Quality and Risk Management in a Tissue Bank

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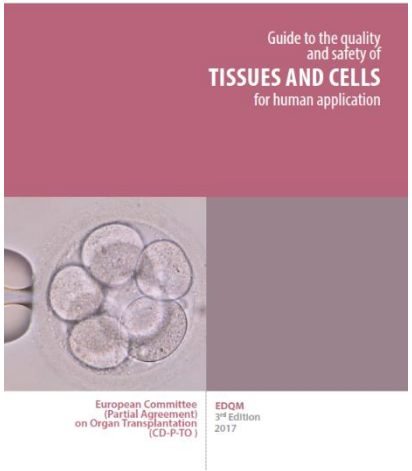
Barcelona Tissue Bank
Banc de Sang i Teixits



Chapter 2

QM is achieved through compliance with the requirements at four levels:

- **Legal framework** provides overall context in which activities for T&C are performed
- **QMS** to ensure that T&C are consistently comply with technical and legal requirements
- **Technical requirements specific to each type of tissues:** ensure Q&S&E
- **Authorisations** in place for specific activities from specific competent authorities

A systematic approach to QM must be implemented and maintained during the whole process:

- Personnel and organization
- Premises
- Equipment & materials
- Outsourced activities managmente (contractual agreements
- Documentation
- Quality control
- Quarantine & release
- Qualification & validation
- Traceability
- Complaints
- Investigation and reporting
- Recall
- Self-assessment
- Quality Risk Management
- Fiscal & continuity planning
- Tools for continuous quality improvement

HISTORY OF A MEDICINAL PRODUCT

INVESTIGATION

1 - 2 years

Research of chemical starting points

- Conception
- Synthesis
- Screening

1 - 2 years

Optimization

- Power
- Selectivity
- Oral absorption
- Duration

DEVELOPMENT

1 - 2 years

Preclinical evaluation in vitro and with animals

- Activity
- Security
- Stability

6 - 8 years

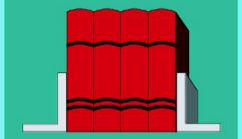
Clinical evaluation in men

Phase I	Phase II	Phase III
Tolerance and pharma-cokinetics	• Biological activity • Optimal dose	Confirmation of therapeutic effect and tolerance

CREATION

1 years

Presentation of the medication registration dossier



PRODUCTION

LIFE

Permanent

Commercia-lization

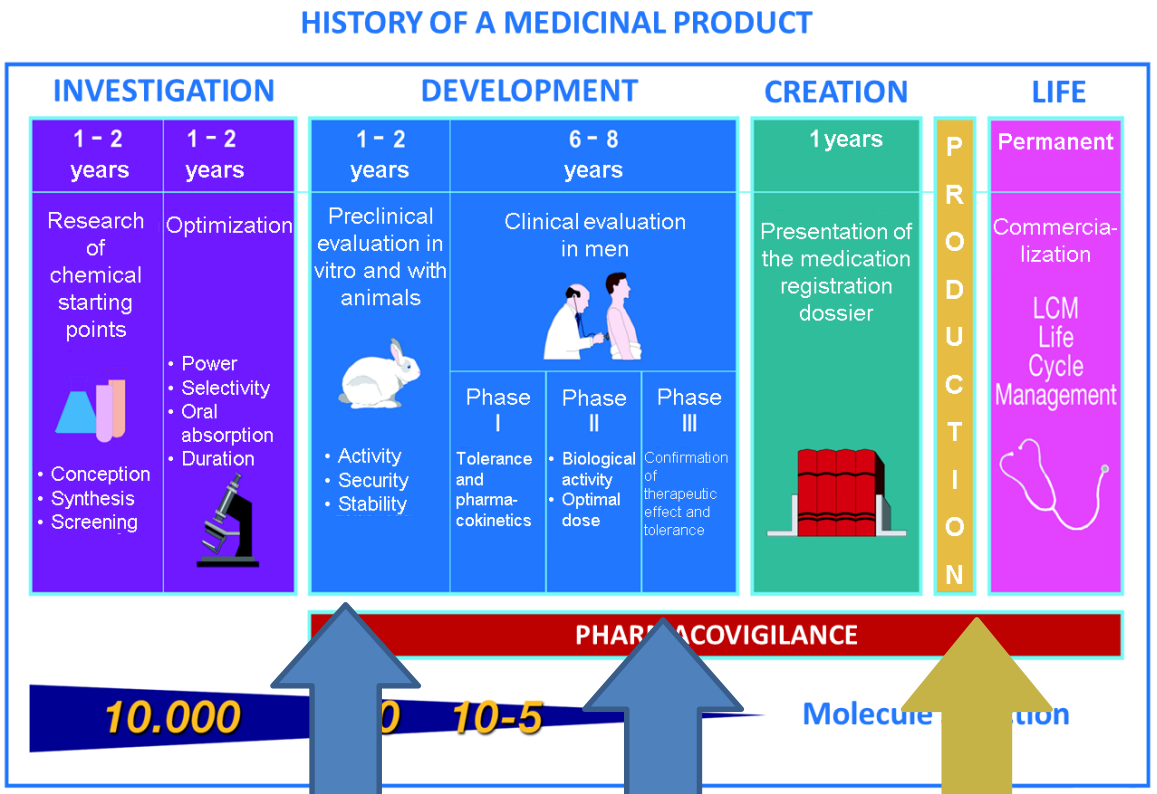
LCM Life Cycle Management

PHARMACOVIGILANCE

10.000 → 50 → 10-5 → 1 **Molecule Selection**

DONOR

Consent
Selection and evaluation
Procurement
Traceability
…



Directive 2004/23/EC
Good Tissue Practices I

Directive 2004/10/EC
Good Laboratory Practices
Good Tissue Practices II

Directive 2001/20/EC
Good Clinical Practices
Good Tissue Practices II

Directive 2001/83/EC
Good Manufacturing Practices
Good Tissue Practices I

Good Tissue Practices I

Directive 2004/23/EC

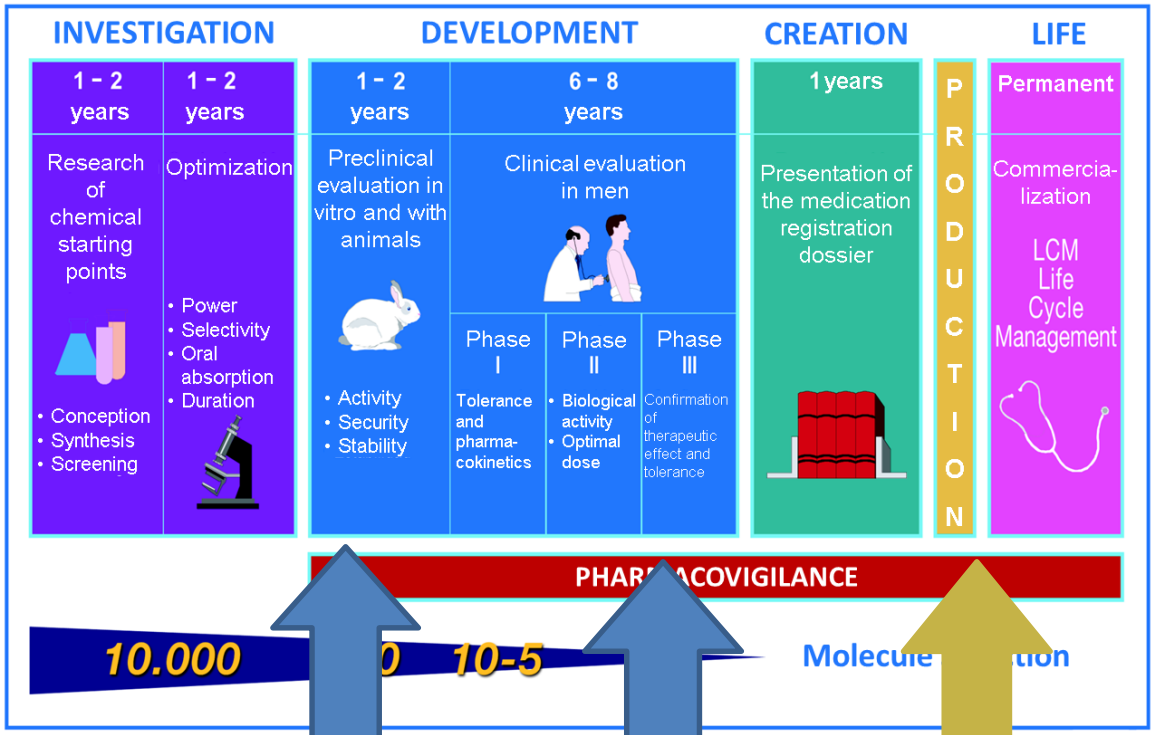
It shall apply to the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells intended for application in humans, as well as processed products derived from human tissues and cells intended for Its application in humans.

When these processed products are regulated by other Directives, this Directive shall only apply to donation, procurement and evaluation.

A.1. PERSONNEL
A.2. FACILITIES AND EQUIPMENT
A.3. DONOR SCREENING
A.4. RECOVERY
A.5. PROCESSING
A.6. STORAGE AND DISTRIBUTION
A.7. QUALITY MANAGEMENT
A.8. BIOVIGILANCE

Consent
Selection and evaluation
Obtaining
Traceability
…

HISTORY OF A MEDICINAL PRODUCT



Directive 2004/23/EC
Good Tissue Practices I

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Directive 2001/83/EC
Good Manufacturing Practices
Good Tissue Practices I

Good Tissue Practices II

Good Practices directed to Tissue and Cell Banks and Organizations Responsible for Clinical Application, which establish methodologies to determine what studies are necessary and therefore, what safety and efficacy data is necessary to provide before such application, so that this is safe and effective.

A.1. EVALUATION OF THE NOVELTY
A.2. RISK ASSESSMENT
A.3. DETERMINATION OF THE SCOPE OF STUDIES

Good Laboratory Practices

Directive 2004/10/EC

The principles of Good Laboratory Practices (GLP) are used to perform tests aimed at obtaining data on the properties and danger to people, animals and the environment of any chemical substance.

