medídee®

Regulatory & Clinical Affairs
Quality Management

Nano-Tera.ch

05 February 2015 – part 4

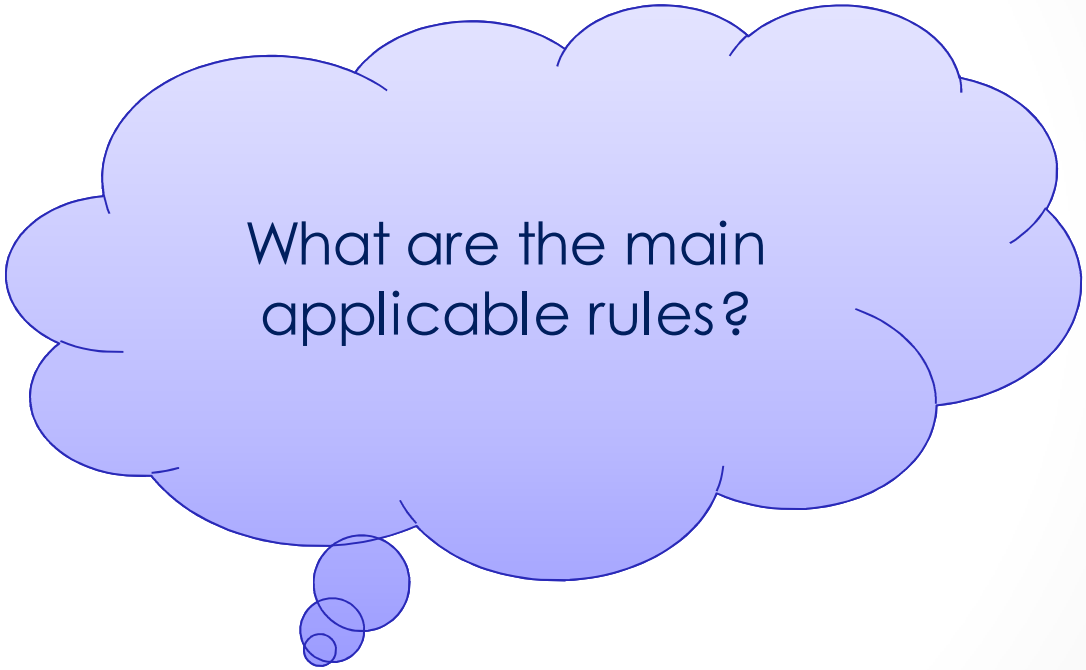
Intro ISO – GMP - GLP

Pierre-Alain Sommer
Pierre-alain.sommer@medidee.com
www.medidee.com

Introduction to ISO 13485, cGMP's and GLP's

- Context
- US approach
- EU approach
- Comparison

Development, manufacture and distribution of medical devices

