

**SoHOs oversight system: a focus on inspection and authorisation process
at national and European level**

SESSION 2 - PREPARATORY TOOLS TOWARDS A EUROPEAN COMMON APPROACH OF THE OVERSIGHT ACTIVITIES

Risk Assessment approach

Rome, March 28th, 2023

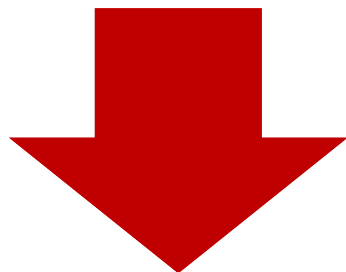
**Jaime Tabera
Barcelona Tissue Bank - Banc de Sang i Teixits**



How technical rules can be kept up to date
at the EU level?

How can we Facilitate the development of a
common and optimal approach to assess
and authorize preparation processes in
blood and tissues establishments?

The challenge of keeping EU legislation up-to-date in a dynamic sector with changing risks

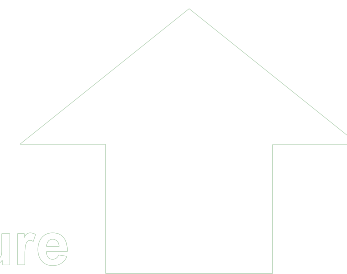


No accessibility
Non efficacious therapies
No sustainability

Legislation



Q&S&E Standards and GXP
International accreditation
Harmonized authorization procedure



Let's focus on: **Q&S&E Standards and GXP**

Good Practices (p.e. EDQM) are more and more written in a **risk management mode** instead of in a **requirements mode**, by incorporating ubiquitous references and specific risk management tools. For instance: Microbiological risk assessment tool (MiRCA) (already included in the 5th ed of the EDQM Guide) and the EuroGTPII risk assessment methodology (coming to the EDQM platform in 2023).

This implies the need for the CA to be provided of sufficient technical knowledge to guarantee an adequate evaluation and a correct interpretation of the risk assessment outcomes.

EU T&C Directives already explicitly mention the need of applying Risk Management tools to diverse situations; e.g. change of any new donor selection or testing criteria; or if a exclusion criteria included in the Directives is not applied.

COMMISSION DIRECTIVE 2006/86/EC

ANNEX II

C. STORAGE AND RELEASE OF PRODUCTS

5. A documented **risk** assessment approved by the responsible person as defined in Article 17 of Directive 2004/23/EC must be undertaken to determine the fate of all stored tissues and cells following the introduction of any new donor selection or testing criterion or any significantly modified processing step that enhances safety or quality.

COMMISSION DIRECTIVE 2006/17/EC

ANNEX I

SELECTION CRITERIA FOR DONORS OF TISSUES AND/OR CELLS (EXCEPT DONORS OF REPRODUCTIVE CELLS) AS REFERRED TO IN ARTICLE 3(a)

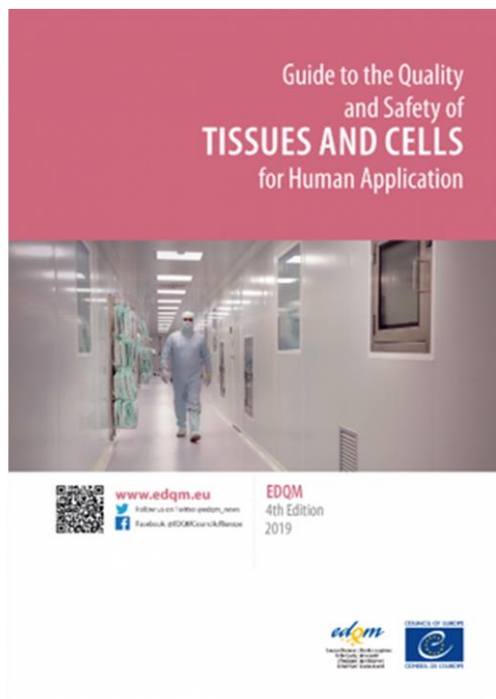
Selection criteria for donors are based on an analysis of the risks related to the application of the specific cells/tissues. Indicators of these risks must be identified by physical examination, review of the medical and behavioural history, biological testing, post-mortem examination (for deceased donors) and any other appropriate investigation. Unless justified on the basis of a documented **risk assessment** approved by the responsible person as defined in Article 17 of Directive 2004/23/EC, donors must be excluded from donation if any of the following criteria applies:

Draft EU regulation quality and safety of SoHO

Article 58, § 5

In the procedures referred to in paragraph 1, **SoHO entities shall mitigate risks arising from microbial contamination** of SoHOs from the environment, the personnel, the equipment, materials or solutions coming into contact with SoHOs during collection, processing, storage, or distribution. **SoHO entities shall mitigate such risks by**, at least, the following measures:

- (a) specifying and verifying the cleanliness of collection areas;
- (b) specifying, **based on a structured and documented risk assessment** for each SoHO preparation, validating and maintaining a defined air quality in processing areas;
- (c) specifying, procuring, and decontaminating equipment, materials and solutions such that their sterility is ensured.



Chapter 2: Quality management, risk management and validation, *page 49*

2.17.	Risk management	61
2.17.1.	Hazard Analysis and Critical Control Points	62
2.17.2.	Failure Mode, Effects and Criticality Analysis	62

Free download at: go.edqm.eu/dl

EudraLex - Volume 4 - Good Manufacturing Practice (GMP) guidelines

Part I - Basic Requirements for Medicinal Products

- [Chapter 1 - Pharmaceutical Quality System](#)   (into operation since 31 January 2013)

Part III - GMP related documents

- Site Master File  
- Q9 Quality Risk Management 

ICH guideline Q9 on quality risk management

Table of contents

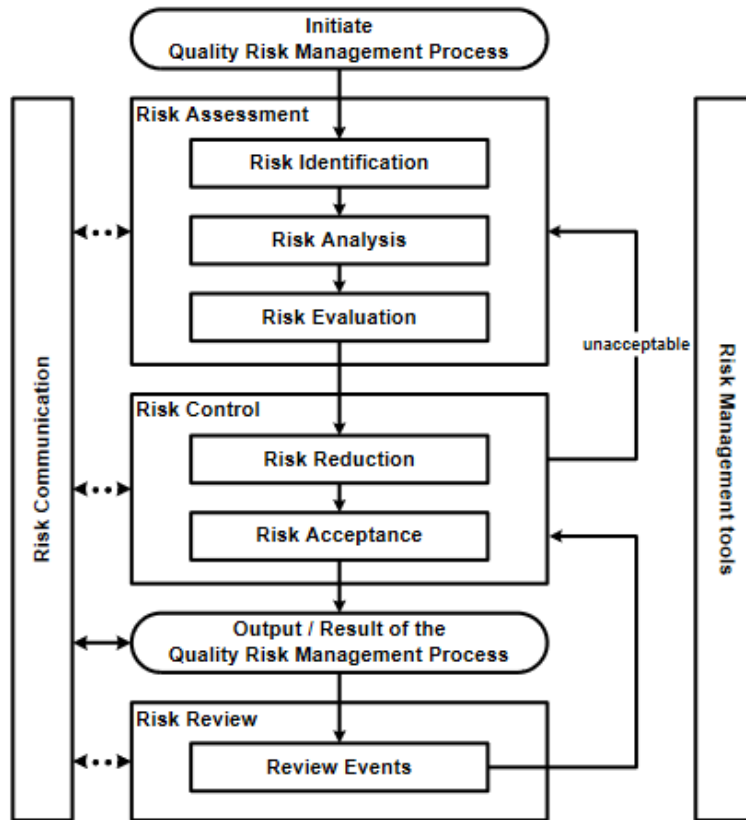
1. Introduction	3
2. Scope	3
3. Principles of quality risk management	4
4. General quality risk management process	4
4.1. Responsibilities	5
4.2. Initiating a quality risk management process	5
4.3. Risk assessment.....	5
4.4. Risk control	6
4.5. Risk communication.....	7
4.6. Risk review	7
5. Risk management methodology	7
6. Integration of quality risk management into industry and regulatory operations	8
7. Definitions	9
8. References	11