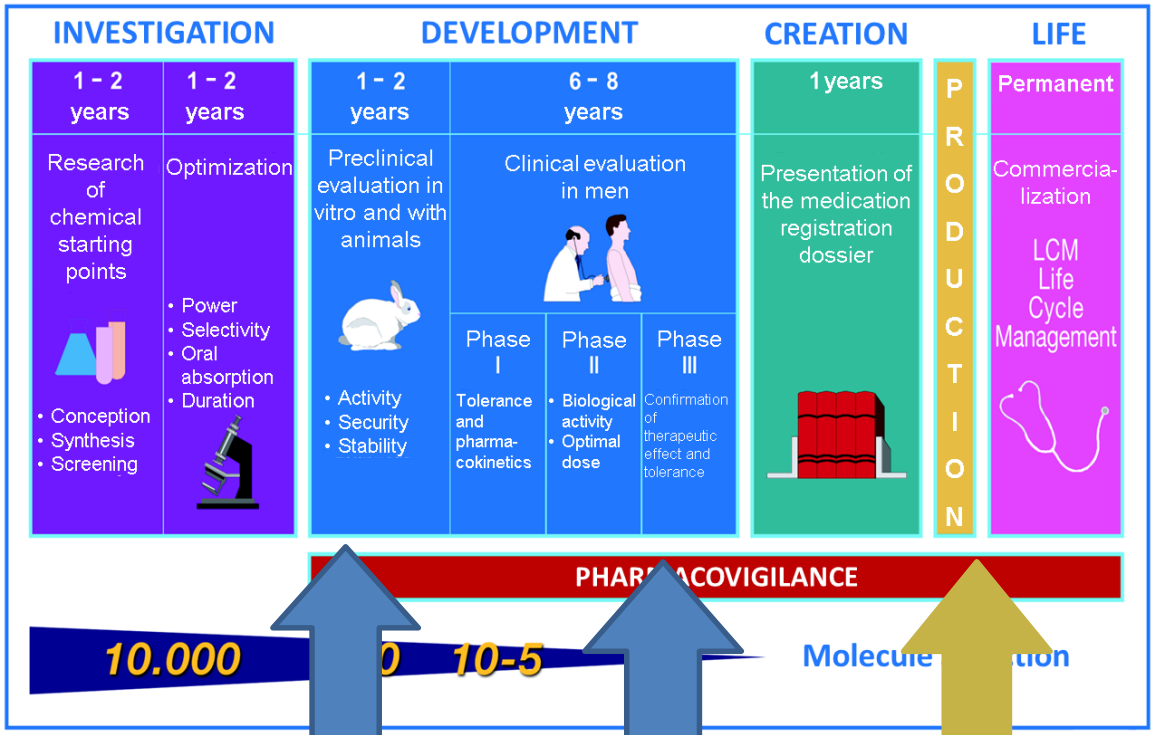
These are non-clinical trials of health and environmental safety carried out, therefore, for regulatory purposes.

The GLPs provide recommended guidelines for the management of these trials and represent a quality system related to the organizational processes and the conditions under which the trials are planned, performed, controlled, recorded, archived and informed, to ensure the quality and validity of data obtained.

1. STAFF
2. QUALITY GUARANTEE PROGRAM
3. FACILITIES
4. EQUIPMENT, MATERIALS AND REAGENTS
5. TEST SYSTEMS
6. TEST SAMPLES
7. SOP
8. REALIZATION OF THE STUDY
9. RESULT REPORTS
10. STORAGE OF RECORDS AND MATERIALS

Consent
Selection and evaluation
Obtaining
Traceability
…

HISTORY OF A MEDICINAL PRODUCT



Directive 2004/23/EC
Good Tissue Practices I

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Good Clinical Practices
Good Tissue Practices II

Directive 2001/83/EC
Good Manufacturing Practices
Good Tissue Practices I

Good Clinical Practices

Directive 2001/20/EC

The Good Clinical Practice Guide (GCP) is an international standard of ethical and scientific quality applicable to the design, conduct, registration and communication of clinical trials in which human beings participate. Compliance with this standard provides a public guarantee of the protection of the rights, safety and well-being of the subjects of the trial in accordance with the principles of the Helsinki Declaration, as well as guarantee the credibility of the clinical trial data.

2. PRINCIPLES OF GCP

2.13. Systems with procedures that ensure the quality of each aspect of the trial will be implemented.

3. ETHICAL CLINICAL RESEARCH COMMITTEE

4. RESEARCHER

5. PROMOTER

6. CLINICAL TRIAL AND MODIFICATIONS PROTOCOL

7. RESEARCHER'S MANUAL

8. ESSENTIAL DOCUMENTS FOR THE PERFORMANCE OF A CLINICAL TRIAL

Consent
Selection and evaluation
Obtaining
Traceability
…

HISTORY OF A MEDICINAL PRODUCT

INVESTIGATION		DEVELOPMENT			NACIMIENTO		LIFE
1 - 2 years	1 - 2 years	1 - 2 years	6 - 8 years		1 years	PRODUCTION	Permanent
Research of chemical starting points • Conception • Synthesis • Screening	Optimization • Power • Selectivity • Oral absorption • Duration	Preclinical evaluation in vitro and with animals • Activity • Security • Stability	Clinical evaluation in men FASE I: Tolerance and pharma-cokinetics FASE II: • Biological activity • Optimal dose FASE III: Confirmation of therapeutic effect and tolerance		Presentation of the medication registration dossier		Commercia-lization LCM Life Cycle Management

PHARMACOVIGILANCE

10.000 … 10-5 … Molecule …

Directive 2004/23/EC
Good Tissue Practices I

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Good Manufacturing Practices
Good Tissue Practices I

Good Manufacturing Practices

Directive 2001/83/EC

These are strict compliance standards for drug manufacturers.
GMP are defined as the part of the quality assurance that ensures that medicines are made and controlled according to the appropriate quality standards for the intended use, controlling all the variables that may affect the final quality of the medicine.

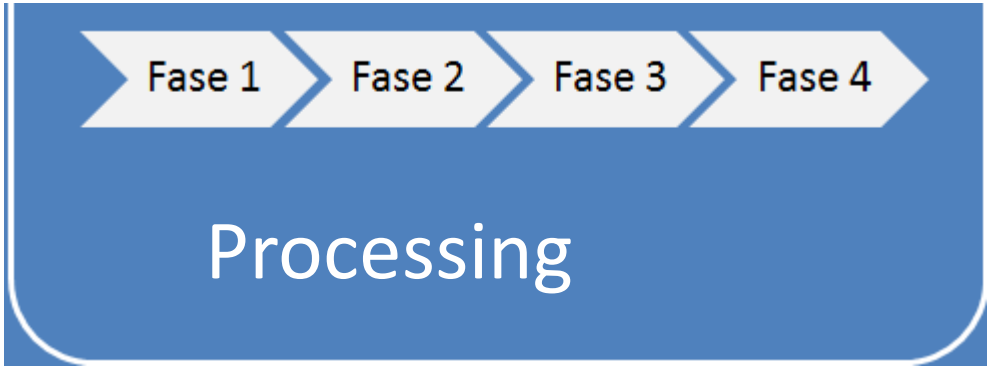
Part I. Basic requirements Medications
Chapter 1. Quality Management
Chapter 2. Staff
Chapter 3. Premises and equipment
Chapter 4. Documentation
Chapter 5. Production
Chapter 6. Quality Control
Chapter 7. Manufacturing and analysis by contract
Chapter 8. Claims and withdrawals
Chapter 9. Self-inspections

Annex 1. Manufacture of sterile medicines
Annex 2. Manufacture of biological medicines for human use.
Annex 13. Manufacture of investigational drugs
Annex 15. Qualification and validation.
Annex 16. Certification by a qualified person and batch release.
Annex 19. Reference samples and retention samples.
Annex 20. Quality risk management

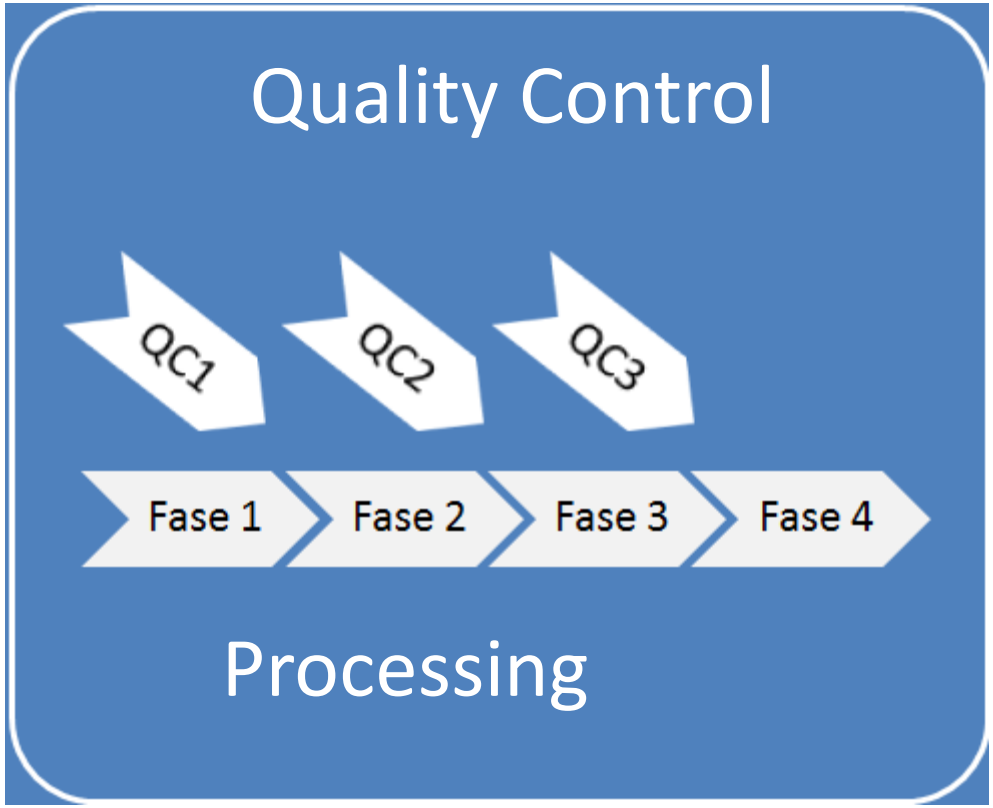
Qualipedia

QUALITY	**COMPLY WITH THE SPECIFICATIONS PREVIOUSLY ESTABLISHED AND REQUIRED (by customers, regulations, medication registration, etc.)**
QUALITY CONTROL	**SET OF ACTIVITIES (sampling and analysis) ESTABLISHED TO ENSURE ADEQUATE QUALITY OF PRODUCED PRODUCTS (composition, physical characteristics)**
QUALITY GUARANTEE	**SET OF ACTIVITIES ESTABLISHED TO ENSURE THAT THE QUALITY CONTROL PROGRAM IS EFFECTIVE (personnel, equipment, facilities, document system, etc.)**