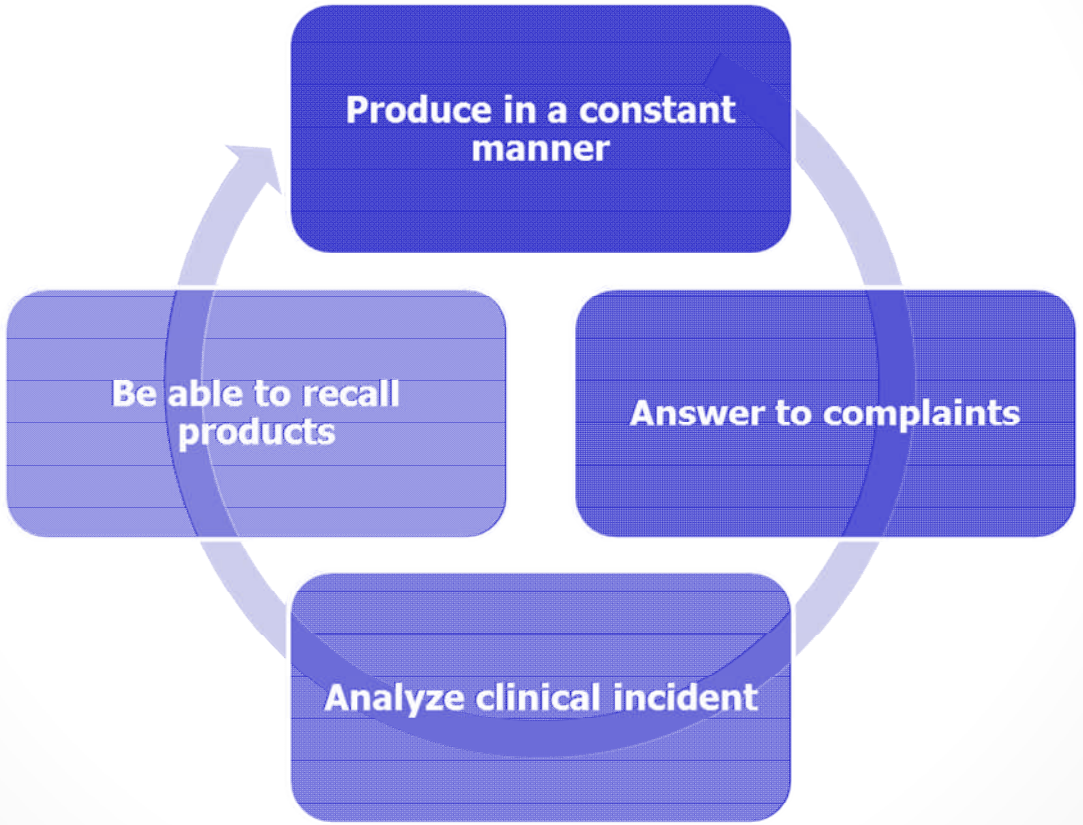


MedTech environment

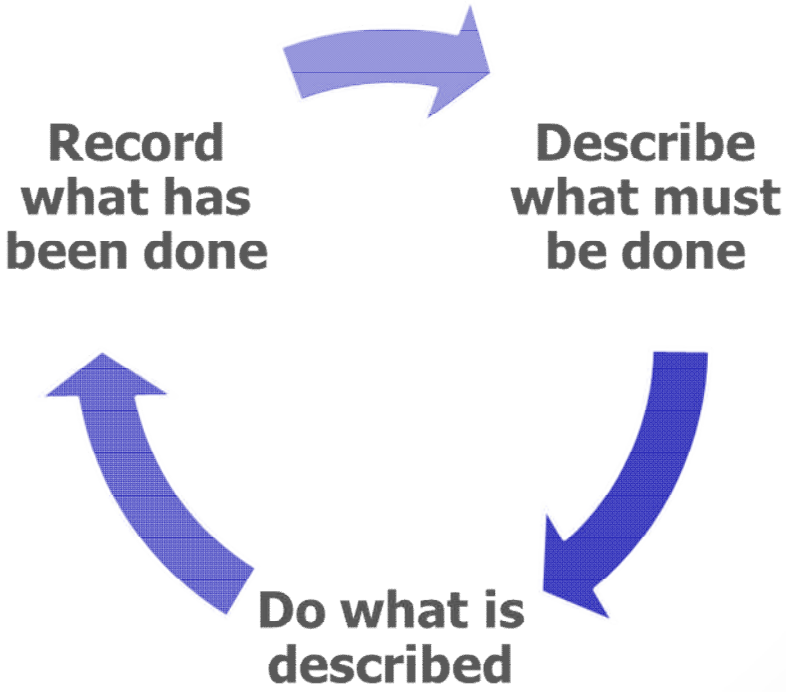
- Legal requirement
- Traceability
- Formalism
- Hygiene
- Cleanliness
- Sterilization
- Products shelf life
- Risk management
- Clinical evaluation
- Market surveillance
- Qualification, validation
- Objective evidences, prove

Safety measures to:

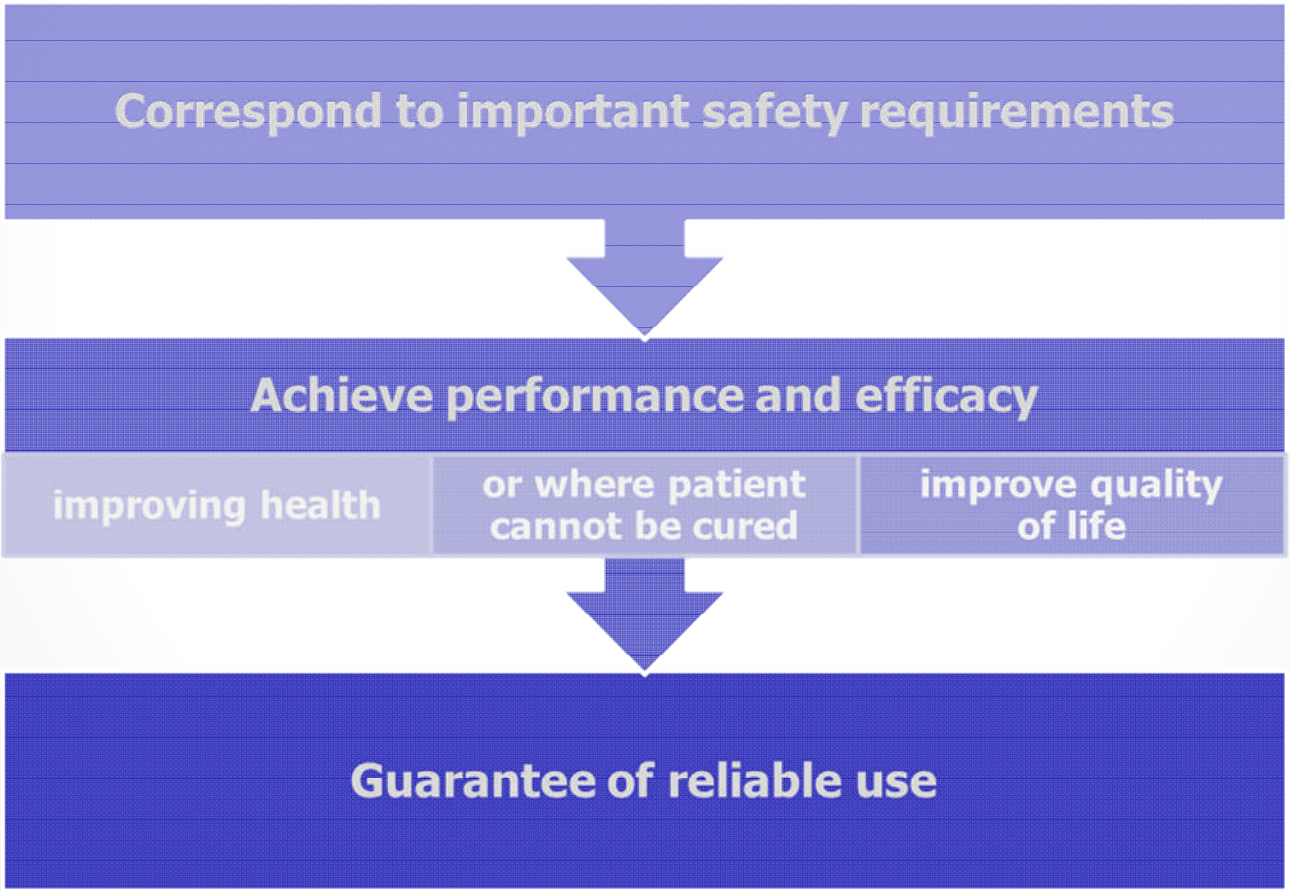
The manufacturer must:



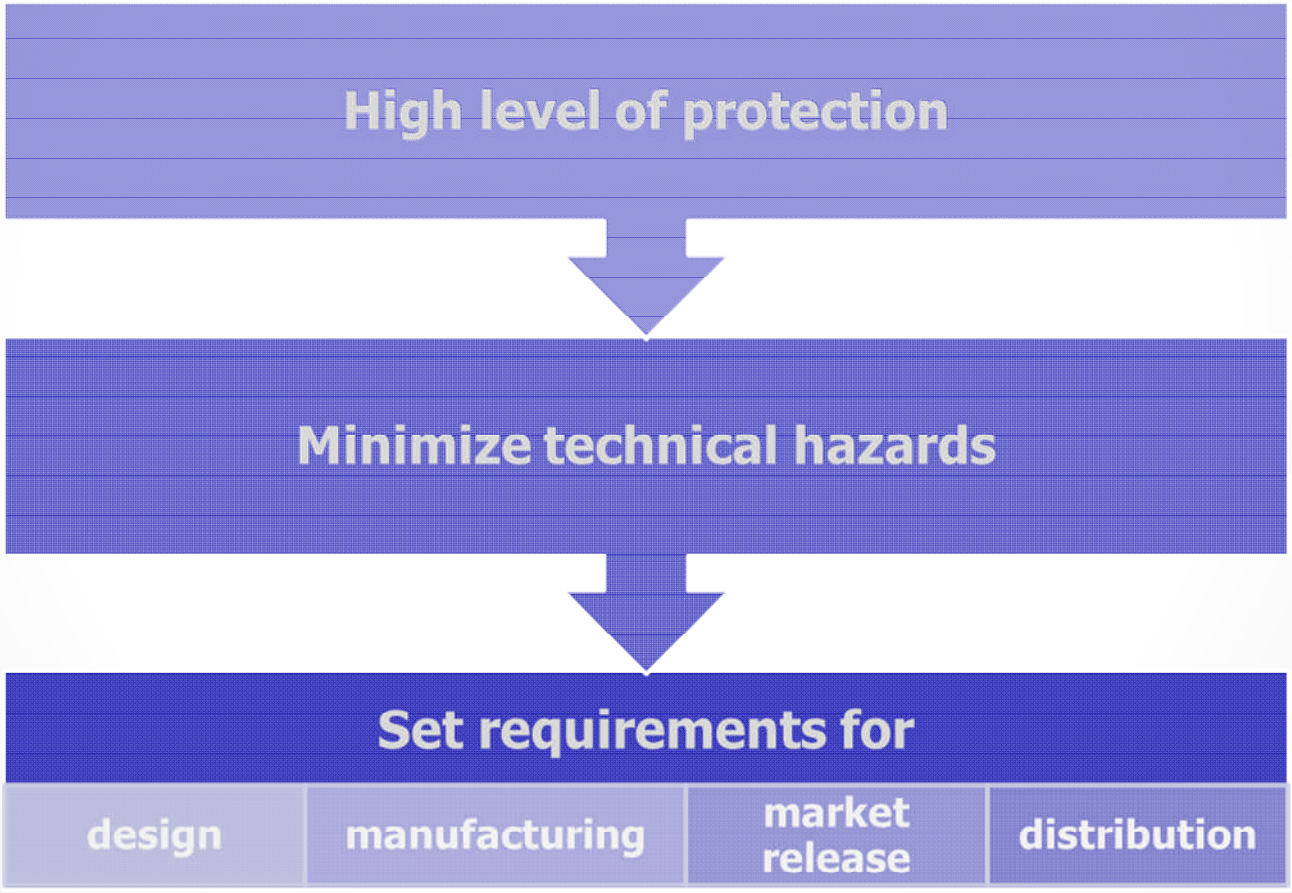
Quality & Regulatory aspects – GMP's basics



For the patients, the users and third parties, the medical devices must:



Therefore, the regulator imposes rules for:



There are several QA systems in common use …

Introduction to ISO 13485, cGMP's and GLP's

- Context
- US approach
- EU approach
- Comparison

Code of Federal Regulations (CFR)

- The Code of Federal Regulations (CFR) is the codification of the general and permanent rules published in the Federal Register by the executive departments and agencies of the Federal Government
- It is divided into 50 titles that represent broad areas subject to Federal regulation
- Each volume of the CFR is updated once each calendar year and is issued on a quarterly basis

USA - Code of Federal Regulations

Multiple regulations covering, for instance:

CFR 7	product recall
CFR 11	e-records and signatures
CFR 801	labeling
CFR 803	medical device reporting
CFR 810	medical device recall
CFR 812	investigational device
CFR 814	premarket approval
CFR 820	quality system regulation
CFR 822	post market surveillance
CFR 860	classification

History	
1963: GMPs for Finished Pharmaceuticals	Current Good Manufacturing Practice in Manufacture, Processing, Packing or Holding. Part 133, 28 FR 6385, 20. June 1963
1970's	Further improvement of product regulation
1975	cGMPs for Blood and Blood Components Final Rule Covering the collection, processing, compatability testing, storage and distribution of blood and blood products
1976: The Medical Device Amendments	Established three regulatory classes for medical devices, based on the degree of control necessary to assure that the various types of devices are safe and effective

History	
1978	GMPs for drugs (21 CFR Parts 210 and 211) and medical devices (21 CFR 820) significantly expanded and finalised
	The aim was to ensure the safety and efficacy of all products
	Described the practices that had to be followed to ensure that drugs met the requirements for safety, strength, identity, quality and purity
	Medical device regulations covered methods, facilities, controls, design, manufacturing, packaging and labelling of all medical devices intended for human use
1979: GLPs 21 CFR Part 58	Good Laboratory Practices
	GLPs define laboratory practices for conducting non-clinical laboratory studies to support applications for research or marketing permits for products regulated by the FDA
	Aim: to ensure the quality and integrity of the safety data submitted to the regulatory authorities

