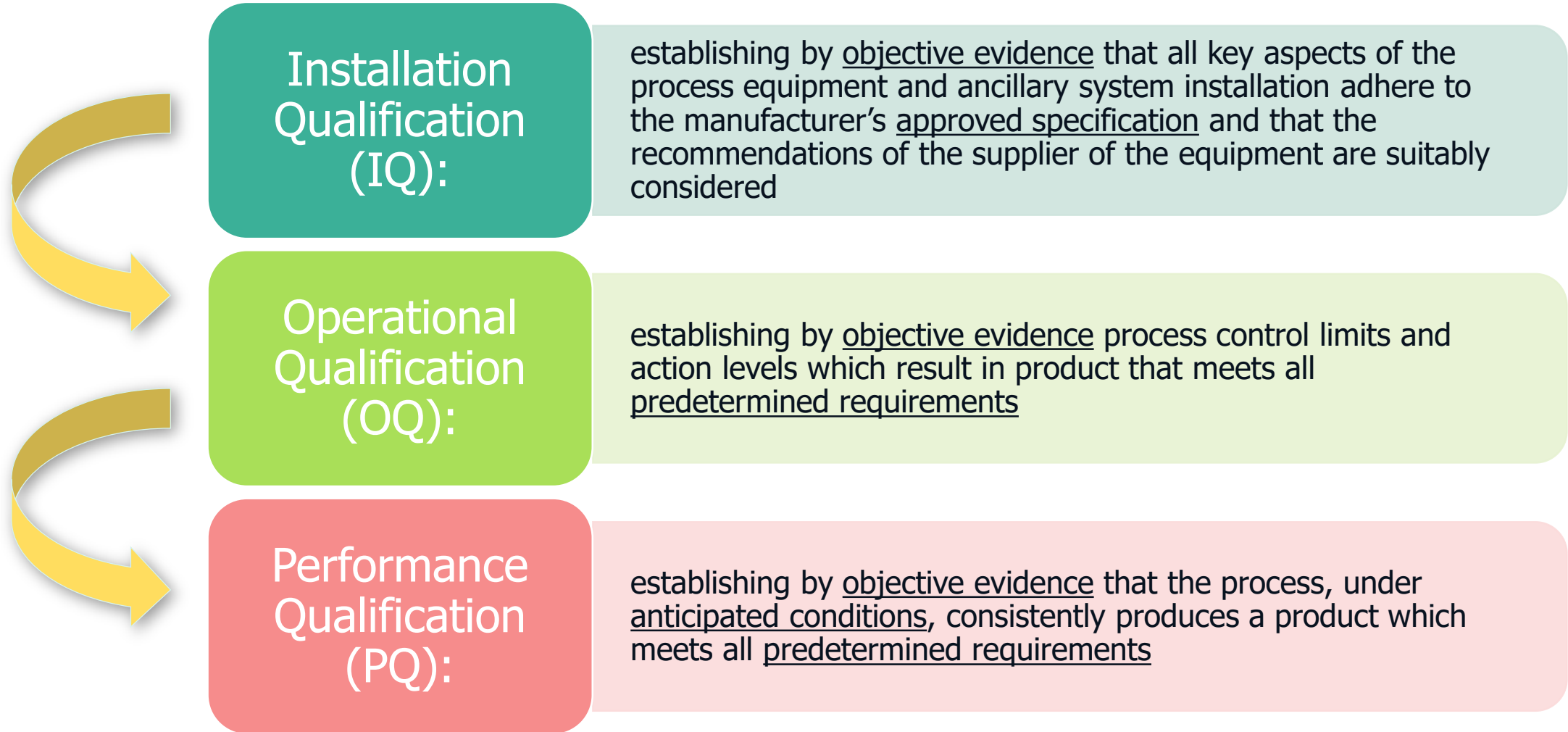Consistency of product

Improve overall quality

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# Process validation
Terminology, standard and regulations

# Process validation terminology

**Installation Qualification (IQ):**
establishing by <u>objective evidence</u> that all key aspects of the process equipment and ancillary system installation adhere to the manufacturer's <u>approved specification</u> and that the recommendations of the supplier of the equipment are suitably considered

**Operational Qualification (OQ):**
establishing by <u>objective evidence</u> process control limits and action levels which result in product that meets all <u>predetermined requirements</u>

**Performance Qualification (PQ):**
establishing by <u>objective evidence</u> that the process, under <u>anticipated conditions</u>, consistently produces a product which meets all <u>predetermined requirements</u>

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# Process validation and a quality management system
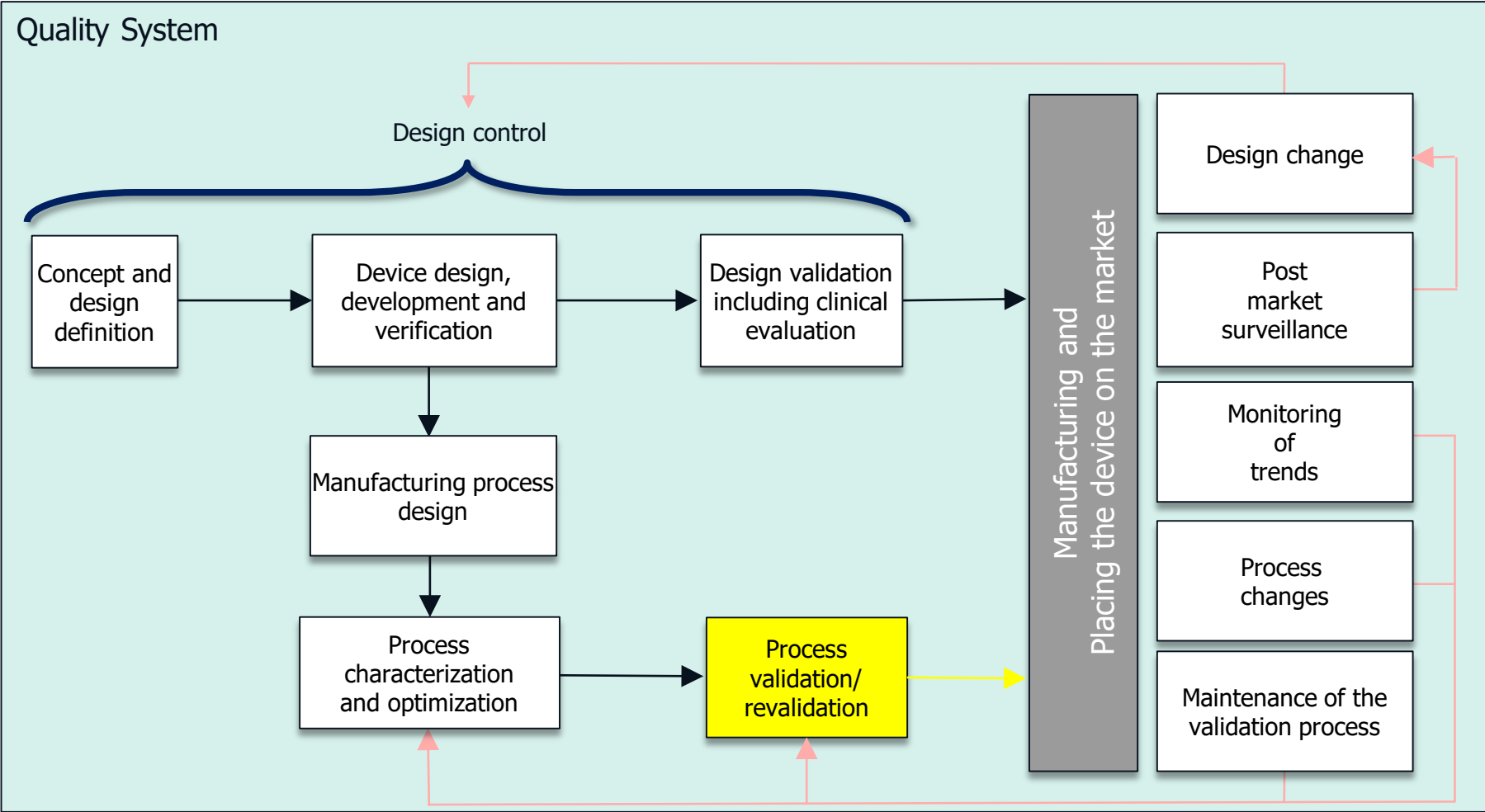
# Process validation
## How to get started

# Approach to process validation

Form a multi-functional team to plan and oversee the validation activities

Plan approach and define requirements

Identify and describe processes

Specify process parameters and desired output

Decide on verification and or/validation

Create a Master Validation Plan

Select tools and methods for the validation

Create validation protocols

Perform IQ, OQ and PQ and document results

Determine continuous process controls

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When is process validation required?