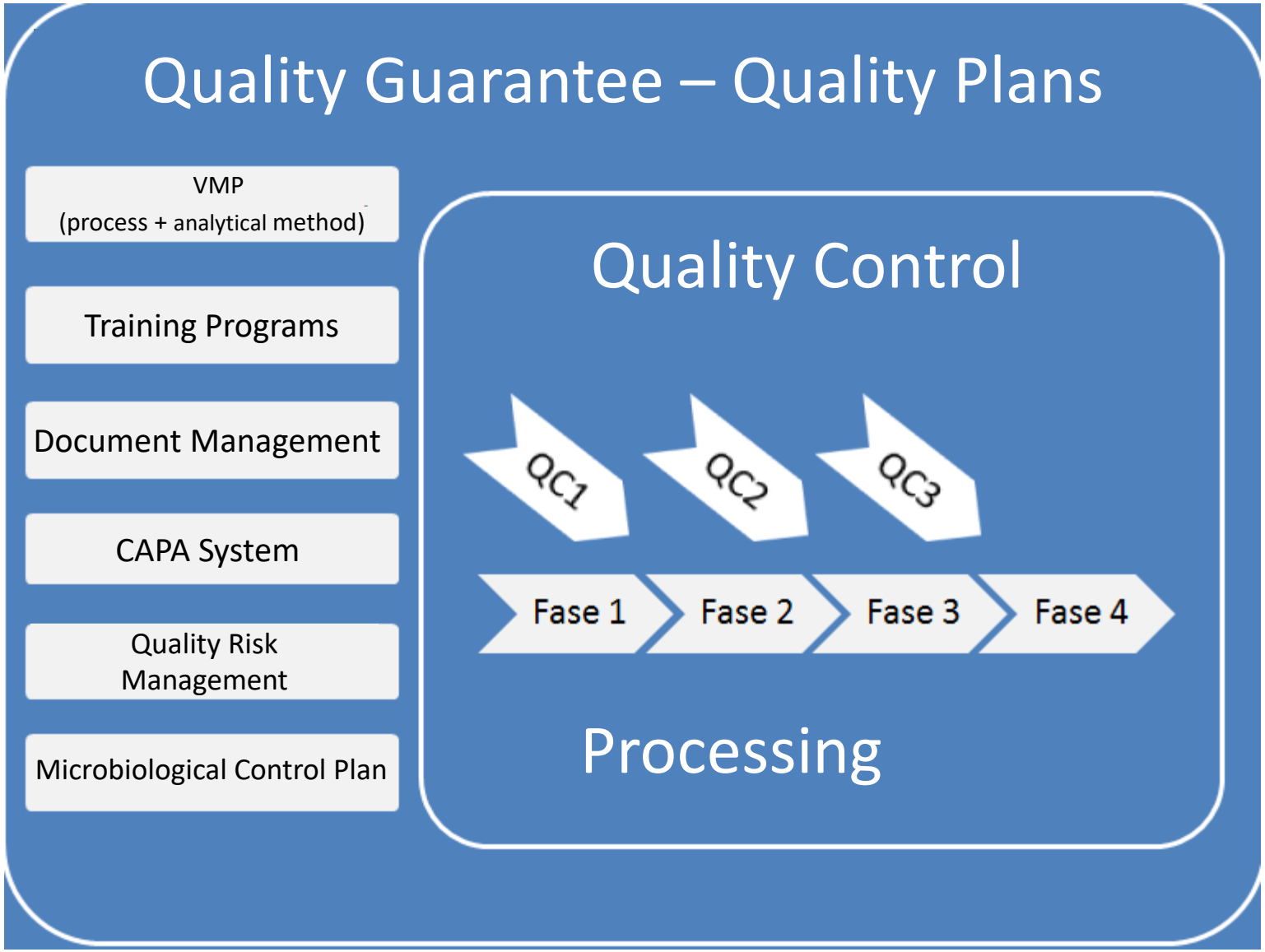
Quality-Control Quality-Quality Guarantee



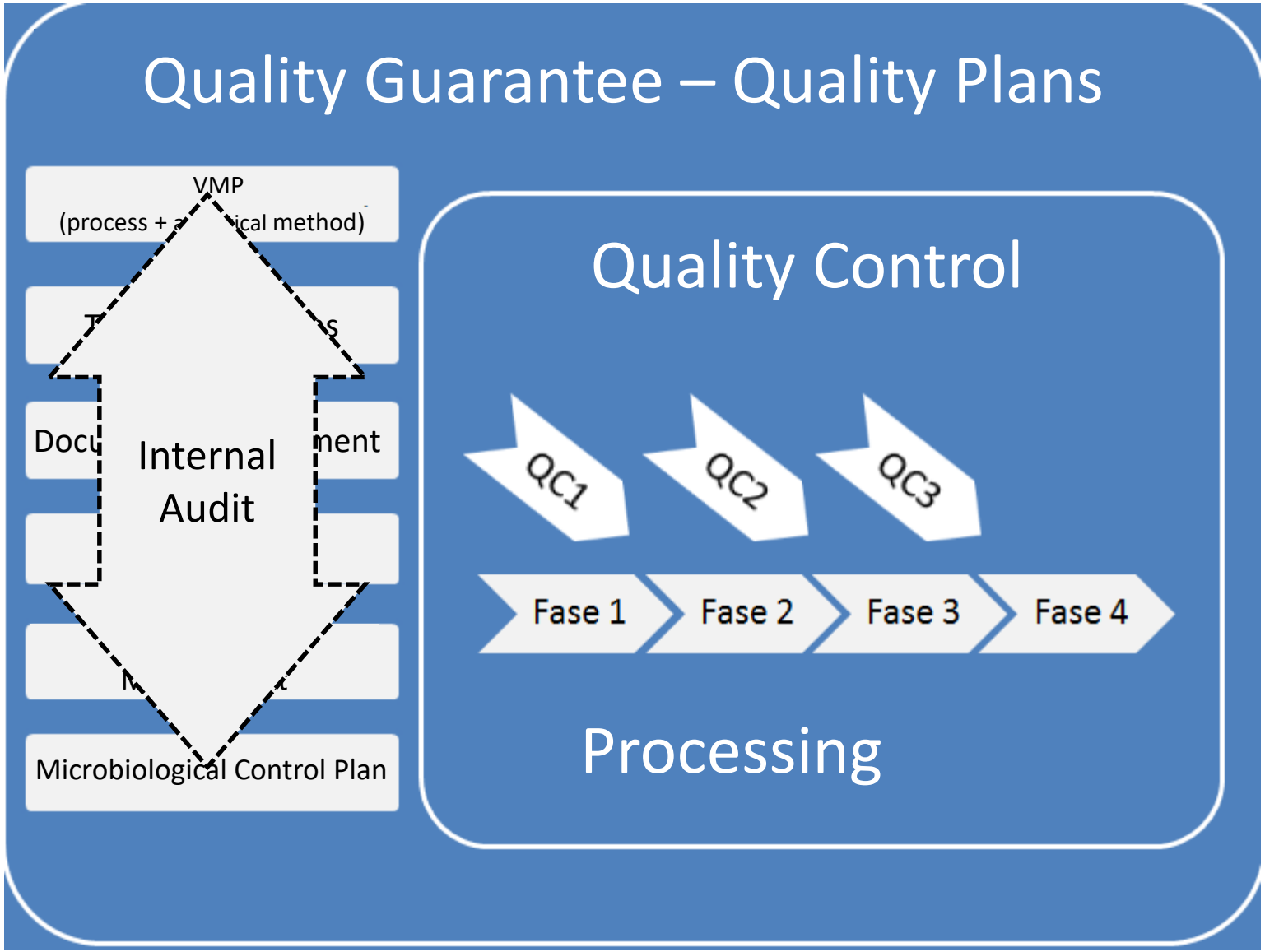
Quality-Control Quality-Quality Guarantee



Quality-Control Quality-Quality Guarantee



Quality-Control Quality-Quality Guarantee



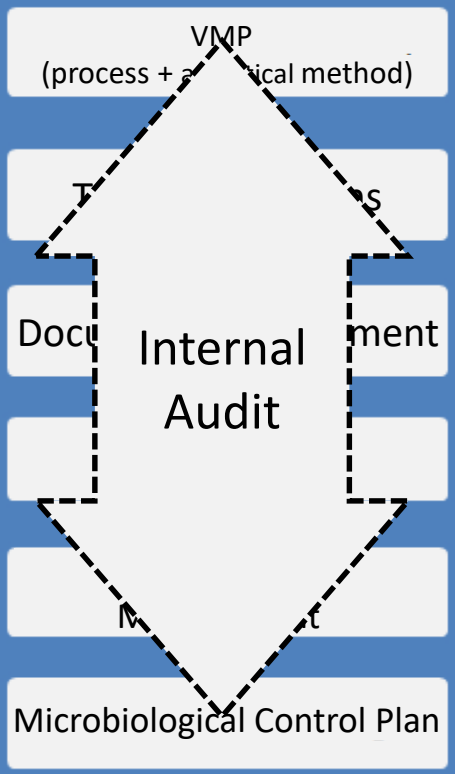
Inspection

AEMPS

OCATT

CLIENTS

Quality Guarantee – Quality Plans



Quality Control

QC1 QC2 QC3

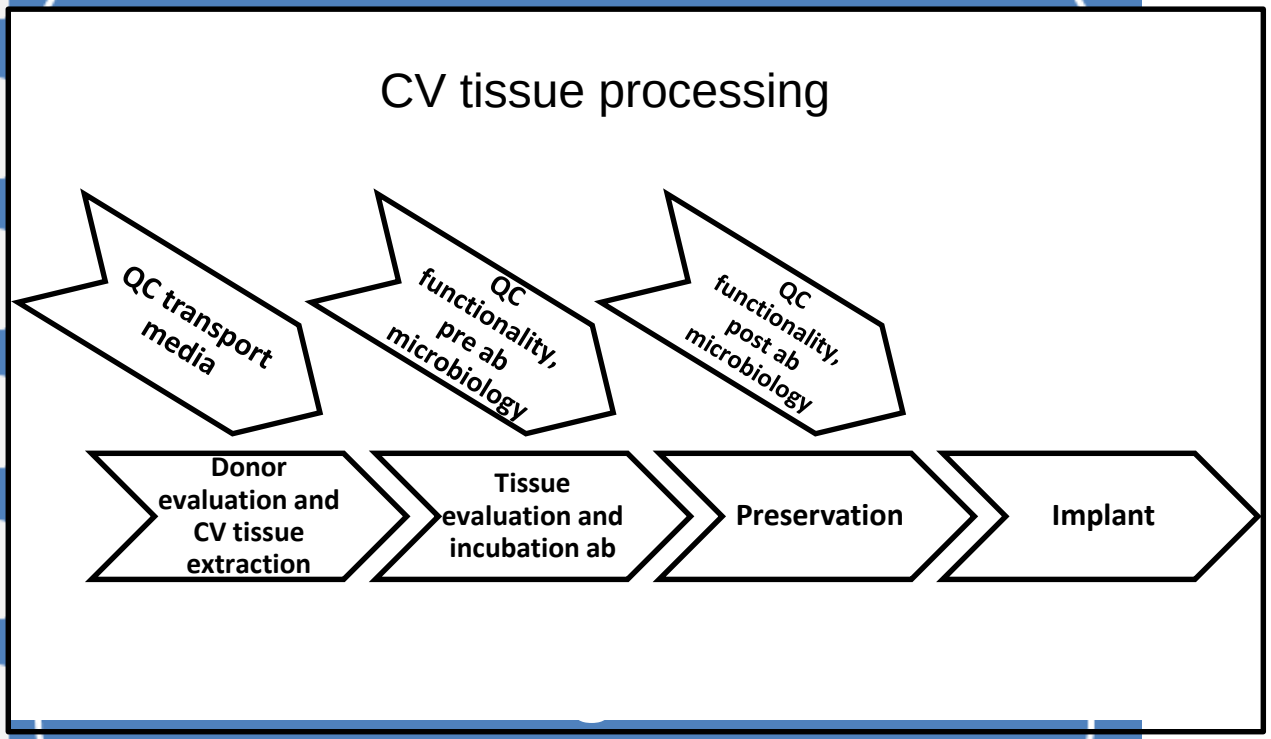
Fase 1 Fase 2 Fase 3 Fase 4

Processing

Quality-Control Quality-Quality Guarantee

Quality Guarantee – Quality Plans

- VMP (process + analytical method)
- Training Programs
- Document Management
- CAPA System
- Quality Risk Management
- Microbiological Control Plan



