



Process Validation Guidance
GHTF/SG3/N99-10:2004
Study Group 3

Introduction

- Purpose & Scope of SG3/N99
- What is process validation?
- How are processes validated?
- What processes must be validated?
- How to maintain state of validation
- Revalidation





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1.1 Purpose

- **To assist manufacturers in understanding quality management system requirements concerning process validation**



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1.2 Scope

- **Applicable to manufacturing, servicing and installation processes for medical devices**
- **Does not cover verification of design output or design validation**





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2.4 Process Validation (Definition)

- Establishing by *objective evidence* that a process *consistently* produces a result or product meeting its *predetermined requirements*.





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2.6 Verification (Definition)

- Confirmation by examination and provision of objective evidence that the specified requirements have been fulfilled.



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Three Elements of Process Validation

- Verify that equipment is installed and operating properly (*Installation Qualification - IQ*)
- Develop process that can produce product or result that meets all specifications (*Operational Qualification - OQ*)
- Verify that process can produce product or result that meets all specifications consistently over time (*Performance Qualification - PQ*)



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Steps in Validating a Process

- Develop validation protocol
- Conduct installation qualification
- Conduct operational qualification
- Conduct performance qualification
- Analyze results and reach conclusions



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Validation Protocol

- A document stating how validation will be conducted, including test parameters, product characteristics, manufacturing equipment, and decision points on what constitutes acceptable test results.
- Criteria for revalidation and extent of revalidation (complete or partial)



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Installation Qualification (IQ)

- 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.



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Some IQ Considerations

- Equipment manufacturer's recommendations
- Electricity: supply, reliability
- Water: supply, pressure, quality
- Air: pressure, quality
- Calibration: schedule, documentation
- Maintenance: schedule, procedures, documentation, spare parts





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Operational Qualification (OQ)

- Establishing by *objective evidence* process control limits and *action levels* which result in product that meets all predetermined requirements.





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Some OQ Considerations

- Things that should be Established:
 - Procedure
 - Process control limits
 - Output specifications
 - Alert levels and action levels
 - Specifications for components, manufacturing materials
- Environmental conditions that may affect process stability
 - Temperature
 - Humidity
 - Light
 - Particle count, contamination
 - Other



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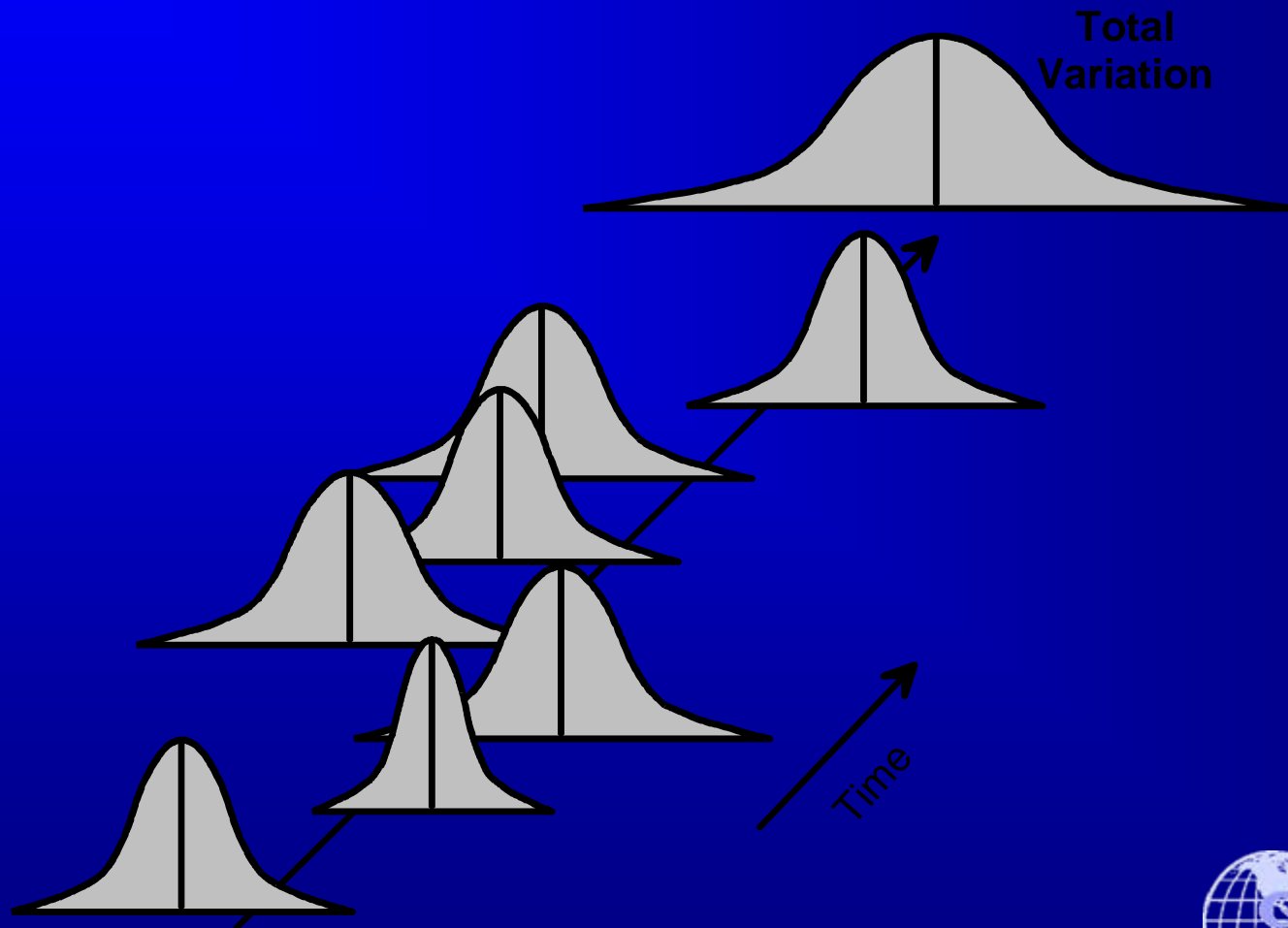
Performance Qualification (PQ)