# Validation versus verification



Verification



Validation

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# When do you validate?

| Process output cannot be verified by 100% inspection and test | Process output can only be verified by destructive testing | Special or critical process: |
|---|---|---|
| • Very high volume combined with long test time | • Sterility<br>• Strength<br>• Complicated curves<br>• Internal dimensions<br>• Very small dimensions | • Sterilization<br>• Clean room conditions<br>• Aseptic filling<br>• Heat treating<br>• Injection molding<br>• Electroplating or polishing<br>• Gluing, bonding or welding assemblies |

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# Process validation plans

# Validation planning – preliminary considerations

What characteristics of devices are being made

How are those characteristics tested

What data are you going to collect?

What method of analysis will be used?

What are the limits of acceptance?

What happens if a failure occurs?

## Validation Plan

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# Validation planning – preliminary considerations

Installation Qualification

Operational Qualification

Performance Qualification
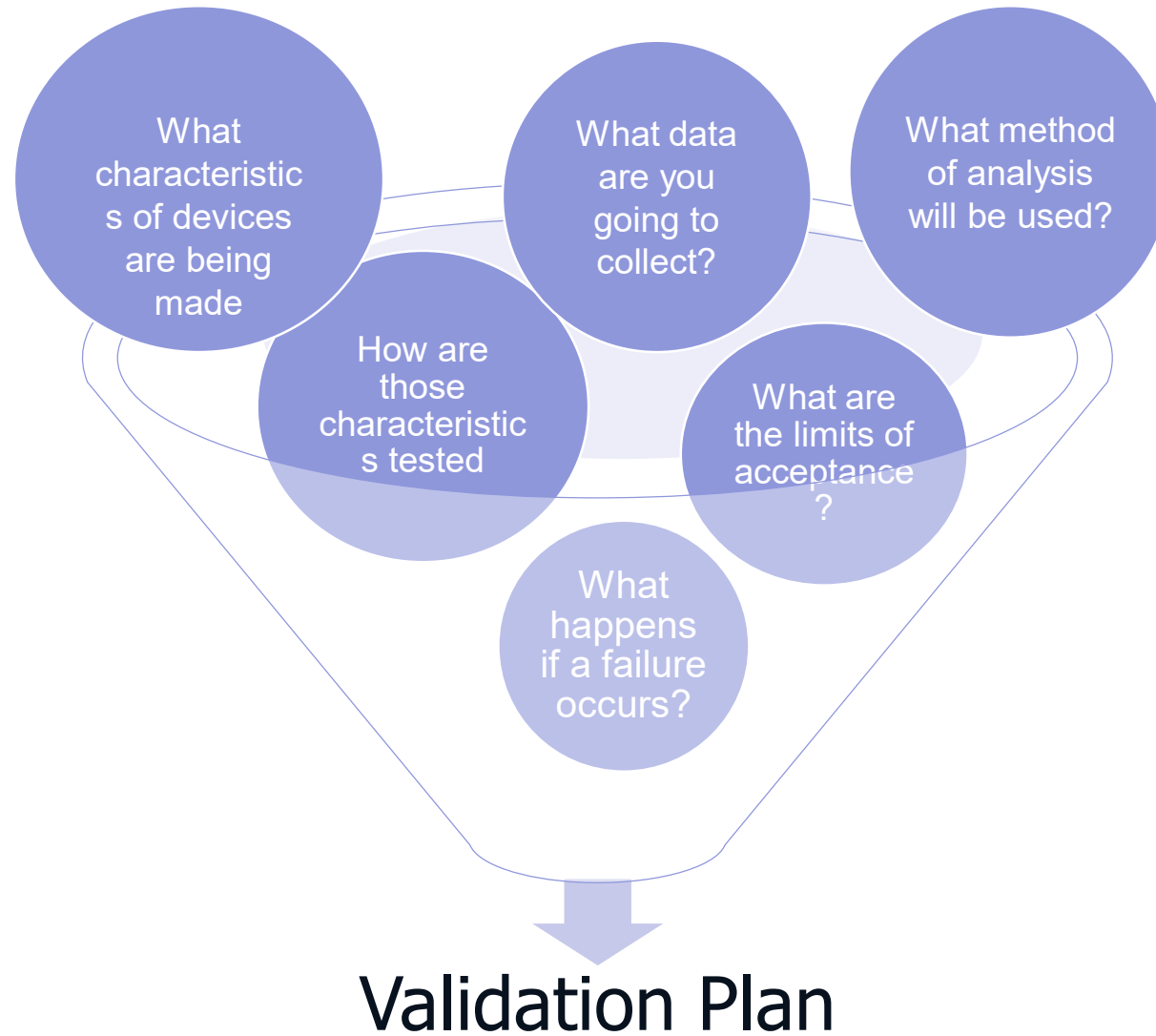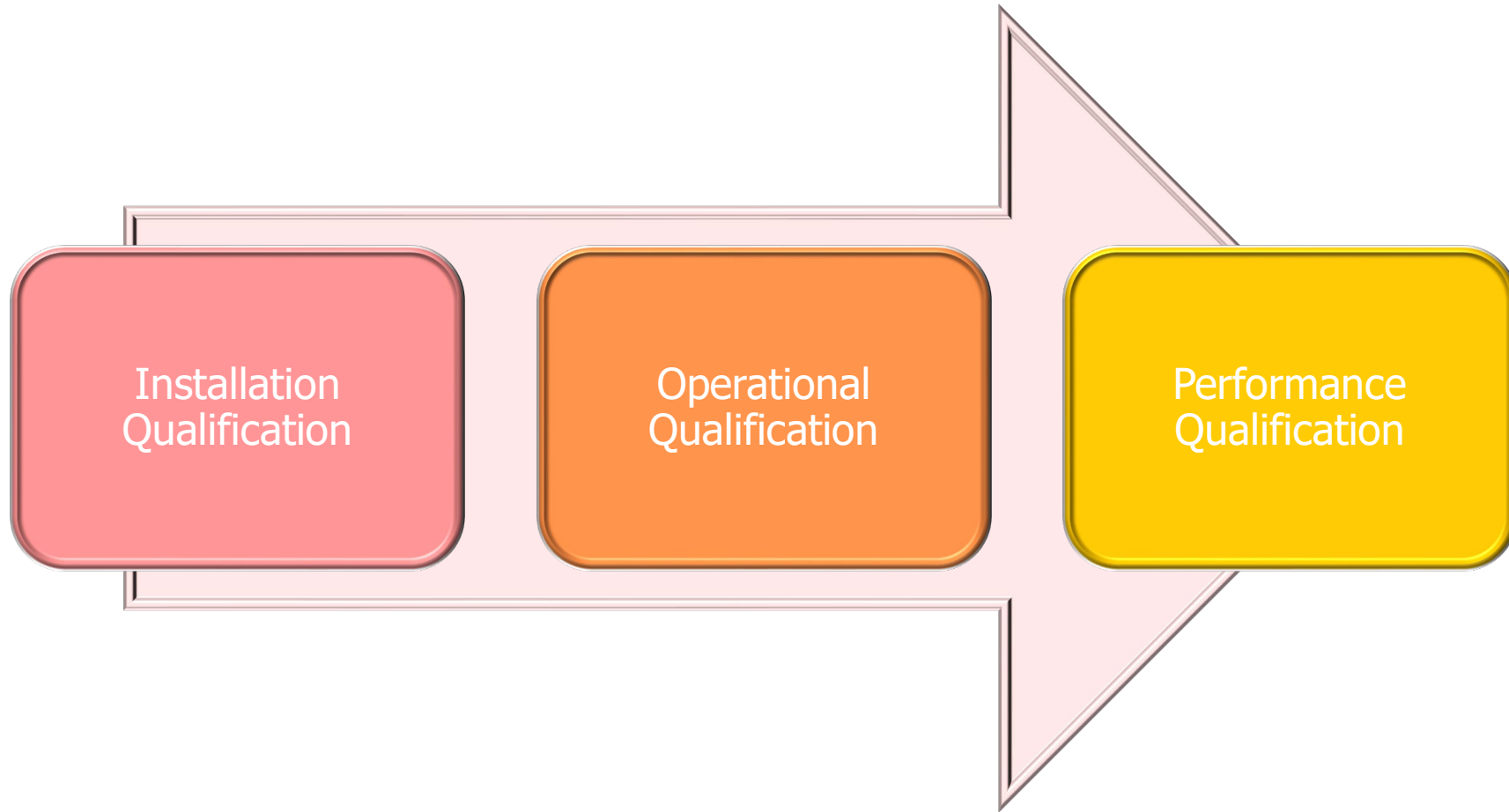
# Validation planning – preliminary considerations
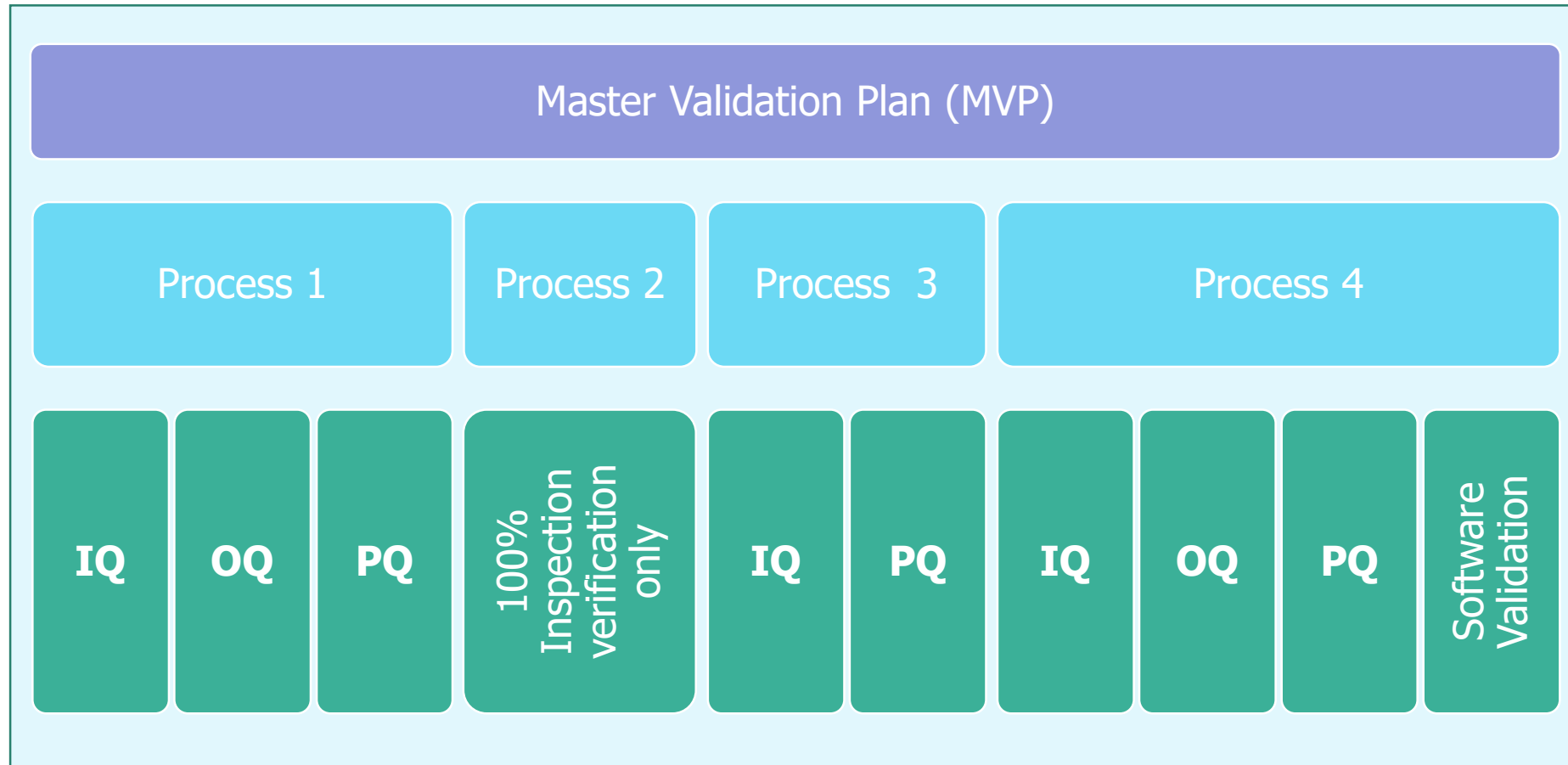
# Different types of process validation