Quality-Control Quality-Quality Guarantee

Quality Guarantee – Quality Plans

VMP

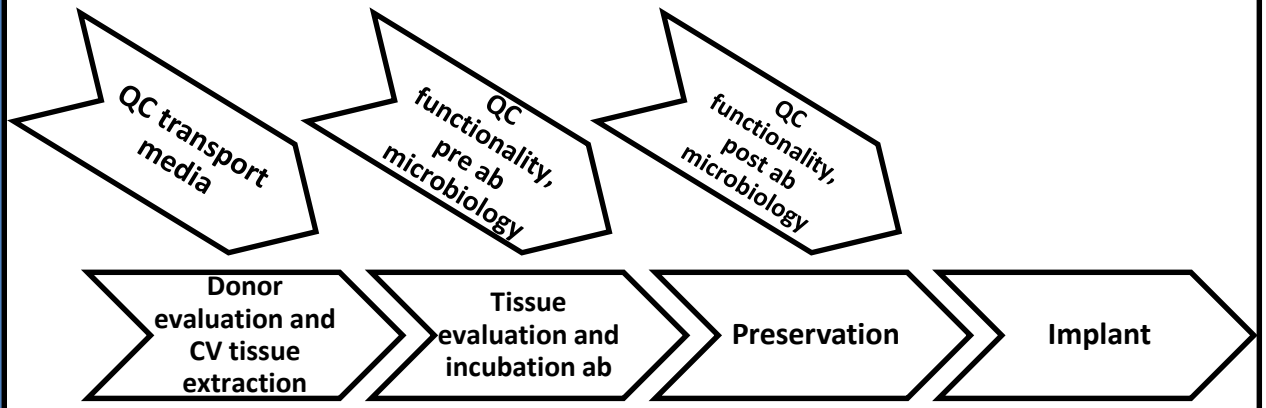
(process + … cal method)

Docu… …nt

Internal Audit

Microbiological Control Plan

CV tissue processing



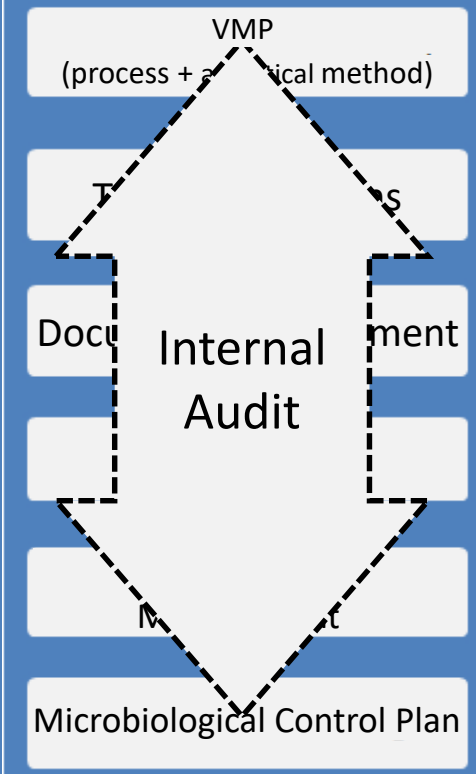
Inspection

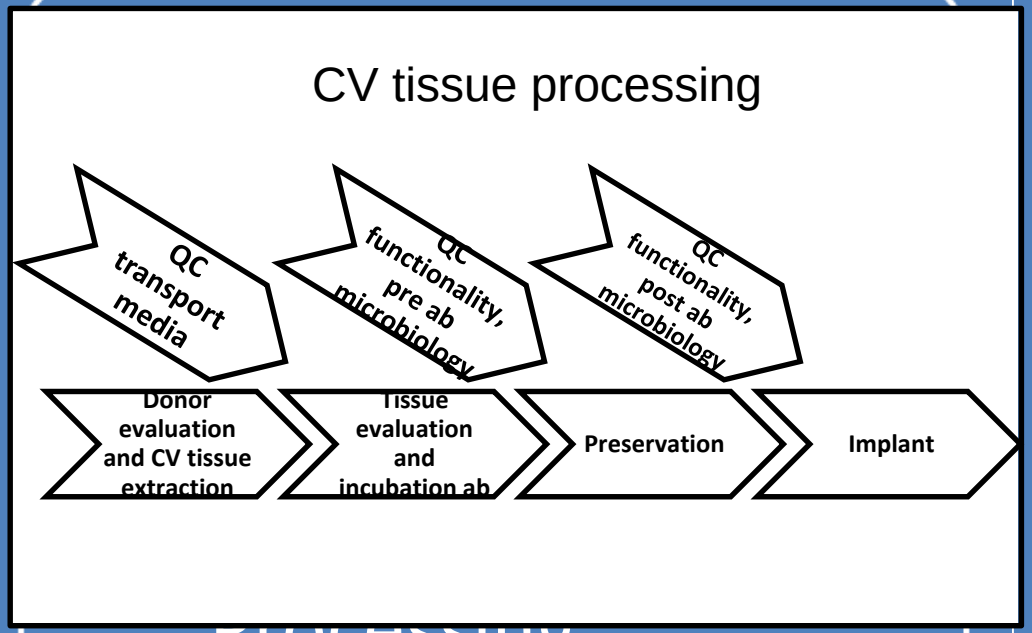
AEMPS

OCATT

CLIENTES

Quality Guarantee – Quality Plans



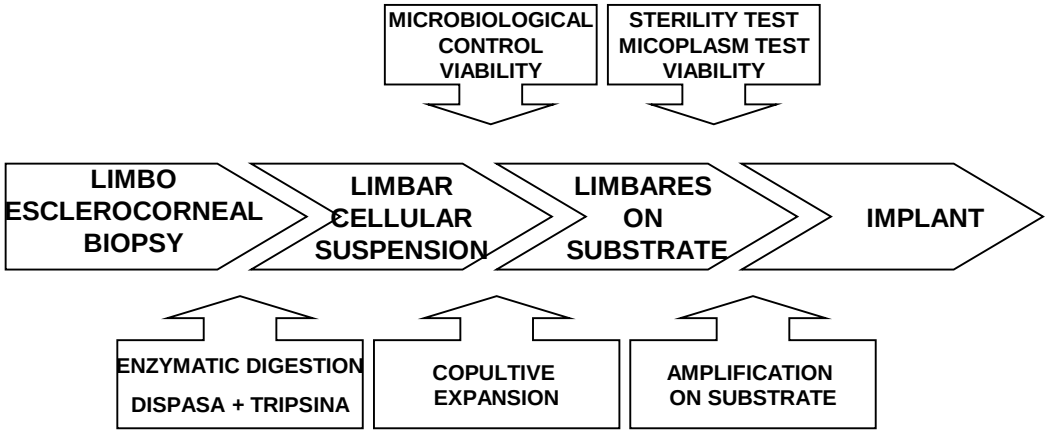


Quality-Control Quality-Quality Guarantee

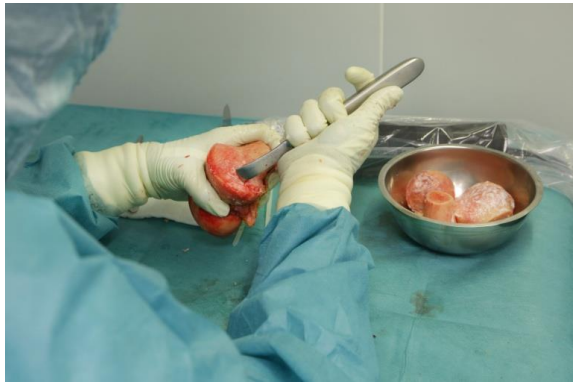
Quality Guarantee – Quality Plans

- VMP (process + analytical method)
- Training Programs
- Document Management
- CAPA System
- Quality Risk Management
- Microbiological Control Plan

Autologous progenitor cells of the sclerocorneal limbus for ocular surface repair