Annex I: risk management methods and tools	12
I.1 Basic risk management facilitation methods	12
I.2 Failure Mode Effects Analysis (FMEA).....	12
I.3 Failure Mode, Effects and Criticality Analysis (FMECA)	12
I.4 Fault Tree Analysis (FTA)	13
I.5 Hazard Analysis and Critical Control Points (HACCP).....	13
I.6 Hazard Operability Analysis (HAZOP).....	14
I.7 Preliminary Hazard Analysis (PHA)	14
I.8 Risk ranking and filtering	14
I.9 Supporting statistical tools.....	15

Annex II: Potential applications for quality risk management	15
II.1 Quality risk management as part of integrated quality management	15
II.2 Quality risk management as part of regulatory operations	16
II.3 Quality risk management as part of development	17
II.4 Quality risk management for facilities, equipment and utilities.....	17
II.5 Quality risk management as part of materials management	18
II.6 Quality risk management as part of production.....	19
II.7 Quality risk management as part of laboratory control and stability studies.....	19
II.8 Quality risk management as part of packaging and labelling.....	20

Risk Assessment approach

Overview of a typical quality risk management process



Applicable to a specific risk management event

- Prospective event; diminish the risk if the event occurs
- Retrospective event; assess risk when the event occurred p.e. deviation from Directives or internal procedures)

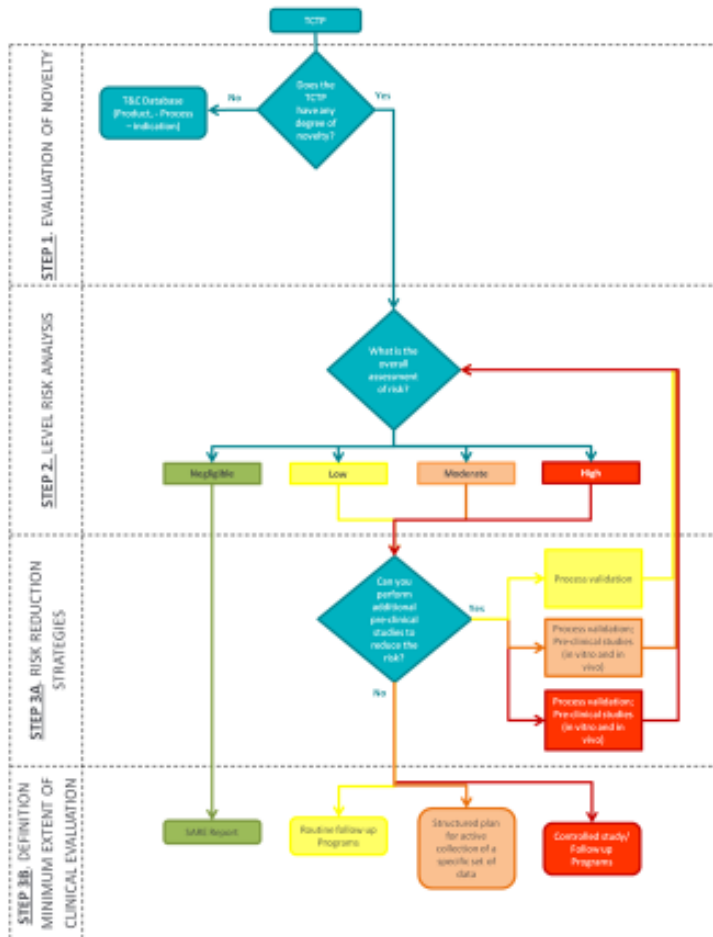
ICH guideline Q9 on quality risk management

Risk Assessment approach



**EURO
GTP II**
Good Tissue
& cell Practices

Methodologies



Applicable to risk management

- for new preparation processes or indications
- Changes in consolidated therapies