Prospective, concurrent and retrospective

# Different types of process validation

**Prospective validation**
- Performed after the product is fully developed and prior to manufacturing the device

**Concurrent validation**
- Performed with the intent of distributing product that has been manufactured in the validation

**Retrospective validation**
- Performed on existing processes where sufficient data is available to demonstrate that the process is in control
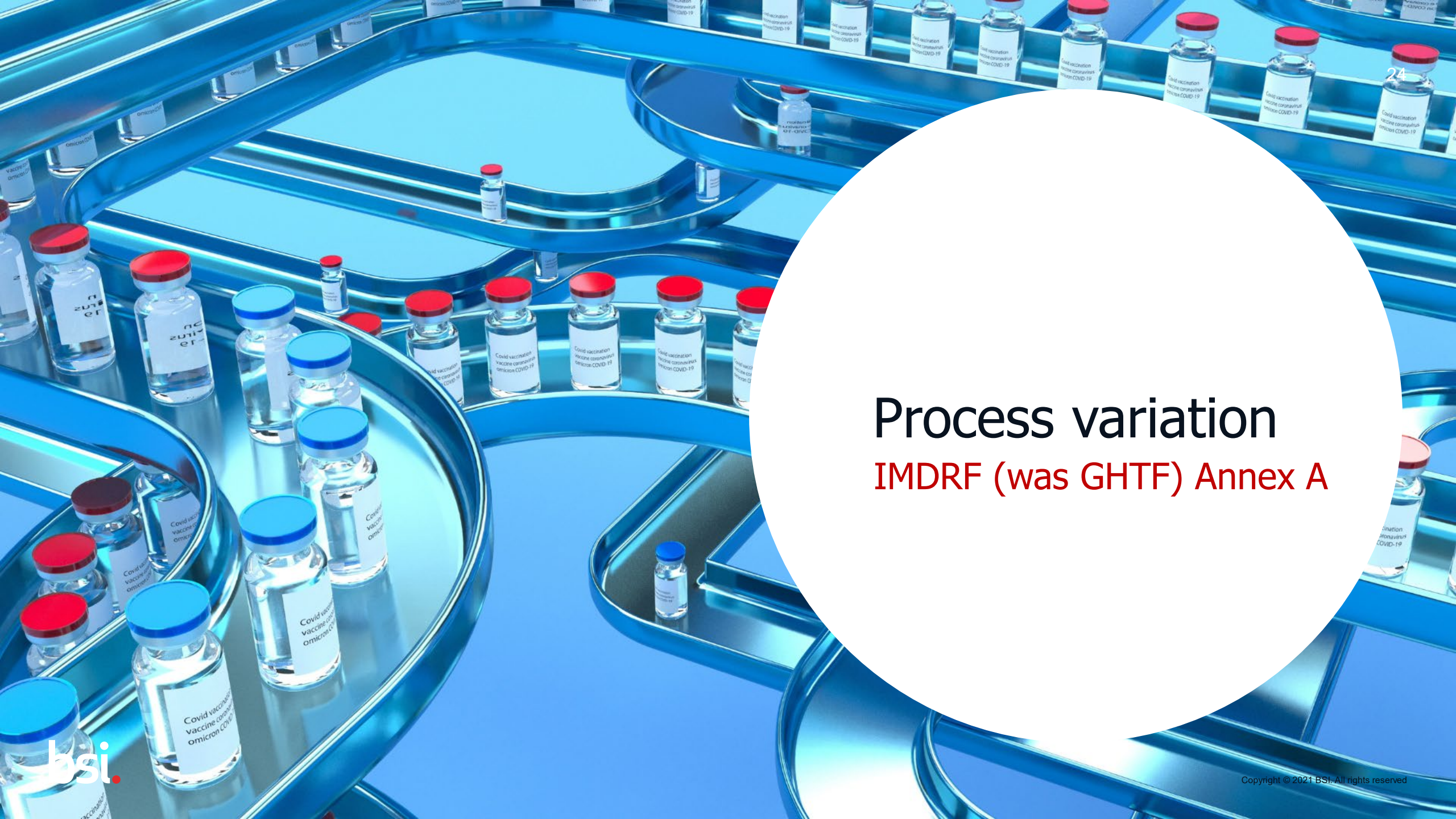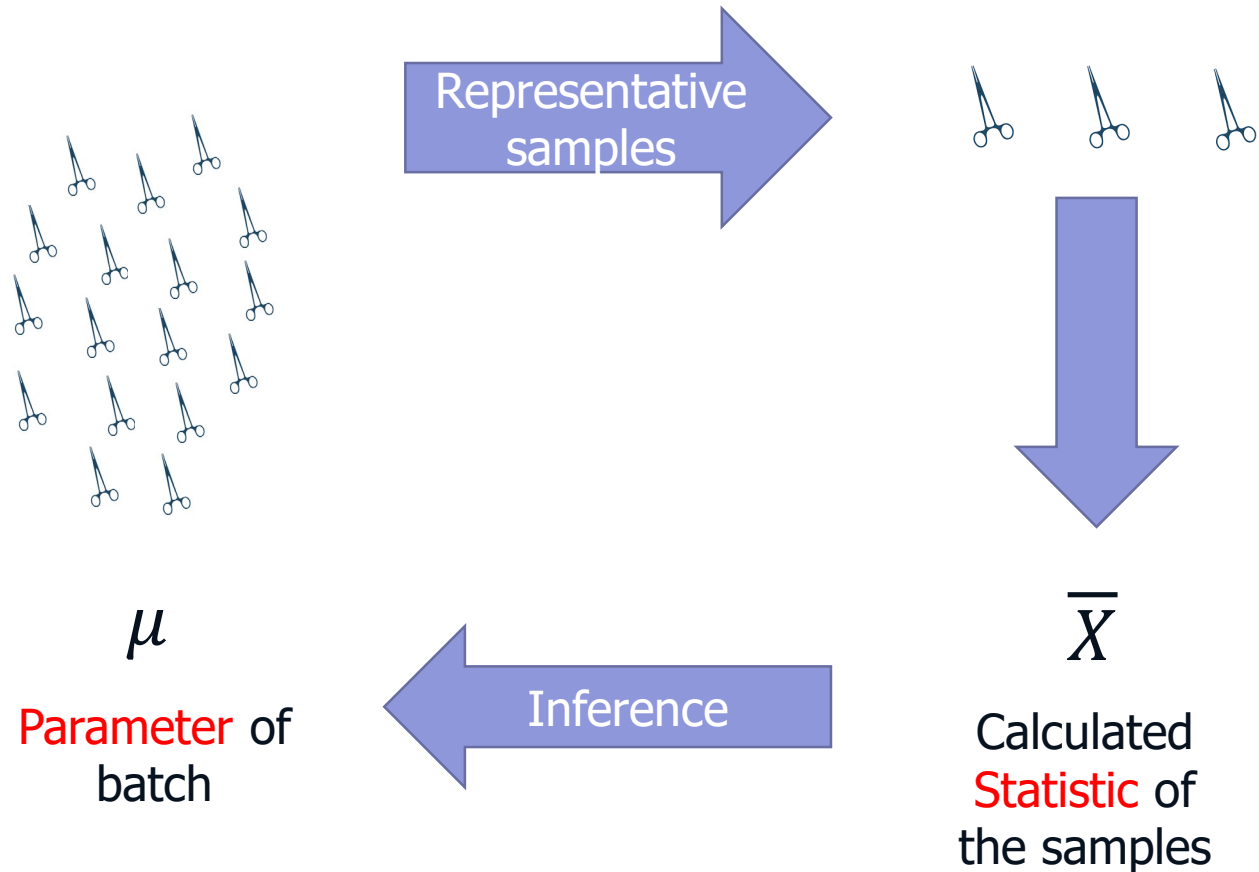
# Process variation
## IMDRF (was GHTF) Annex A

GHTF/SG3/N99-10:2004 (Edition 2)

**GHTF**

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http://www.imdrf.org/docs/ghtf/final/sg3/technical-docs/ghtf-sg3-n99-10-2004-qms-process-guidance-04010.pdf

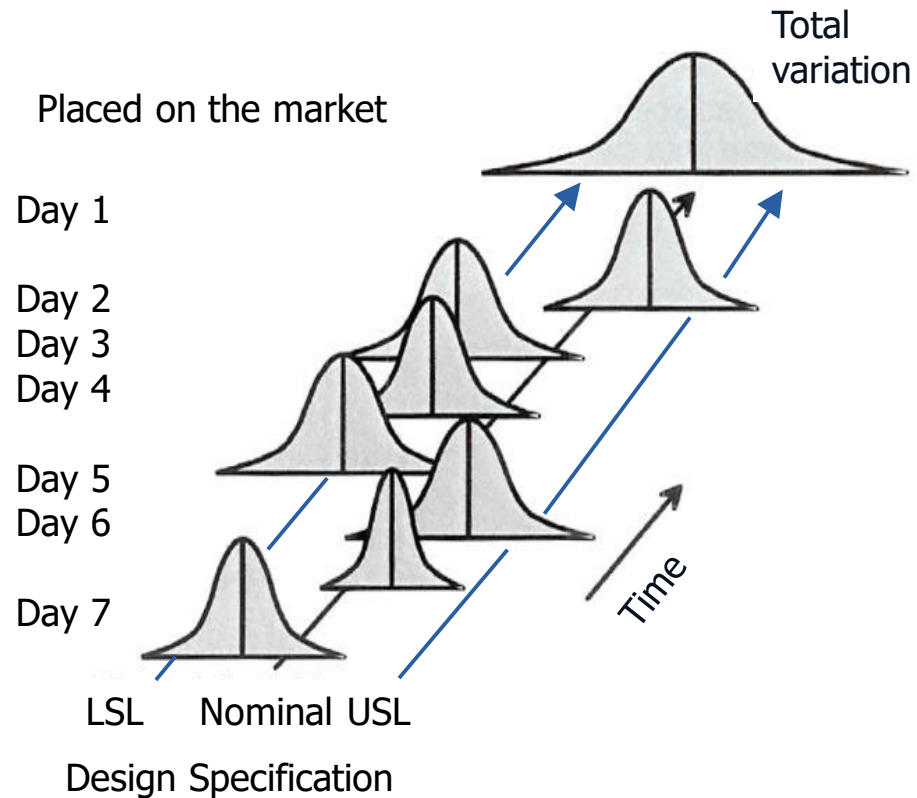Click here

# Sampling

Need to know the sharpness of the scissors of the whole batch

Measuring sharpness on every device is too time consuming, instead will measure a sample of those made