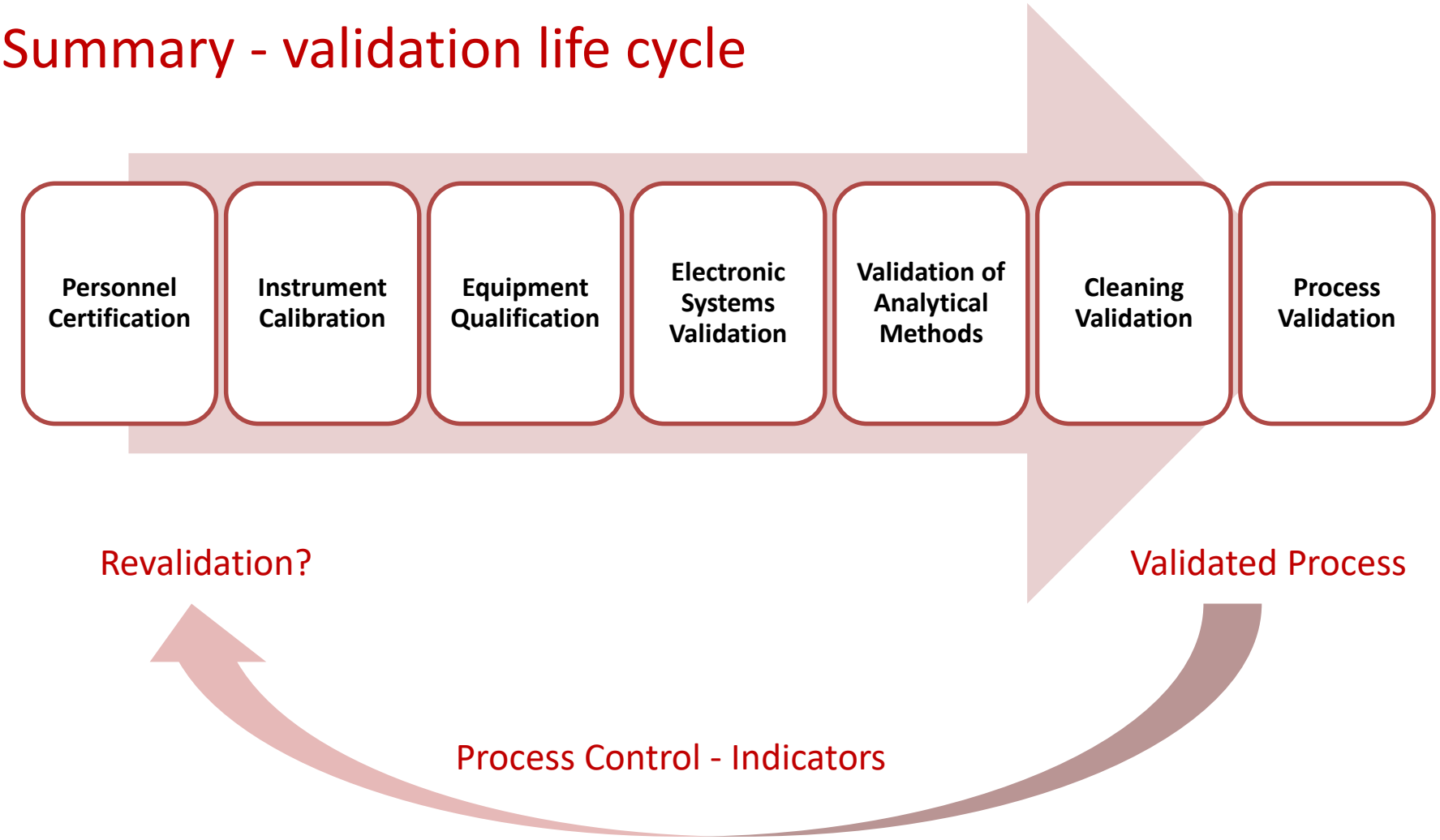
Quality-Control Quality-**Quality Guarantee**



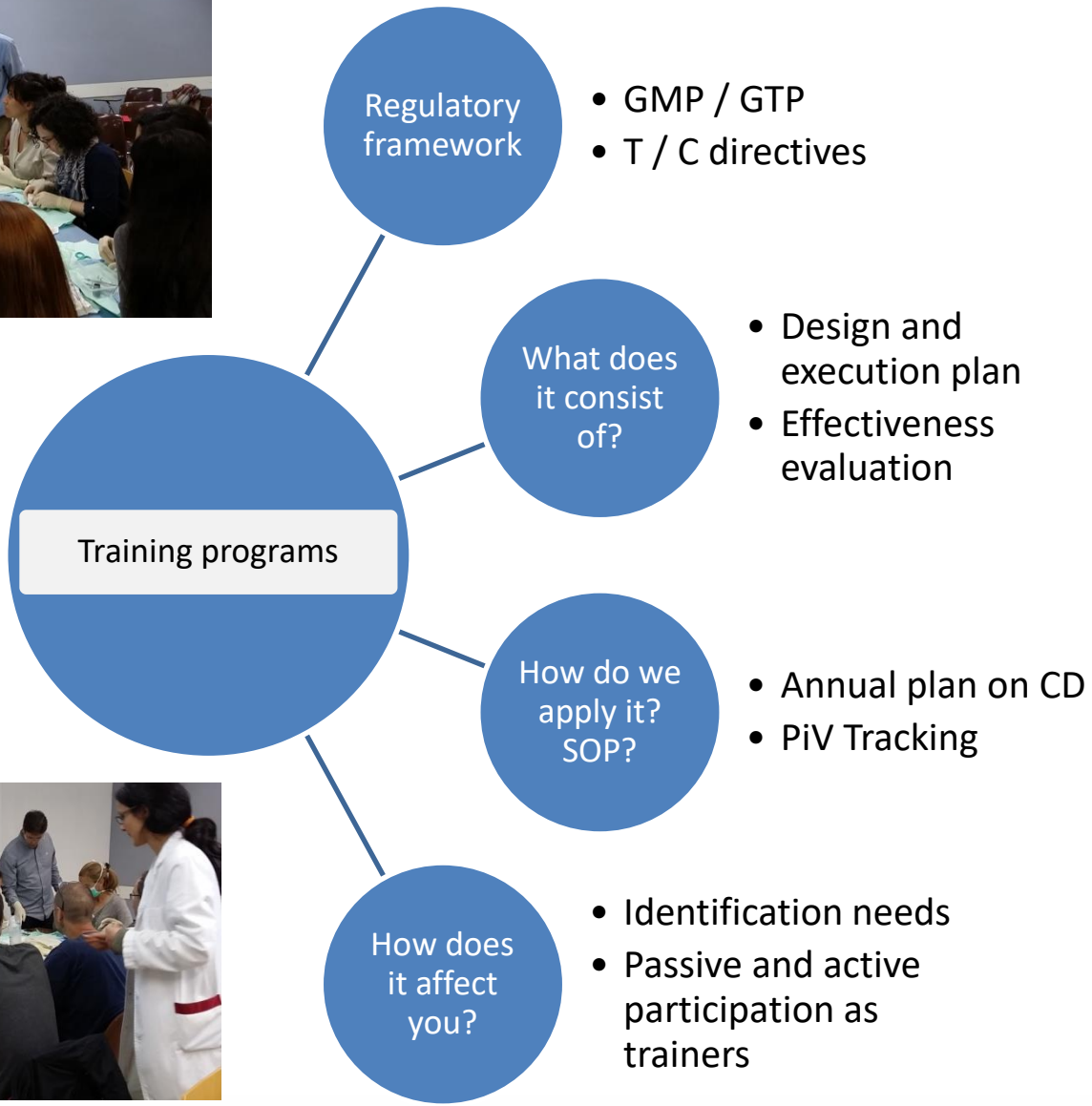
VMP
(process + analytical method)

- Regulatory Framework
  - GMP/GTP
  - Directives T/C
- What does it consist of?
  - Risk analysis
  - Test planning
- How do we apply it? PNT?
  - PMV intern
  - Central quality
- How does it affect you?
  - Identification of critical attributes and parameters
  - Respect for validated procedures