- Establishing by objective evidence that the process, under *anticipated conditions, consistently* produces a product which meets all predetermined requirements



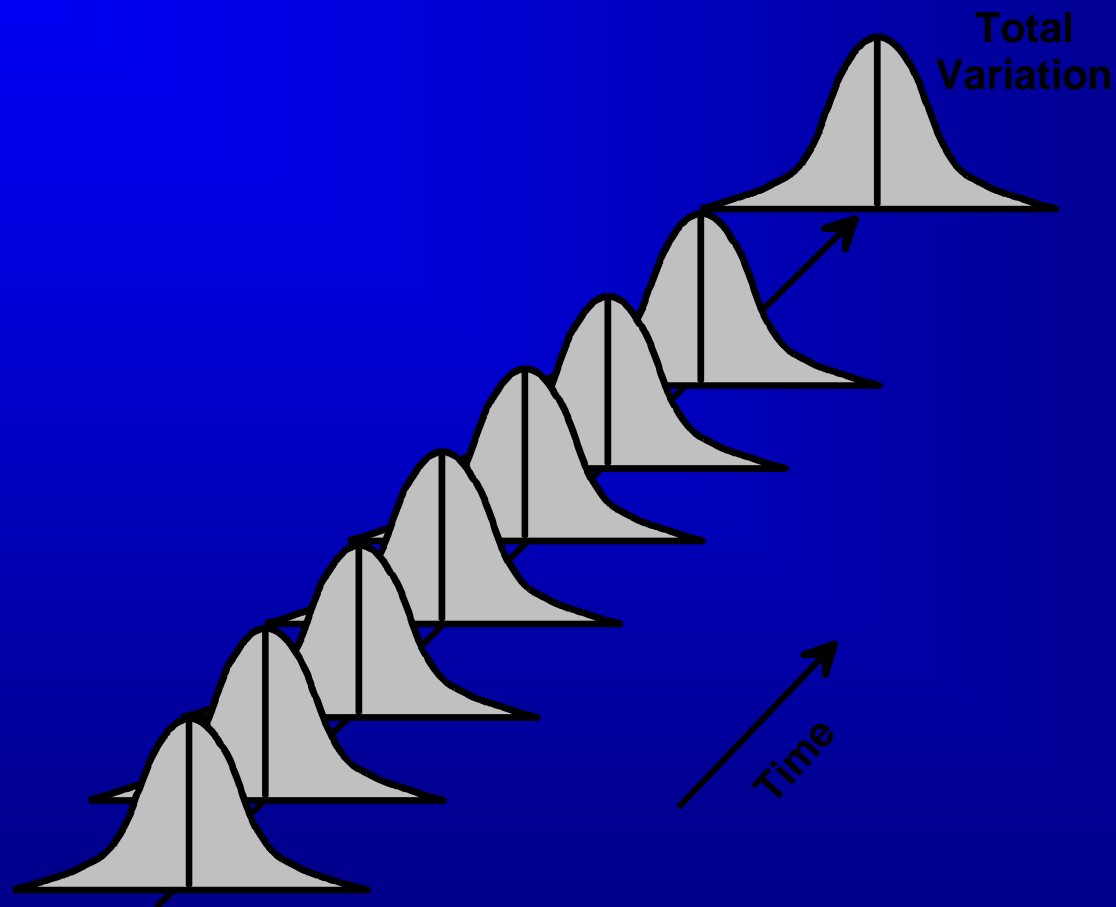


UNSTABLE PROCESS





STABLE PROCESS



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Monitor and control process

- Purpose: to ensure process remains within established parameters under anticipated conditions
- Investigate deviations from established parameters
- Take corrective action
- Consider whether revalidation is necessary



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Changes in process or product

- Evaluate changes in process, product, procedures, equipment, personnel, environment, etc. to determine effect of change
- Is revalidation necessary?
- How much revalidation is necessary to assure process is capable and stable?



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Periodic revalidation

- Consider periodic revalidation where *cumulative* minor changes to process and raw materials may eventually affect process
- Sterilization processes typically are revalidated periodically (once a year) as specified in voluntary standards



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Some reasons for revalidation

- Change in process that may affect quality or validation status
- Negative trend in quality indicators
- Change in the product design that affects the process
- Process is moved within facility or transferred from one facility to another
- Change in the application of the process



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Using historical data for validation

- Validation can be partially based on accumulated historical manufacturing, testing, control and other data
- Sources of historical data:
 - batch or lot records
 - manufacturing log books
 - test and inspection results
 - control charts
 - customer feedback
 - field failure reports
 - service reports
 - audit reports
 - generic feedback



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Using historical data for validation

- All appropriate data must have been collected AND collected in a manner that allows adequate analysis
- Historical pass/fail manufacturing data usually is not adequate



Summary

- Key features of Process Validation Guidance
GHTF/SG3/N99-10:2004
- IQ, OQ, and PQ



GHTF SG3 Training Summary