Representative samples

$\mu$

Parameter of batch

Inference

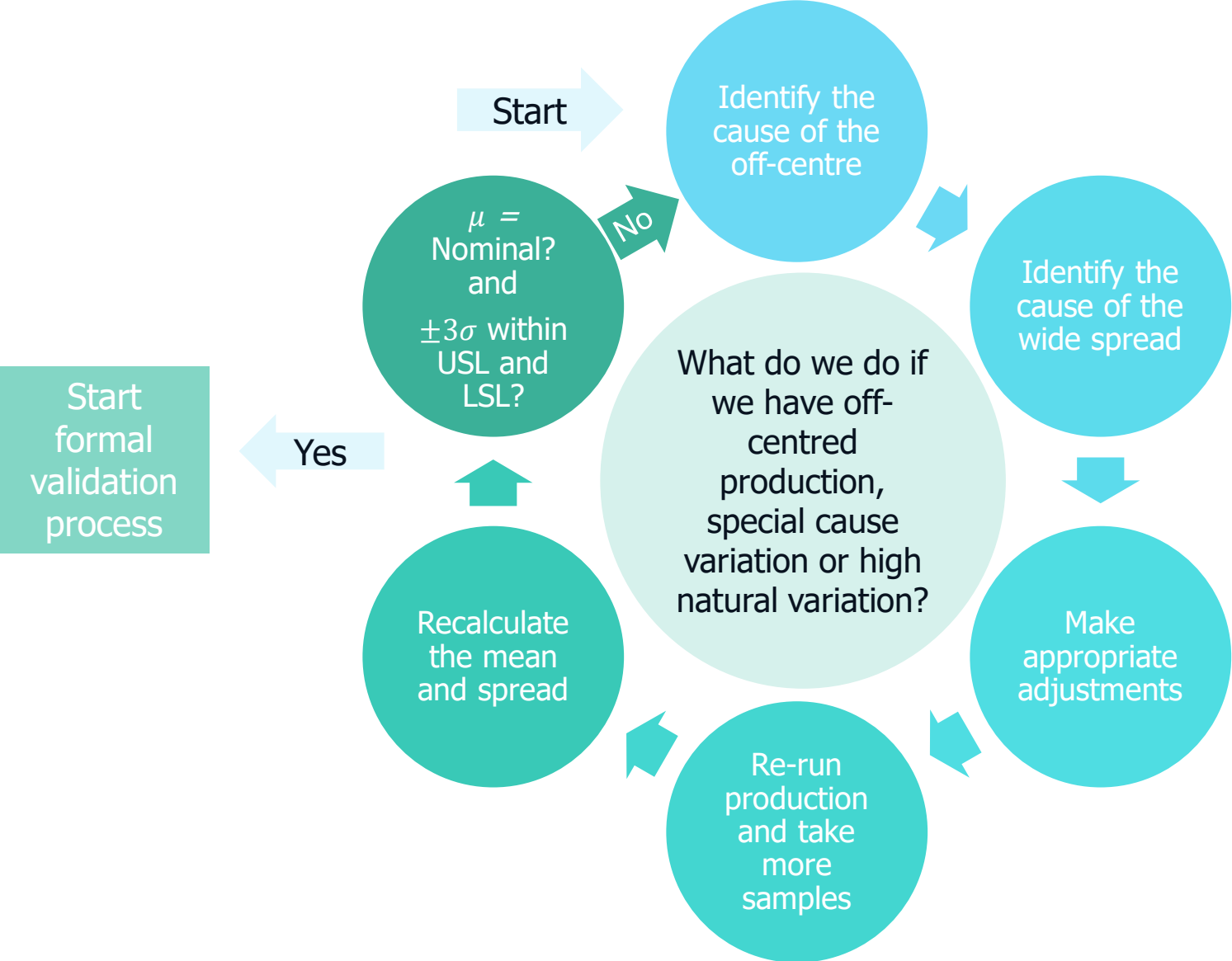$\overline{X}$

Calculated Statistic of the samples

# Process variation over time

To achieve a <u>capable and stable</u> manufacturing process, variation needs to be reduced to well within design limits, and be central



Figure 1 - Unstable process

Total variation

Placed on the market

Day 1

Day 2
Day 3
Day 4

Day 5
Day 6

Day 7

Time

LSL    Nominal USL

Design Specification

Figure 3
Stable and capable

Figure 2
Stable but not capable

Time

LSL    Nominal  USL

Design Specification
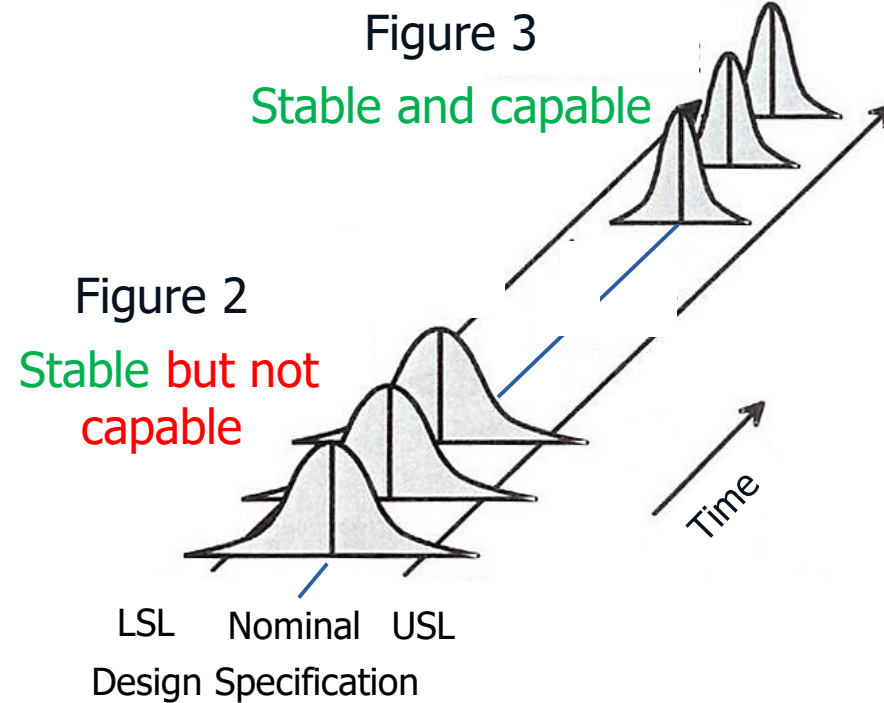
# Process variation – reducing variation

# Evaluating process capability

- Cpk compared to the engineering specification.
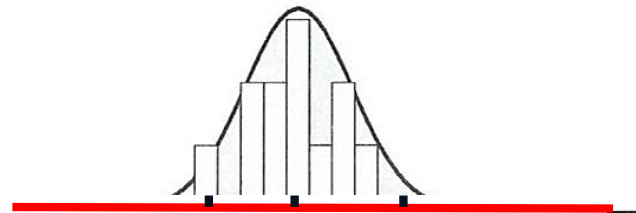