History	
1990: Safe Medical Devices Act	The first important device amendment to the federal Food, Drug, and Cosmetic Act since the Medical Device Amendments of 1976
	Regulates the safety and effectiveness of medical devices and diagnostic products
1997: FDA Modernisation Act	Designed to reform the regulation of medical products, food and cosmetics
	To encourage innovation in manufacturing in order to improve products
1997-1999: further regulations	cGMPs for Medical Devices (quality system regulation) final rule
	Electronic Records Final Rule (21 CFR Part 11)
	QSIT Inspection Handbook: new FDA approach for inspecting device companies

21 CFR Part 58 - Good Laboratory Practice

- FDA promulgated these regulations in response to public concerns that several important studies supporting the safety of FDA-regulated products were seriously flawed due to poor research practices and laboratory misconduct.

- The GLP regulations apply to nonclinical laboratory studies supporting research or marketing applications for FDA-regulated products

21 CFR Part 58 - Good Laboratory Practice

- These regulations set forth the minimum basic requirements for:
  - study conduct – personnel – facilities – equipment - written protocols - operating procedures - study reports - system of quality assurance

- To help assure the safety of FDA-regulated products.

21 CFR Part 58 – GLP - nonclinical laboratory study

- in vivo or in vitro experiment in which a test article is studied prospectively in a test system under laboratory conditions to determine its safety (21 CFR 58.3(d))

- test article is a medical device for human use
- or any other article subject to regulation

- GLP regulations do not apply to human clinical studies

21 CFR Part 58 – GLP - nonclinical laboratory study

- GLP's do not include "basic exploratory studies carried out to determine whether a test article has any potential utility . . . ."
- Basic exploratory studies carried out to determine whether a device has any potential utility, or to determine physical or chemical characteristics of a device, are not subject to the GLP regulations (21 CFR 58.3(d))
- However, the design and implementation of such studies should be based on good science, and data collection should be such that the integrity and quality of the study remain robust.

The Applicability of Good Laboratory Practice in Premarket Device Submissions: Questions & Answers

---

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.
Document issued on: August 28, 2013

Introduction to ISO 13485, cGMP's and GLP's

- Context
- US approach
- EU approach
- Comparison

Major legislation - Europe

- Contents of European Directives
- List of Essential Requirements of those directives
- CE mark
- ISO 13485
- Harmonized technical standards