- 1. GHTF SG3 – Role, Members, Documents**
- 2. Quality Management Systems: History and Evolution**
- 3. ISO13485:2003 - An Overview**
- 4. Risk Management Principles and Activities Within a Quality Management System**
- 5. Process Validation**





END

Regulatory Links & Sources of Standards



Additional information

European Medical Device Directive 93/42/EEC:

<http://www.newapproach.org/Directives/DirectiveList.asp>

European Medical Device Directive Guidance documents:

<http://www.meddev.info>

Canadian Medical Devices Regulations:

<http://laws.justice.gc.ca/en/f-27/sor-98-282/126598.html>

Australian Medical Devices Regulations:

<http://scaleplus.law.gov.au/html/pastereq/3/1762/top.htm>

Global Harmonization Task Force:

<http://www.ghtf.org>

Japan MHLW:

<http://www.mhlw.go.jp/english/index.html>

China:

CNCA: <http://www.cnca.gov.cn/index.htm> or <http://www.cnca.gov.cn/download/english.html>

SFDA: <http://www.sfda.gov.cn/eng/>



Additional information (cont.):

FDA:

General:

<http://www.fda.gov>

FDA site searchable for QSR and Electronic Records & Signature (21 CFR Parts 820 and 11) :

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm>

FDA Guidance documents

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfGGP/Search.cfm>

GEHC Internal sites:

Americas: http://supportcentral.ge.com/products/sup_products.asp?prod_id=23217

Europe: <http://gein.euro.med.ge.com/engineering/qualsys/>

Asia: <http://3.28.123.6/free/qmc/qasr/newQASRasia/>



Additional information (cont.)

Council Directive 93/42/EEC of 14 June 1993 concerning medical devices Official Journal L169, 12/07/1993 P. 0001 - 0043 can be found at:

http://3.70.4.1/~qualsys/regulatory/MDD/1993L0042_consolid.pdf

Guidance on Technical Files developed by the Co-ordination of Notified Bodies - Medical Devices (NB-MED) can be found at:

http://www.meddev.info/documents/R2_5_1-5_rev4.pdf

Guidance on “Essential Principles of Safety and Performance of Medical Devices on a Global Basis” developed by Study Group 1 of the Global Harmonization Task Force can be found at:

<http://www.ghtf.org/sg1/inventorysg1/sg1-n20r5.pdf>



Sources of Standards - IEC

The International Electrotechnical Commission (IEC) is the leading global organization that prepares and publishes international standards for all electrical, electronic and related technologies.