9.9    10    10.1

LSL    Nom    USL
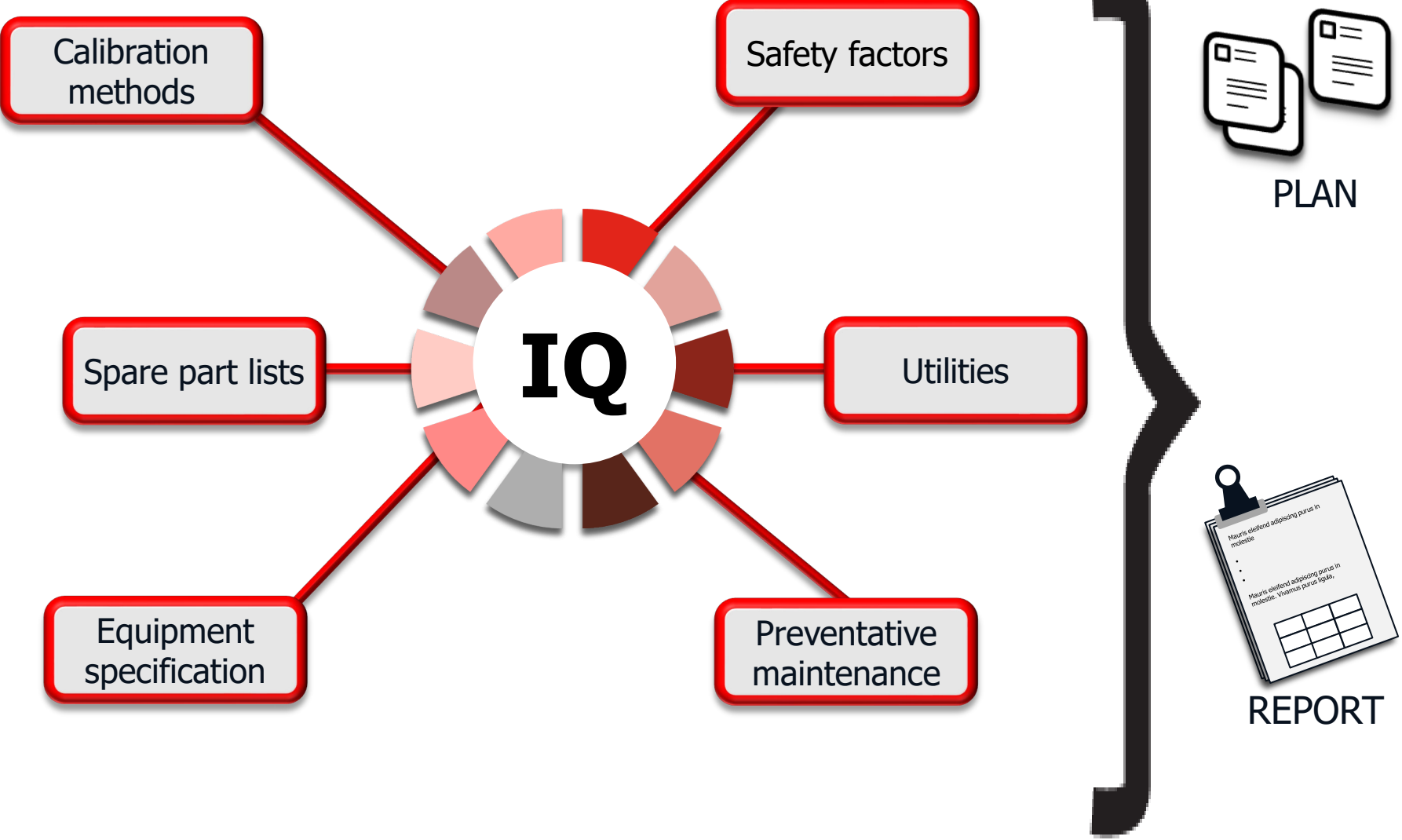
Cpk  <1

9.9    10    10.1

LSL    Nom    USL

Cpk = 1

9.9    10    10.1

LSL    Nom    USL

Cpk >1

Common starting point Cpk=1.33

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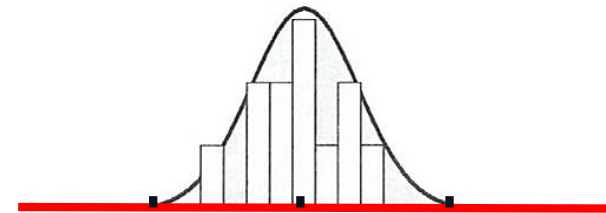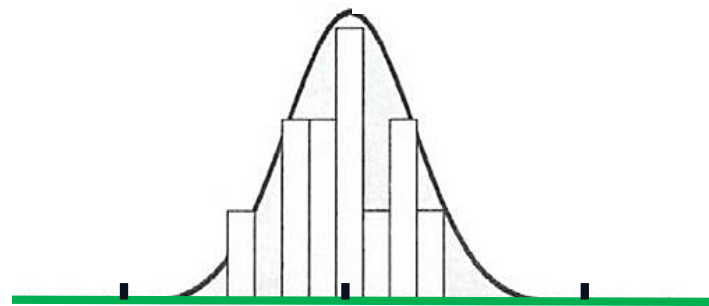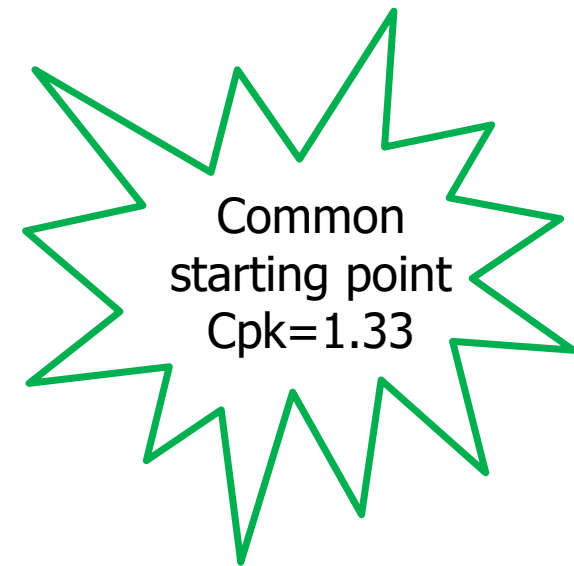
# Process validation protocols

