



# PROCESS VALIDATION

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# DEFINITIONS

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- From ISO 9000:2000
  - Verification - confirmation, through the provision of objective evidence, that specified requirements have been fulfilled
  - Validation - confirmation, through the provision of objective evidence, that the requirements for a specific intended use or application have been fulfilled
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# VALIDATION REQUIREMENTS

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- ISO 9001:2000 & DIS 13485(2002) Clause 7.5.2
- The organization shall validate any processes for production and service provision where the resulting output cannot be verified by subsequent monitoring or measurement. This includes any processes where 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.

# VALIDATION

## REQUIREMENTS

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ISO 9001:2000 & DIS 13485(2002) Clause 7.5.2 continued

The organisation shall establish arrangements for these processes including, as applicable

- >defined criteria for review and approval of the processes

- >approval of equipment and qualification of personnel

- >use of specific methods and procedures

- >requirements for records, and

- >revalidation

# DIS 13485 >> ISO13485:2003

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## Clause 7.5.2.2.1

The organization shall establish documented procedures for the validation of the application of computer software (and changes to such software and/or its application) for production and service operations and measuring and monitoring operations that affect the ability of the product to conform to specified requirements. Such software applications shall be validated prior to initial use.

The results of validation shall be recorded.

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# DIS 13485 CONTINUED

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Clause 7.5.2.2.2 – for **sterile** medical devices

The organization shall establish documented procedures for the validation of sterilization processes. Sterilization processes shall be validated prior to initial use.

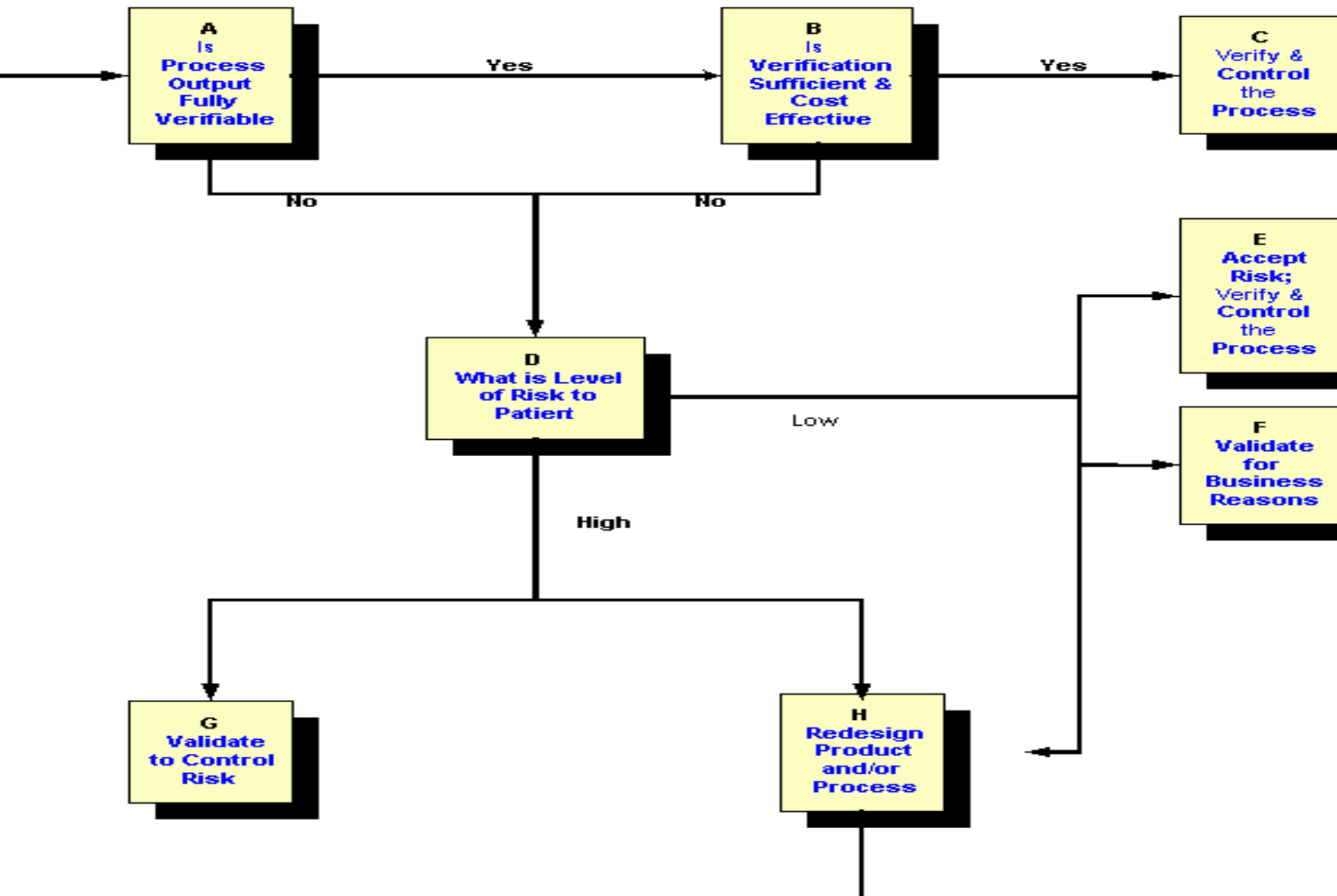
The results of sterilization process validation(s) shall be recorded, and shall identify the process parameters of the sterilization process necessary to demonstrate control.