Rather a system approach

Standards history - Europe

EN 46001/2

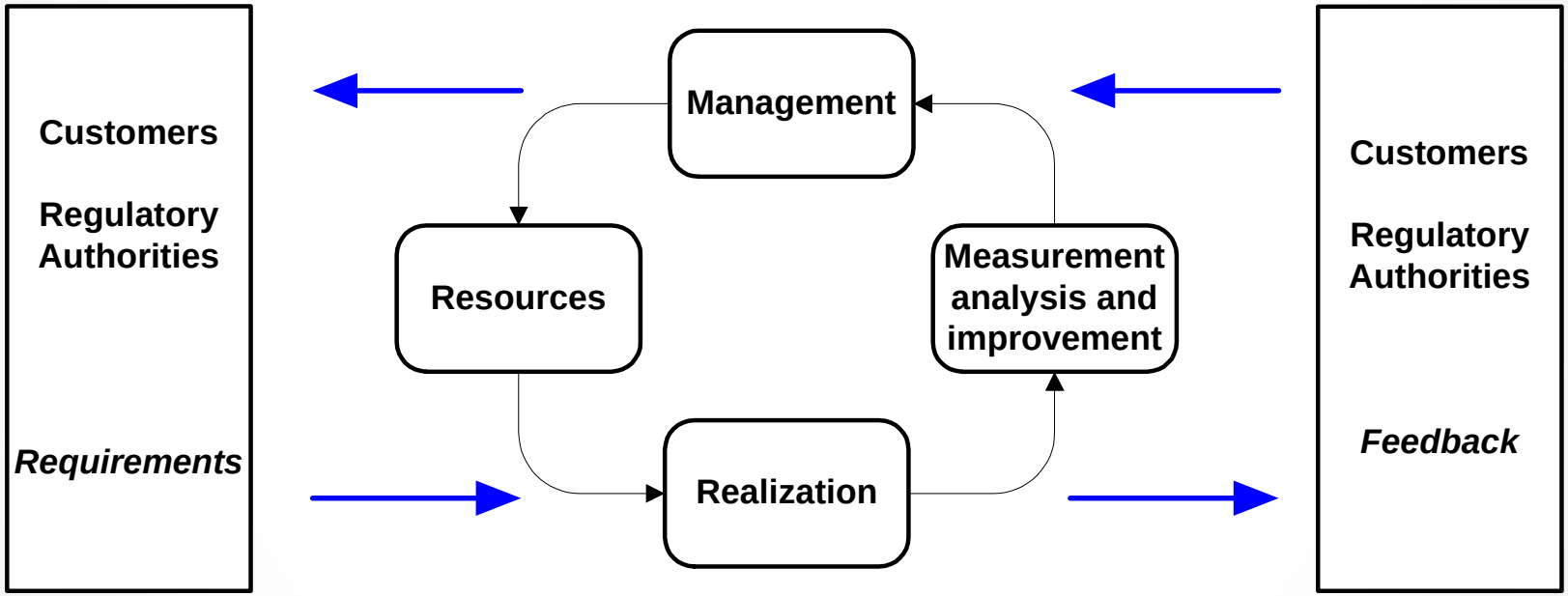
ISO 13485/8

ISO 13485 : 2003

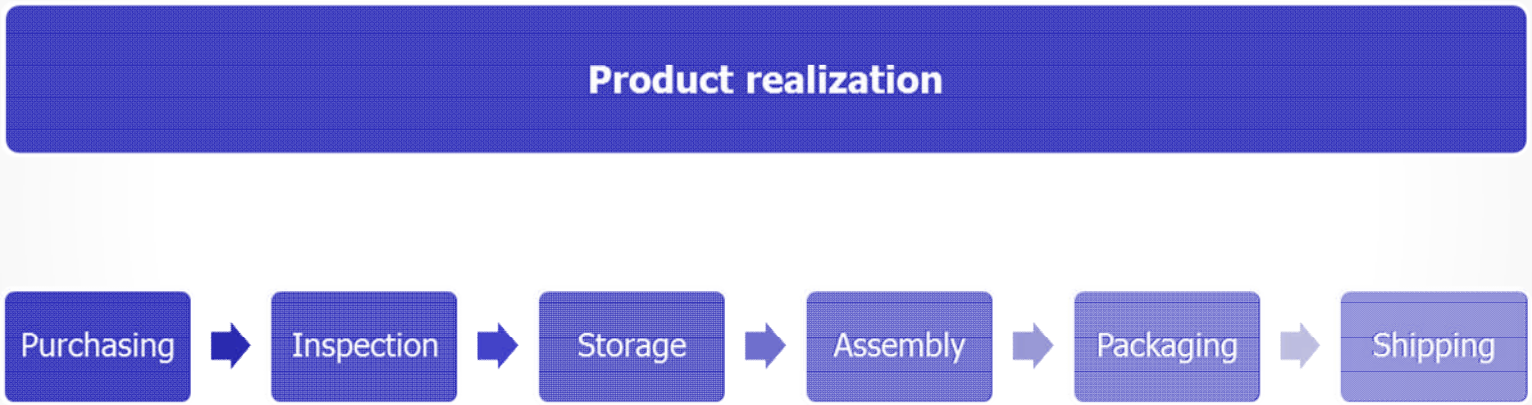
EN ISO 13485 : 2012

EN ISO 13485 : 20xx

Process-based quality management system - ISO 13485



Good Manufacturing Practices apply mainly to the product realization process



Introduction to ISO 13485, cGMP's and GLP's

- Context
- US approach
- EU approach
- Comparison

Europe and USA

- ✓ Two similar approaches, with different origins:
  - focused on « product », in the USA
  - focused on « system », in Europe
- ✓ Serve as models for the rest of the world
- ✓ The European system is younger than the American one
- ✓ Systems tend to merge with time

USA – Food and Drug Administration

QUALITY SYSTEM REGULATION

21 CFR Part 820

Medical Devices;

current Good Manufacturing Practice

Historically a product approach

Effective June 1, 1997,
replacing the 1978 GMP for medical devices

The Development of GMPs

- In the past GMPs have often been developed as a reaction to tragedy
- Public outrage following tragedies result in new laws and regulations, to try to prevent similar events in the future
- Current initiatives are more proactive than reactive
- Nevertheless tragedies may still occurring

Summary

- Standards have improved steadily as drug manufacturing, testing and marketing have become more regulated
- Regulations have become more complex and are often restrictive
- Harmonisation between different regulatory authorities is required for global products

End of part
4. Intro to ISO – GMP – GLP

Followed by part 5 Conformity Assessment Europe