IQ, OQ and PQ

Calibration methods

Safety factors

Spare part lists

Utilities

Equipment specification

Preventative maintenance

PLAN

REPORT

# Operational qualification



Test maximum limits

Qualified utilities

Test minimum limits

Raw materials

Trained operators

Process inputs

OQ

PLAN

REPORT
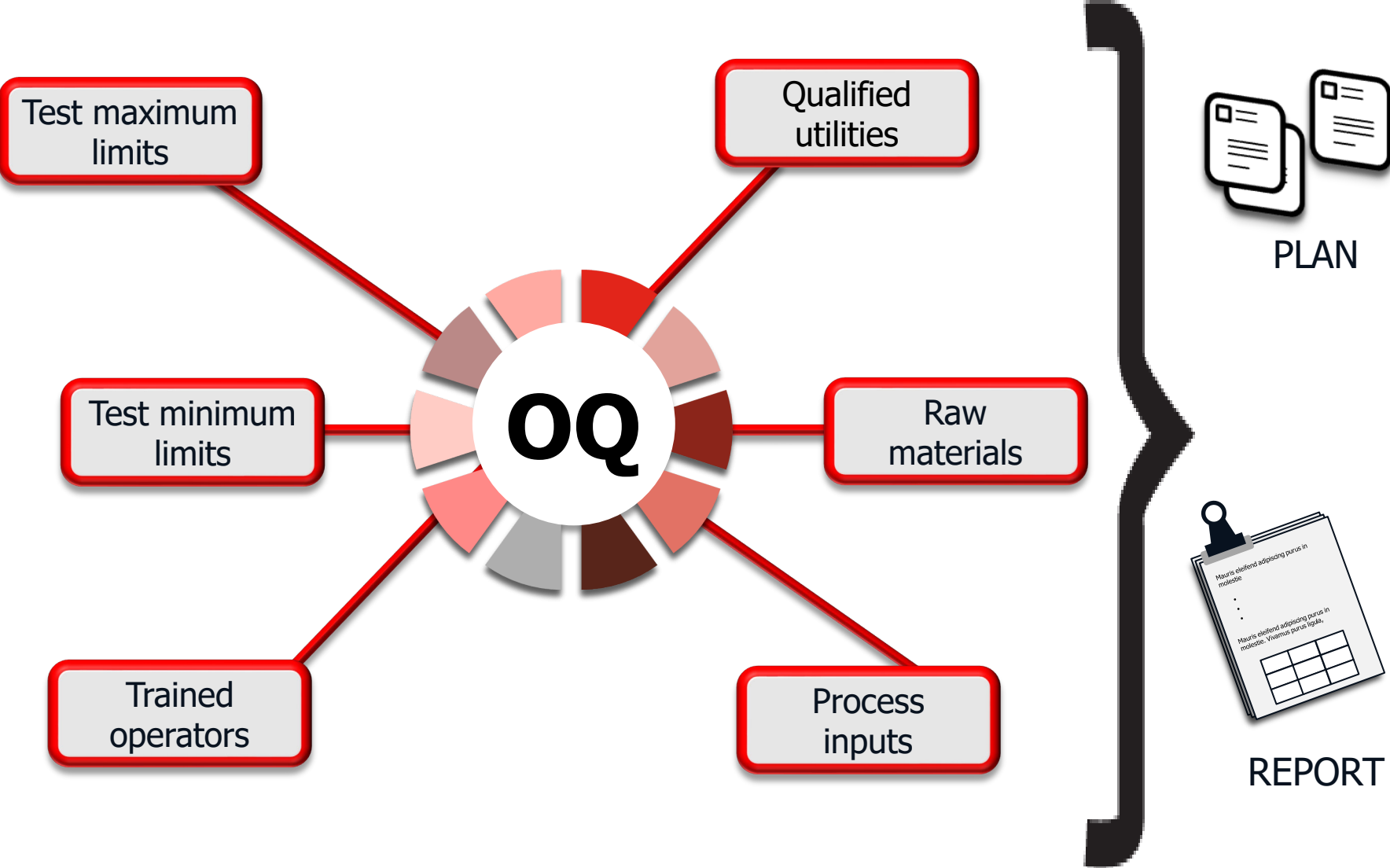
# Relationship between OQ and PQ



**Bar Sealer**

**Label Printer**

Machine settings

Temperature range

Pressure range

Speed range

Overlap area represents process settings where the device specification(s) were achieved

Process settings taken forward into PQ studies

# Performance qualification



Test with challenge pieces

Process parameters established in OQ

Multiple raw material suppliers

**PQ**

Real manufacturing conditions

Multiple shifts

Multiple batches

PLAN

REPORT

# The validation protocol



**What?**

- Characteristics of the device
- Characteristics of the process

**How?**

- Measurement methods

**How many?**

- Statistical significance
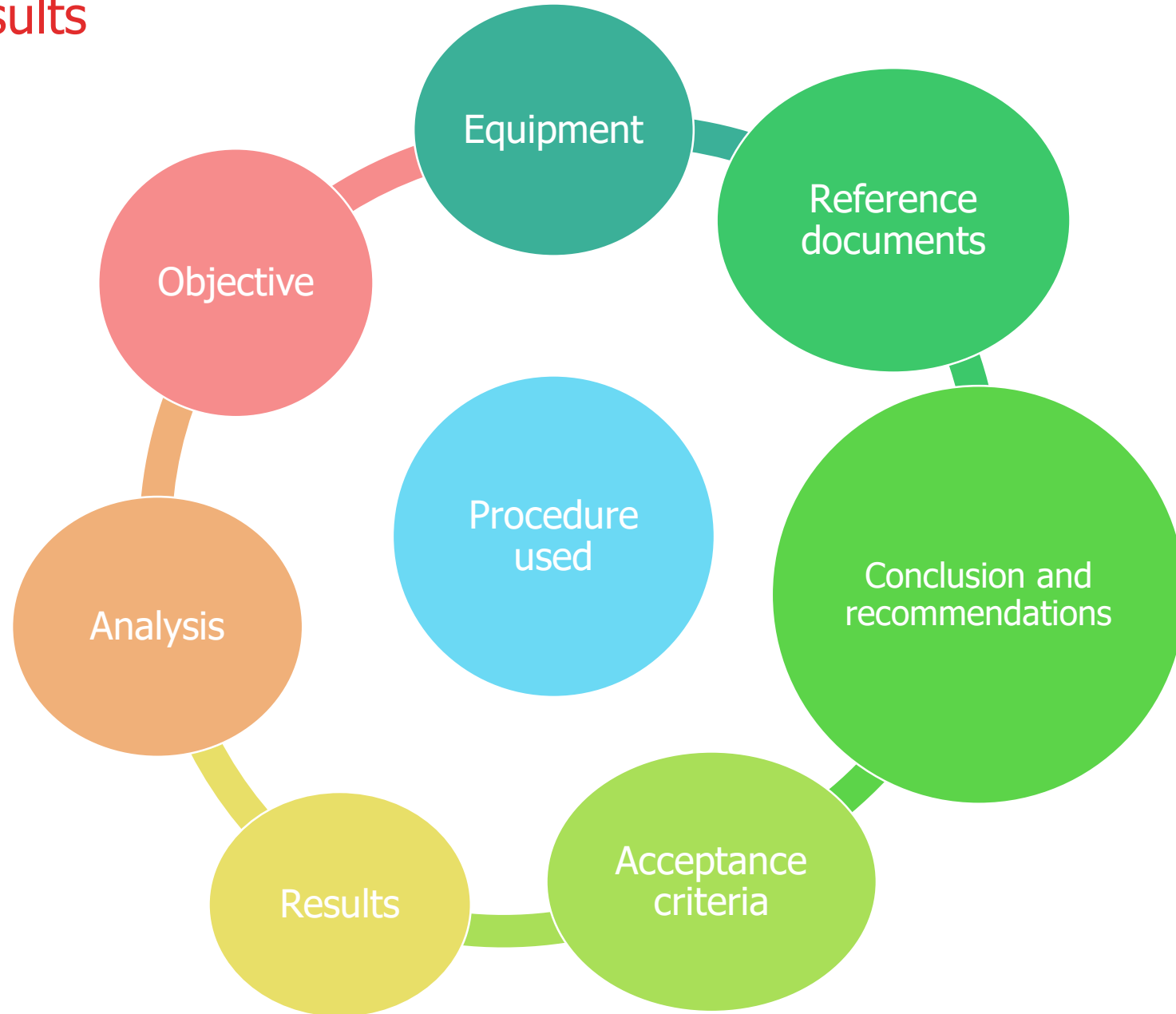- Statistical methodology