International Electromedical Commission (IEC)

Central Office of the IEC

3, rue de Varembe

P.O. Box 131

CH-1211 Geneva 20

Switzerland

Telephone: (+41) 22 919 02 11

Fax: (+41) 22 919 03 00

Web Site: <http://www.iec.ch>



Sources of Standards - ISO

ISO is a non-governmental organization, consisting of a network of the national standards institutes of 148 countries, on the basis of one member per country, with a Central Secretariat in Geneva, Switzerland, that coordinates the system

International Organization for Standardization (ISO)

1, rue de Varembe

Case postale 56

CH-1211 Geneve 20

Switzerland

Telephone: (+41) 22 749 01 11

Fax: (+41) 22 733 34 30

e-mail: central@iso.ch

Web Site: <http://www.iso.ch>



Sources of Standards - CEN

CEN, the European Committee for Standardization, develops voluntary technical standards which promote free trade, the safety of workers and consumers, interoperability of networks, environmental protection, exploitation of research and development programs, and public procurement.

European Committee for Standardization (CEN)

Rue de Stassart, 36

B-1050 Brussels

Belgium

Telephone: (+32) 2 550 08 11

Fax: (+32) 2 550 08 19

E-Mail: infodesk@cenorm.be

Web Site: <http://www.cenorm.be/cenorm/index.htm>



Sources of Standards - CENELEC

CENELEC is a non-profit technical organization set up under Belgian law and composed of the National Electrotechnical Committees of 28 European countries. CENELEC prepares voluntary electrotechnical standards.

Comite Europeene de Normalisation Electrotechnique (CENELEC)

Rue de Stassart, 35

B-1050 Brussels

Belgium

Telephone: (+32) 2 519 68 71

Fax: (+32) 2 519 69 19

E-Mail: info@cenelec.org

Web Site: <http://www.cenelec.org>



Sources of Standards - ASTM

ASTM International develops voluntary technical standards for materials, products, systems, and services.

American Society for Testing and Materials (ASTM)

100 Barr Harbor Drive

West Conshohocken, PA, 19428-2959

USA

Telephone: (610) 832-9500

Fax: (610) 832-9555

Web Site: <http://www.astm.org>



Sources of Standards - ANSI

The American National Standards Institute (ANSI) is a private, non-profit organization (501(c)3) that administers and coordinates the U.S. voluntary standardization and conformity assessment system.

American National Standards Institute (ANSI)

1819 L Street, NW, Suite 600

Washington, DC 20036

USA

Telephone: (202) 293-8020

Fax: (202) 293-9287

Web Site: <http://www.ansi.org>



Sources of Standards - AAMI

The AAMI standards program consists of over 100 technical committees and working groups that produce Standards, Recommended Practices, and Technical Information Reports for medical devices.

Association for the Advancement of Medical Instrumentation (AAMI)

1110 North Glebe Road, Suite 220

Arlington, VA 22201-4795

USA

Telephone: (703) 525-4890

Fax: (703) 276-0793

Web Site: <http://www.aami.org>



Sources of Standards - NEMA

NEMA provides a forum for the standardization of electrical equipment and develops technical standards.

National Electrical Manufacturers Association (NEMA)

1300 N. 17th Street, Suite 1847

Rosslyn, VA, 22209

USA

Telephone: (703) 841-3200

Fax: (703) 841-5900

E-Mail: webmaster@nema.org

Web Site: <http://www.nema.org>



Sources of Standards - UL

Underwriters Laboratories Inc. (UL) is an independent, not-for-profit product-safety testing and certification organization, as well as a developer of safety standards

Underwriters Laboratories, Inc.

333 Pfingsten Road

Northbrook, IL 60062-2096

USA

Telephone: (847) 272-8800

Fax: (847) 272-8129

E-mail: northbrook@us.ul.com

Web Site: <http://www.ul.com>



Sources of Standards - CNCA

Certification Accreditation Administration Of The
People's Republic Of China (CNCA)

9A Madian Street

Haidian District

Beijing 100088

China

Telephone: (+86) 10 - 82260766 or 82262775

Fax: (+86) 10 - 82260767

E-Mail: webmaster@cnca.gov.cn

Web Site: <http://www.cnca.gov.cn>



Sources of Standards - JISC

- JISC consists of many national committees and plays a central role in standardization activities in Japan.

Japanese Industrial Standards Committee (JISC)

1-3-1 Kasumigaseki

Chiyoda-ku

Tokyo 100-8901

Japan

Telephone: not available at time of this writing

Fax: not available at time of this writing

E-Mail: jjisc@meti.go.jp

Web Site: <http://www.jjisc.go.jp/eng/>