Summary - validation life cycle



Quality-Control Quality-**Quality Guarantee**

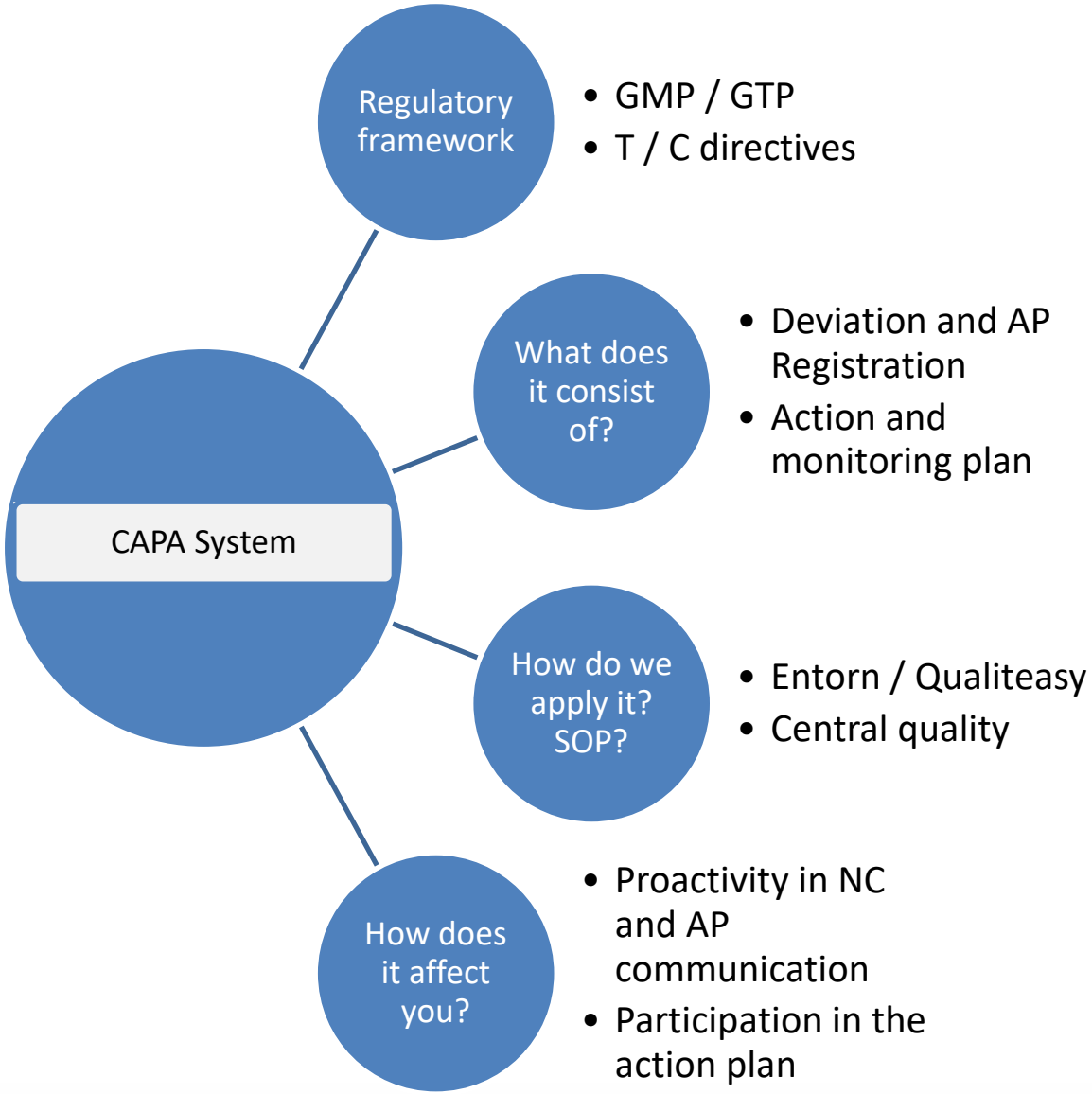


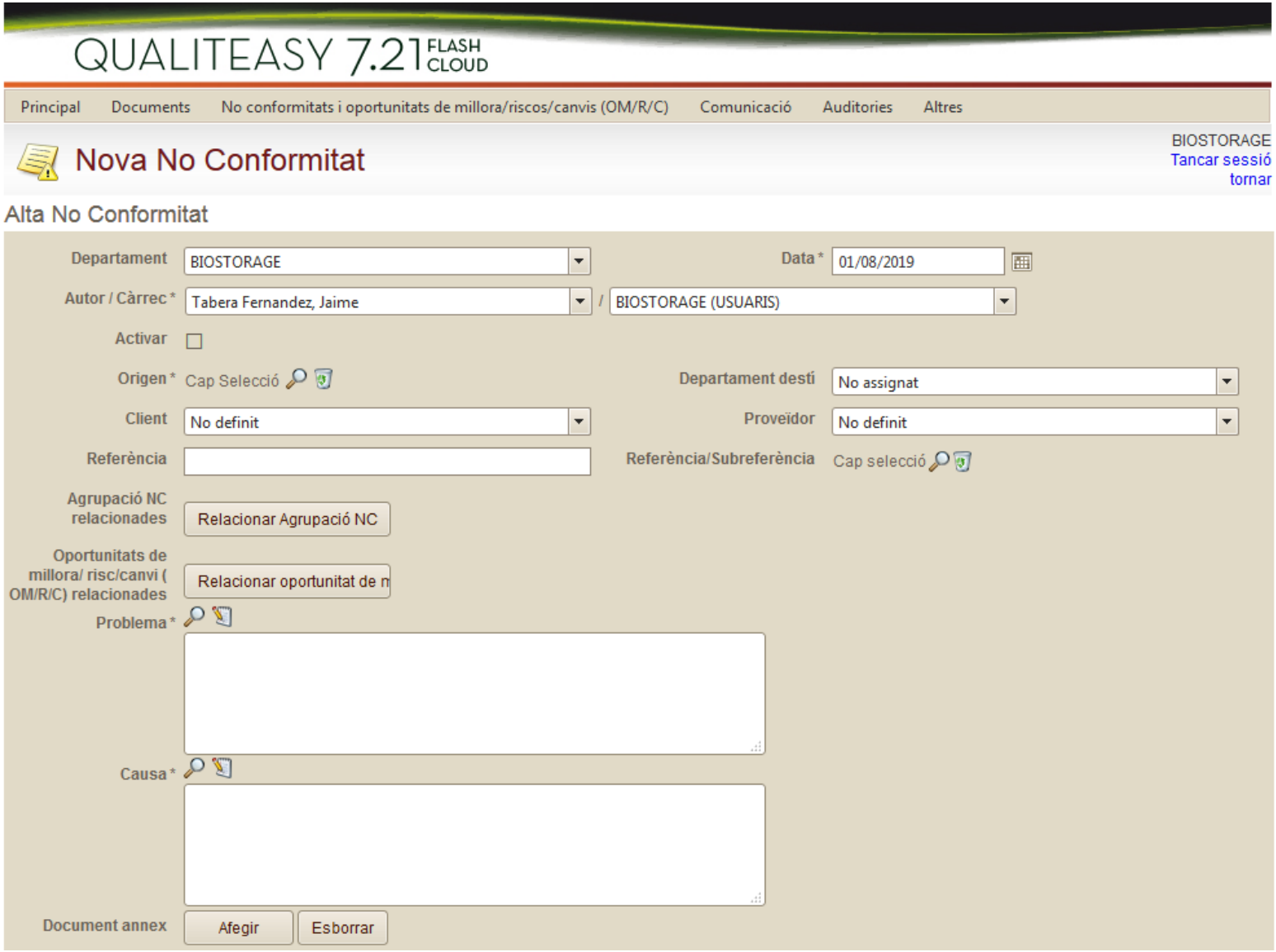
Quality-Control Quality-**Quality Guarantee**

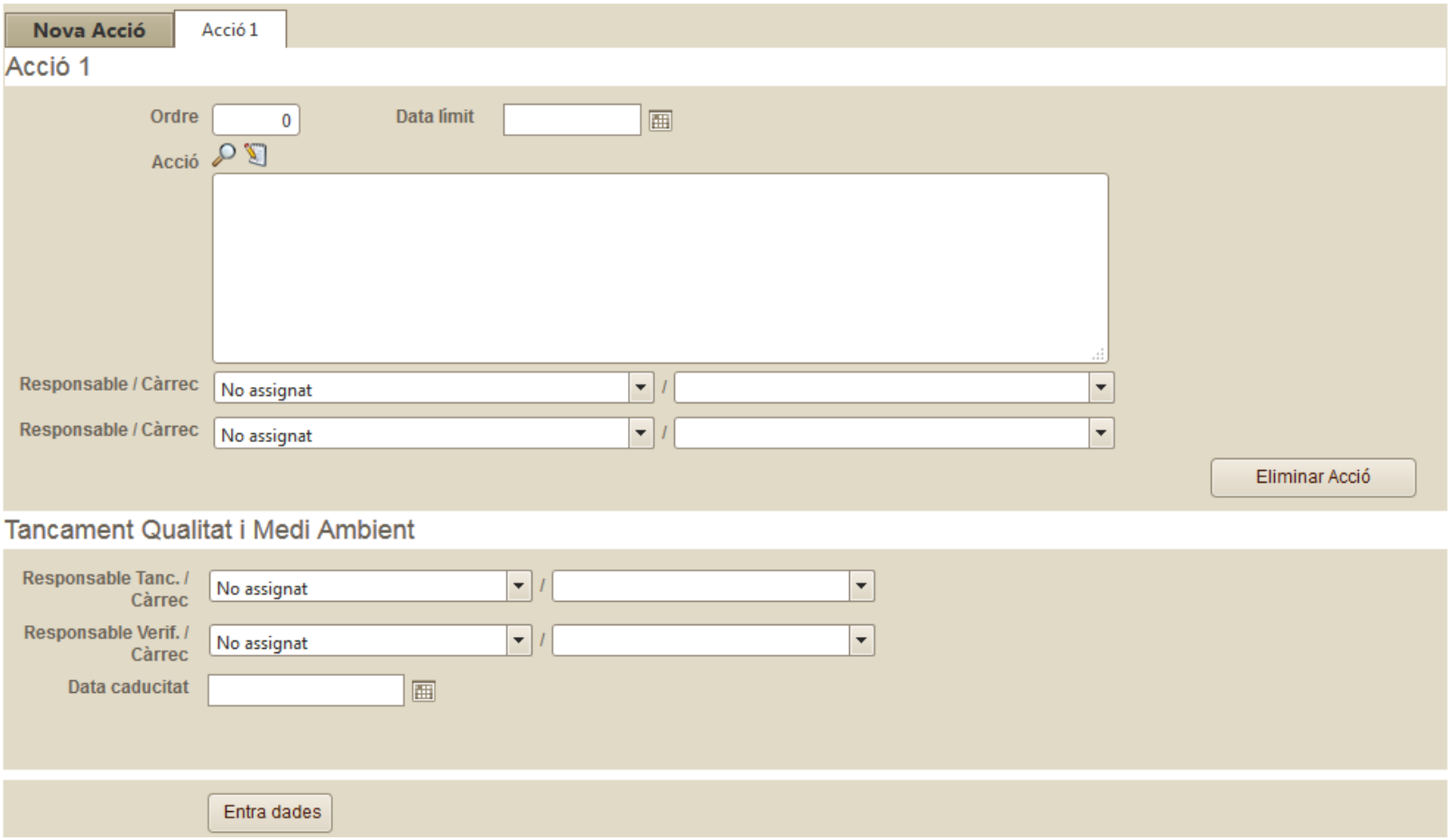
Document Management

- **Regulatory framework**
  - GMP / GTP
  - T / C directives
- **What does it consist of?**
  - Document management system
  - Current versions and update
- **How do we apply it? SOP?**
  - Qdoc / Qualiteasy
  - Central quality
- **How does it affect you?**
  - Doc Review and Update
  - Respect for current docs

Quality-Control Quality-**Quality Guarantee**




QUALITEASY 7.21 FLASH CLOUD
Principal
Documents
No conformitats i oportunitats de millora/riscos/canvis (OM/R/C)
Comunicació
Auditories
Altres
Nova No Conformitat
BIOSTORAGE
Tancar sessió
tornar
Alta No Conformitat
Departament
BIOSTORAGE
Data *
01/08/2019
Autor / Càrrec *
Tabera Fernandez, Jaime
/
BIOSTORAGE (USUARIS)
Activar
Origen *
Cap Selecció
Departament destí
No assignat
Client
No definit
Proveïdor
No definit
Referència
Referència/Subreferència
Cap selecció
Agrupació NC relacionades
Relacionar Agrupació NC
Oportunitats de millora/ risc/canvi (OM/R/C) relacionades
Relacionar oportunitat de n
Problema *
Causa *
Document annex
Afegir
Esborrar