**When?**

- Where in the process are the measurements taken?
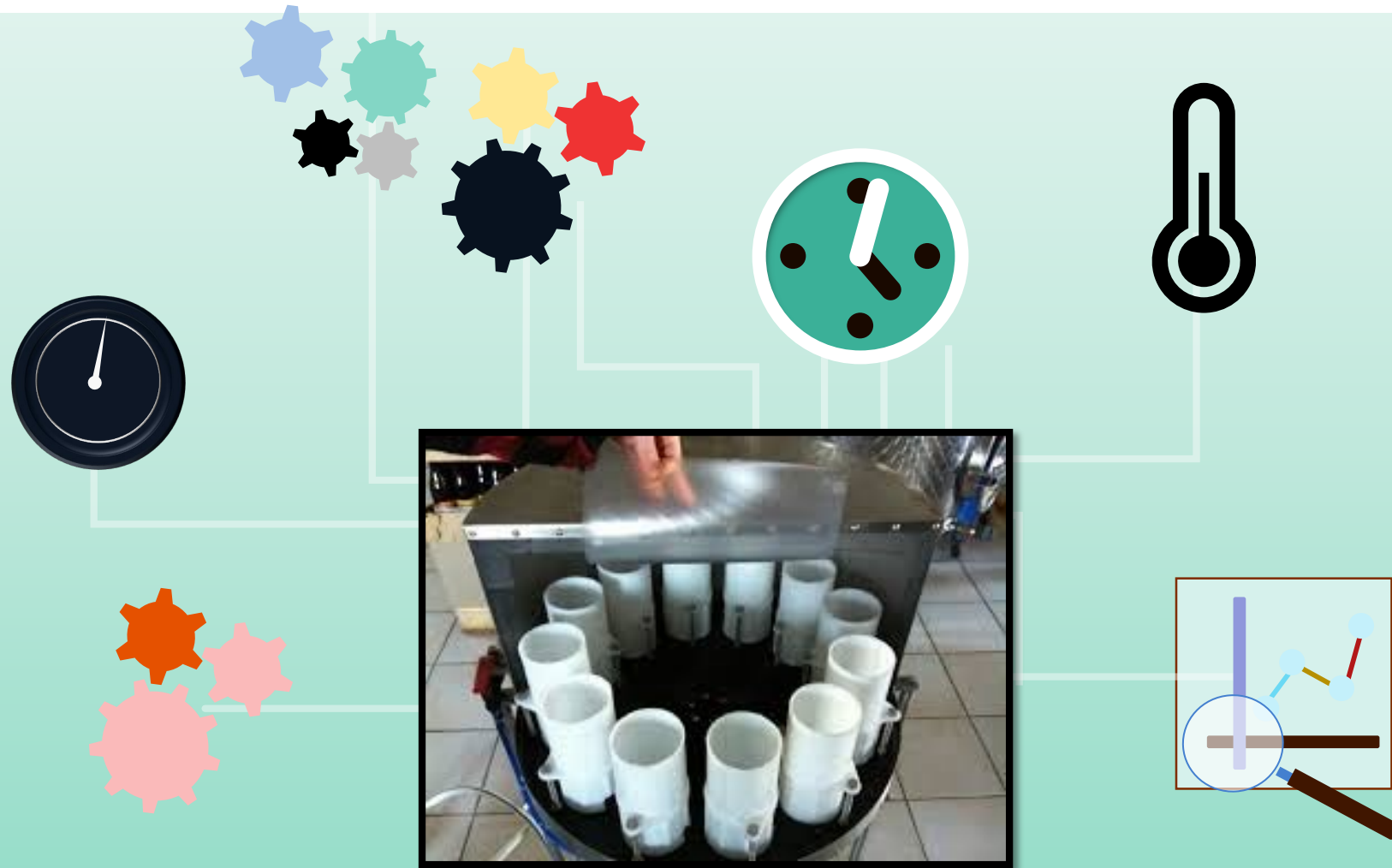
**Criteria?**

- Pass/fail limits

PLAN

# How to report results

# Monitoring the state of process validation

# Monitoring a state of validation

Process revalidation

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# Review and reflect

What can go wrong?

# Reflective quiz

## Thank you
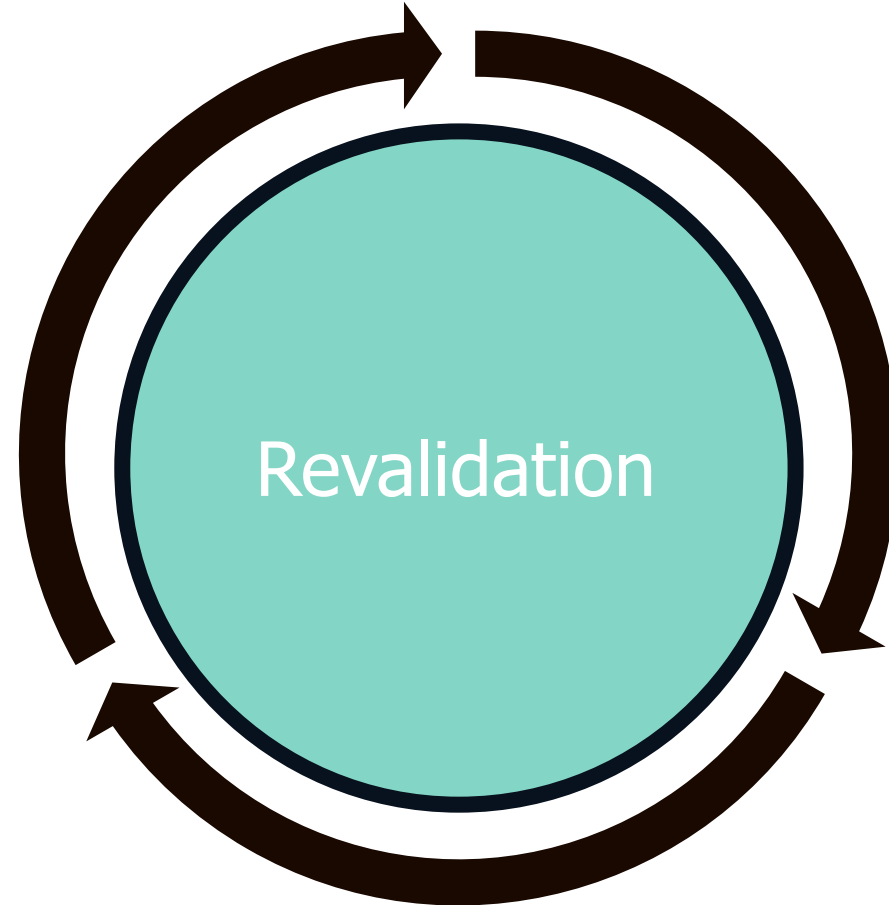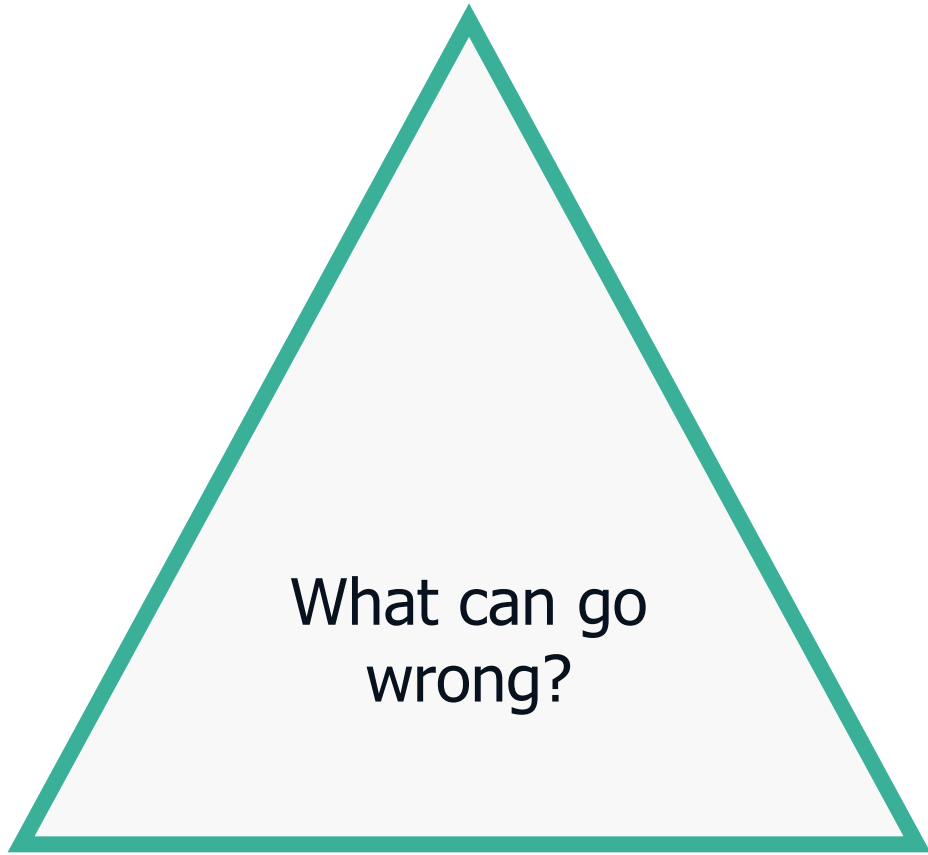
# Further Information & Support

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