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# GHTF GUIDANCE

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- Available on GHTF website ([www.gh tf.org](http://www.gh tf.org))
  - Document GHTF.SG3.N99-10
  - Dated June 29, 1999
  - Written by GHTF SG 3 – Kim Trautman (US FDA) Convenor
  - Active participation from regulators and industry from USA, Europe, Japan, Canada, Australia
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# GHTF GUIDANCE

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Examples of processes which should be validated

- > Sterilization processes
  - > Clean room ambient conditions
  - > Aseptic filling processes
  - > Sterile packaging sealing processes
  - > Lyophilization processes
  - > Heat treating processes
  - > Plating processes
  - > Plastic injection moulding processes
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# GHTF GUIDANCE

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Processes which may be satisfactorily covered by verification

- > manual cutting processes
- > Testing for colour, turbidity, total pH of solutions
- > Visual inspection of printed circuit boards
- > Manufacturing and testing of wiring harnesses

Processes which **may** need to be validated

- > Cleaning processes
  - > Certain human assembly processes
  - > Numerical control cutting processes
  - > Filling processes
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# GETTING STARTED

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- Form multi-functional team for validation
  - Plan the approach and define the requirements
  - Identify and describe the processes
  - Specify process parameters and desired output
  - Create a master validation plan
  - Select methods and tools for validation
  - Create validation protocols
  - Perform IQ, OQ, PQ and document results
  - Determine continuous process controls
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# MORE DEFINITIONS

Installation qualification (IQ): establishing by objective evidence that all key aspects of the process equipment and ancillary system installation adhere to the manufacturers approved specification and that the recommendations of the supplier of the equipment are suitably considered.

Operational qualification (OQ): establishing by objective evidence process control limits and action levels which result in product that meets all predetermined requirements.

# MORE DEFINITIONS 2

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Performance qualification (PQ): establishing by objective evidence that the process, under anticipated conditions, consistently produces a product which meets all predetermined requirements.

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# INSTALLATION QUALIFICATION      IQ

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Is the equipment installed correctly ?

- >Equipment design features
  - >Installation conditions
  - >Calibration, preventative maintenance, cleaning
  - >Safety
  - >Supplier documentation – drawings, manuals etc
  - >Software documentation
  - >Spare parts
  - >Environmental conditions
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# OPERATIONAL QUALIFICATION

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OQ

Process control limits

>Software parameters

>Raw material Specifications

>Process operating procedures

>Material handling requirements

>Process change control

>Training

>Short term stability and capability

>Potential failure modes, action levels and worse case conditions

>Statistically valid techniques

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# PERFORMANCE

## QUALIFICATION

## PQ

Demonstrate that the process will consistently produce acceptable product under normal operating conditions

- > Produce actual product under process parameters established in OQ

- > Check acceptability of product

- > Assure process capability

- > Check process repeatability and long term process stability

# GHTF GUIDANCE

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- Statistical methods
  - Stable / Unstable processes
  - Process capability
  - Transmission of variation
  - Control charts
  - Useful tools
  - Example validation of a Heat Sealer machine
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# SUMMARY

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This guidance provides general suggestions on ways manufacturers may prepare for and carry out process validations

Some regulatory requirements state that **every** process that cannot be fully verified by subsequent inspection or test **must** be validated

Records of every step in the process are most important for reference and audit

Frequency of revalidation is the responsibility of the manufacturer and should be carefully defined