Nova Acció
Acció 1
Acció 1
Ordre
0
Data límit
Acció
Responsable / Càrrec
No assignat
/
Responsable / Càrrec
No assignat
/
Eliminar Acció
Tancament Qualitat i Medi Ambient
Responsable Tanc. / Càrrec
No assignat
/
Responsable Verif. / Càrrec
No assignat
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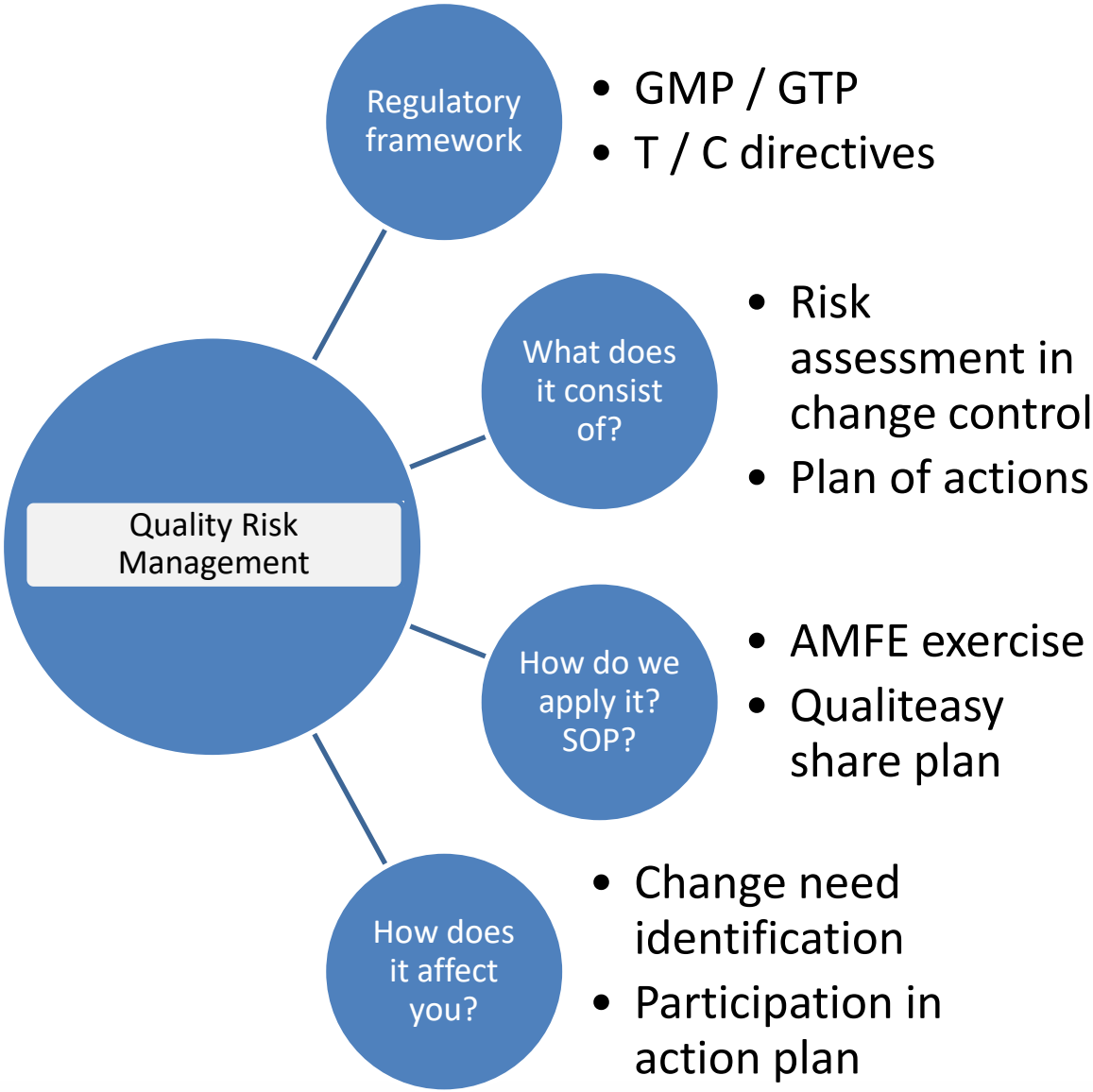
Data caducitat
Entra dades

Quality-Control Quality-**Quality Guarantee**



- GMP / GTP
- T / C directives

- Risk assessment in change control
- Plan of actions

- AMFE exercise
- Qualiteasy share plan

- Change need identification
- Participation in action plan

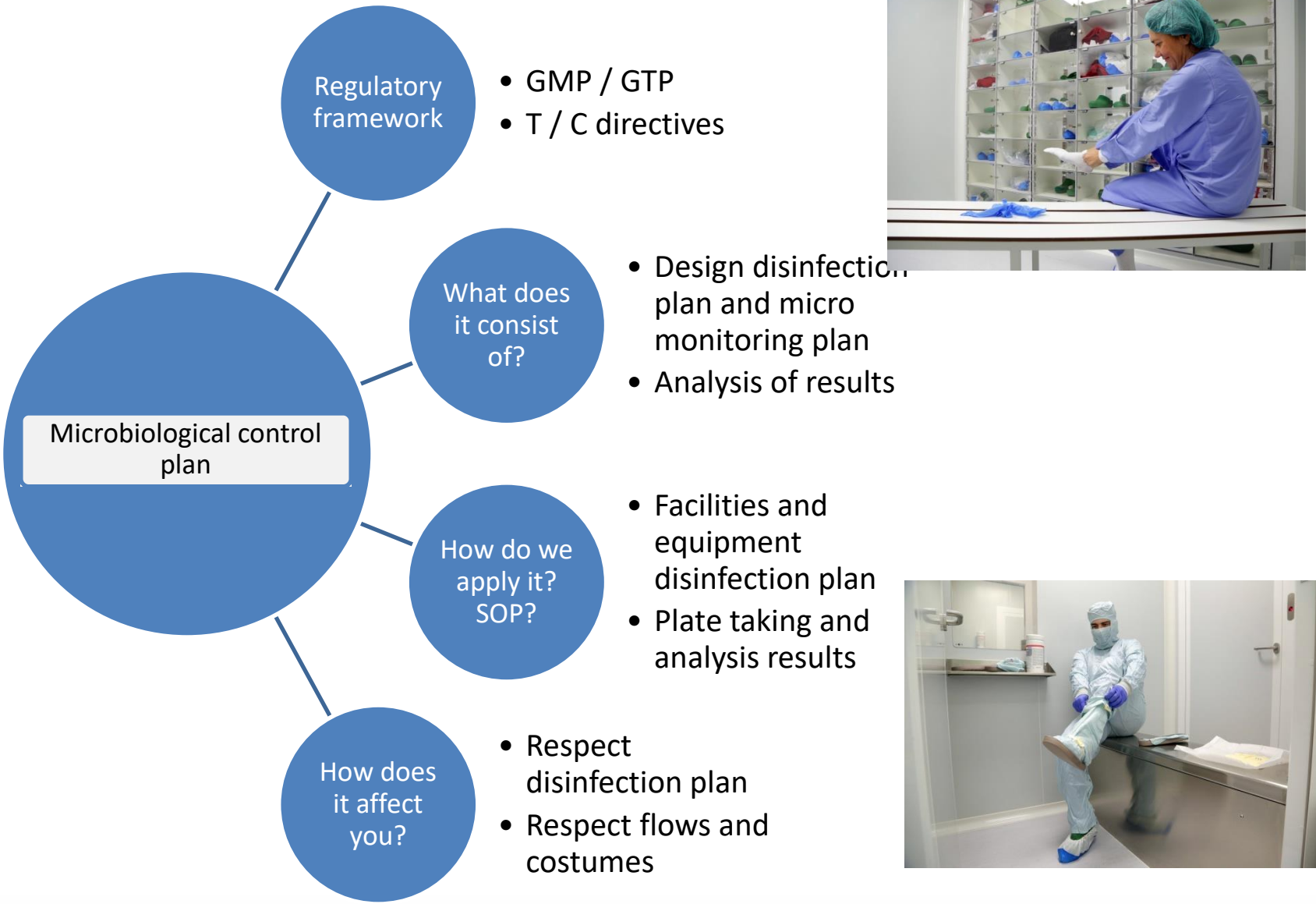
Quality-Control Quality-**Quality Guarantee**

PROCESO	REQ. REGULATORIO	RISK ASSESSMENT						
		FALLO	EFECTO	CAUSA	S	P	D	SPD

RISK CONTROL					
Actual mecanismo de reducción	Riesgo residual	Nuevo mecanismo de reducción	Se introducen nuevos riesgos?	Prioridad	Nuevo riesgo residual
estrategia de control de calidad de donante y tejido implementada	no aceptado por riesgo de distribuir corneas cultivadas contaminadas	1.revisión de historias de los donantes 2. revisión de las guías de procesamiento para	No (se limita la manipulación de las corneas para evitar introducir	alta	se espera a resultados de las acciones de 'nuevo mecanismo de reducción'

CHANGE CONTROL				Solicitante y fecha
Causa	Impacto global	Acciones	Seguimiento	
extensión de los controles de calidad para detectar posible contaminación de tejido en stock	aumento de coste aceptado	las cciones establecidas en 'nuevo mecanismo de reducción' son accioens de investigación. De momento no se decide realizar ningún cambio sobre los procedimientos vigentes.	acciones inmediatas	Jaime Tabera 03.08.17

Quality-Control Quality-**Quality Guarantee**

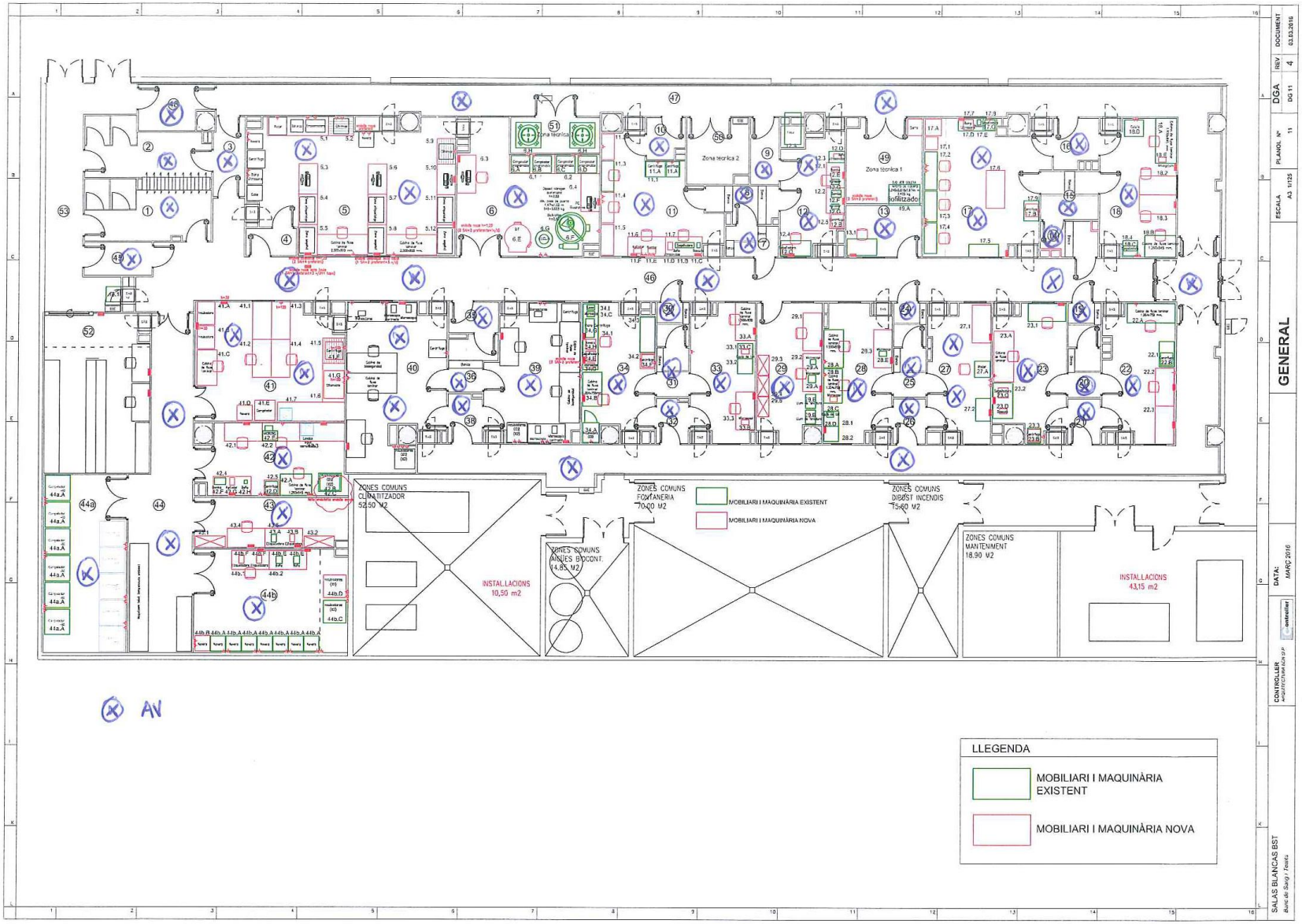


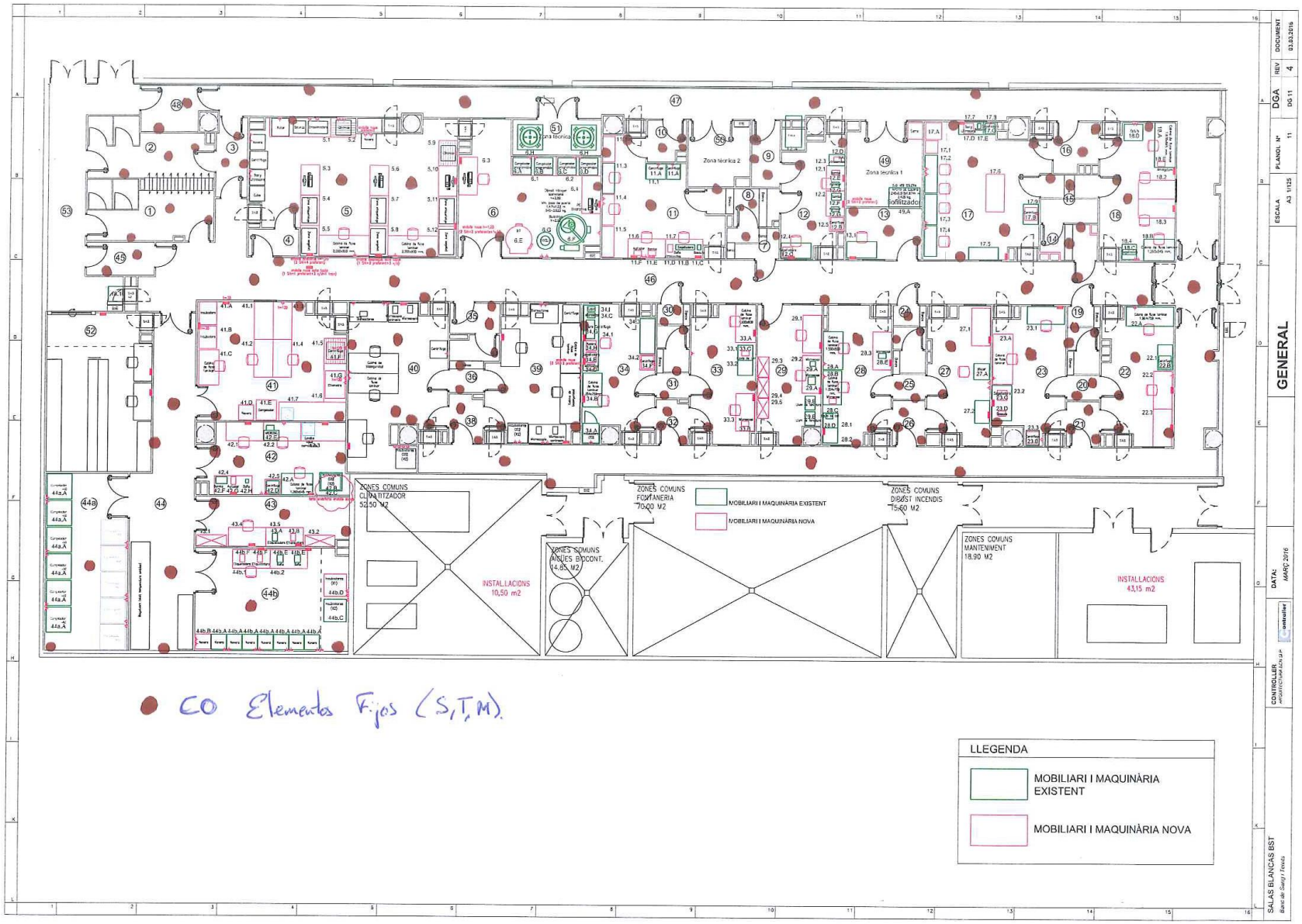
- GMP / GTP
- T / C directives

- Design disinfection plan and micro monitoring plan
- Analysis of results

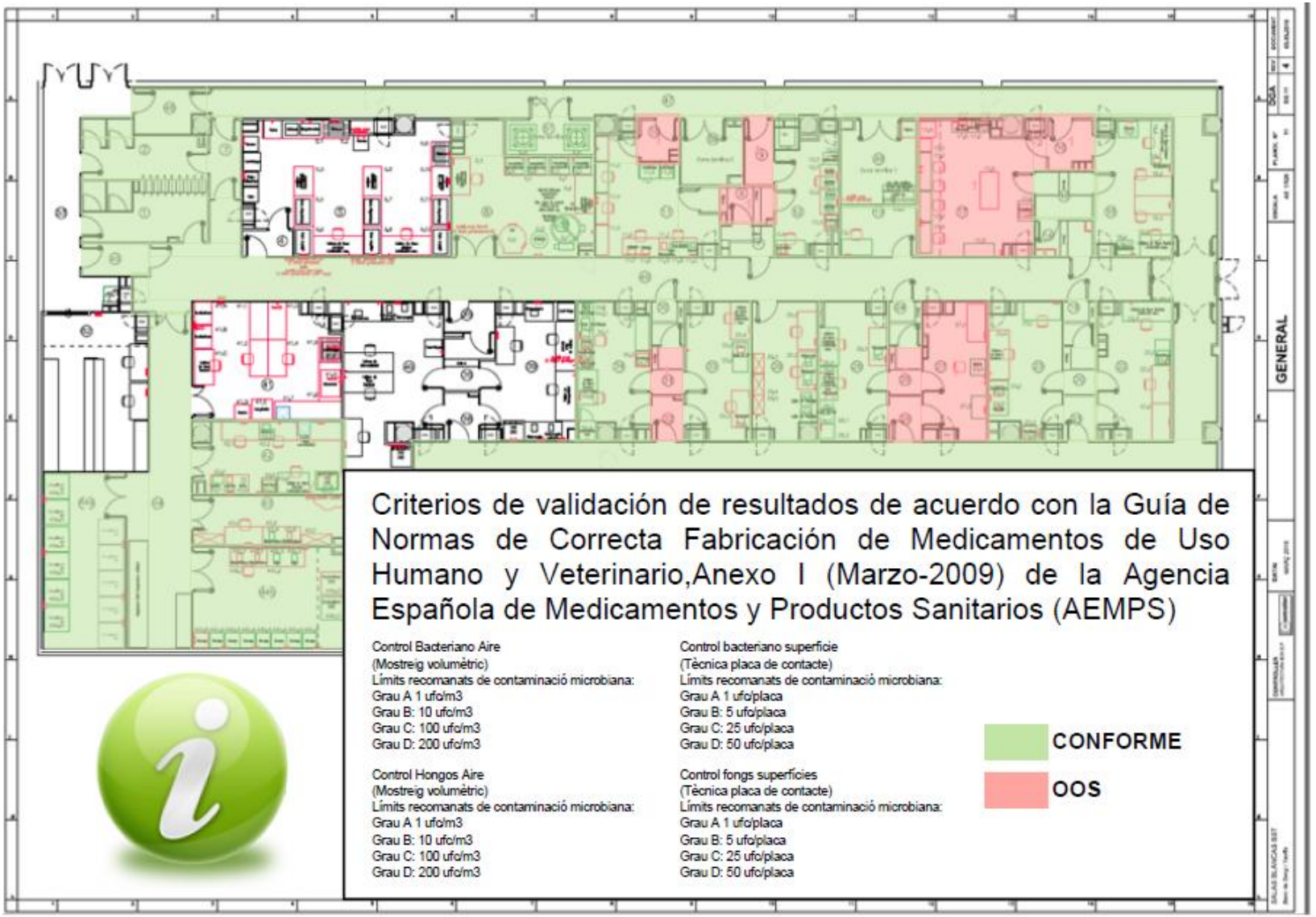
- Facilities and equipment disinfection plan
- Plate taking and analysis results

- Respect disinfection plan
- Respect flows and costumes


ZONES COMUNS
CLIMATITZADOR
52,50 M2
INSTAL.LACIONS
10,50 m2
ZONES COMUNS
ANNEXES BIOCONT.
14,85 M2
ZONES COMUNS
FONTANERIA
70,00 M2
MOBILIARI I MAQUINÀRIA EXISTENT
MOBILIARI I MAQUINÀRIA NOVA
ZONES COMUNS
DIBOST INCENDIS
15,60 M2
ZONES COMUNS
MANTENIMENT
18,90 M2
INSTAL.LACIONS
43,15 m2
Zona tècnica
Zona tècnica 2
Zona tècnica 1
AV
LLEGENDA
MOBILIARI I MAQUINÀRIA EXISTENT
MOBILIARI I MAQUINÀRIA NOVA
DGA
REV 4
DOCUMENT 03.03.2016
PLANOL Nº 11
DG 11
ESCALA A3 1/125
GENERAL
DATA: MARÇ 2016
CONTROLLER
SALAS BLANCAS BST
Àrea de Salut i Casos



CO Elementos Fijos (S,T,M).



Criterios de validación de resultados de acuerdo con la Guía de Normas de Correcta Fabricación de Medicamentos de Uso Humano y Veterinario,Anexo I (Marzo-2009) de la Agencia Española de Medicamentos y Productos Sanitarios (AEMPS)

Control Bacteriano Aire
(Mostreig volumètric)
Límits recomanats de contaminació microbiana:
Grau A 1 ufc/m3
Grau B: 10 ufc/m3
Grau C: 100 ufc/m3
Grau D: 200 ufc/m3

Control Hongos Aire
(Mostreig volumètric)
Límits recomanats de contaminació microbiana:
Grau A 1 ufc/m3
Grau B: 10 ufc/m3
Grau C: 100 ufc/m3
Grau D: 200 ufc/m3

Control bacteriano superficie
(Tècnica placa de contacte)
Límits recomanats de contaminació microbiana:
Grau A 1 ufc/placa
Grau B: 5 ufc/placa
Grau C: 25 ufc/placa
Grau D: 50 ufc/placa

Control fongs superfícies
(Tècnica placa de contacte)
Límits recomanats de contaminació microbiana:
Grau A 1 ufc/placa
Grau B: 5 ufc/placa
Grau C: 25 ufc/placa
Grau D: 50 ufc/placa

CONFORME

OOS