Risk Assessment approach

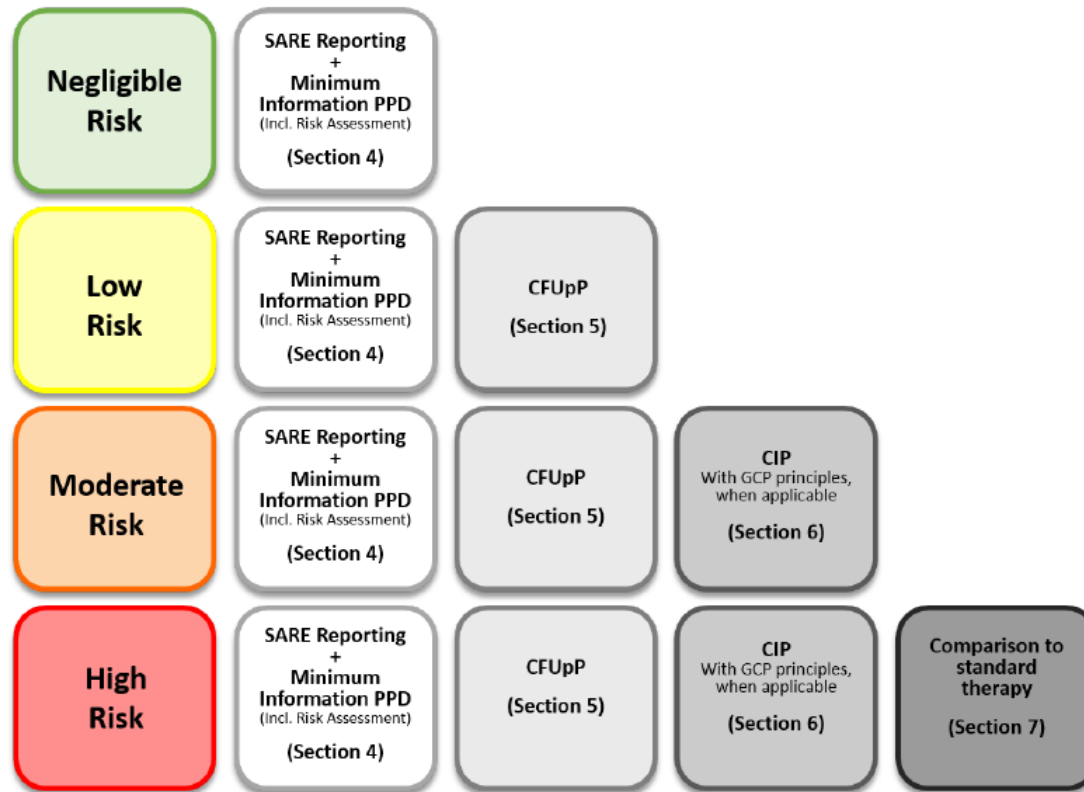


Figure 1. The extent of plan for collecting clinical data included in the clinical component of the PPD is based on the risk level.



Microbiological Risk of Contamination Assessment tool for tissues and cells (MiRCA)

Substances of Human Origin (SoHO) are being used in an increasing variety of new ways and many of these developments also raises questions of safety, quality and efficacy.

This platform aims to support professionals on a practical level and increase the rate of successful clinical applications, complement the guidance provided in EDQM technical guides.

At present, you will find here the MIRCA (**M**icrobiological **R**isk of **C**ontamination **A**ssessment) tool.

MiRCA TOOL

The aseptic procurement and processing of tissues and cells are some of the more difficult processes conducted. Process steps may lead to microbiological contamination and loss of tissues and cells, or even pose potential risks for clinical application.

The MIRCA tool is aimed at:

- helping users identify potential risks in novel, existing or changed aseptic processes;
- alerting users to the degree of risk of introducing microbiological contamination during the procurement and processing;
- supporting decisions and changes to mitigate risks during aseptic processes.

The tool will generate a summary report detailing the risks identified and the risk scores, and will prompt user actions to be taken to support them.

To access the tool, users need to create an account where all their assessments will be stored and remain available.

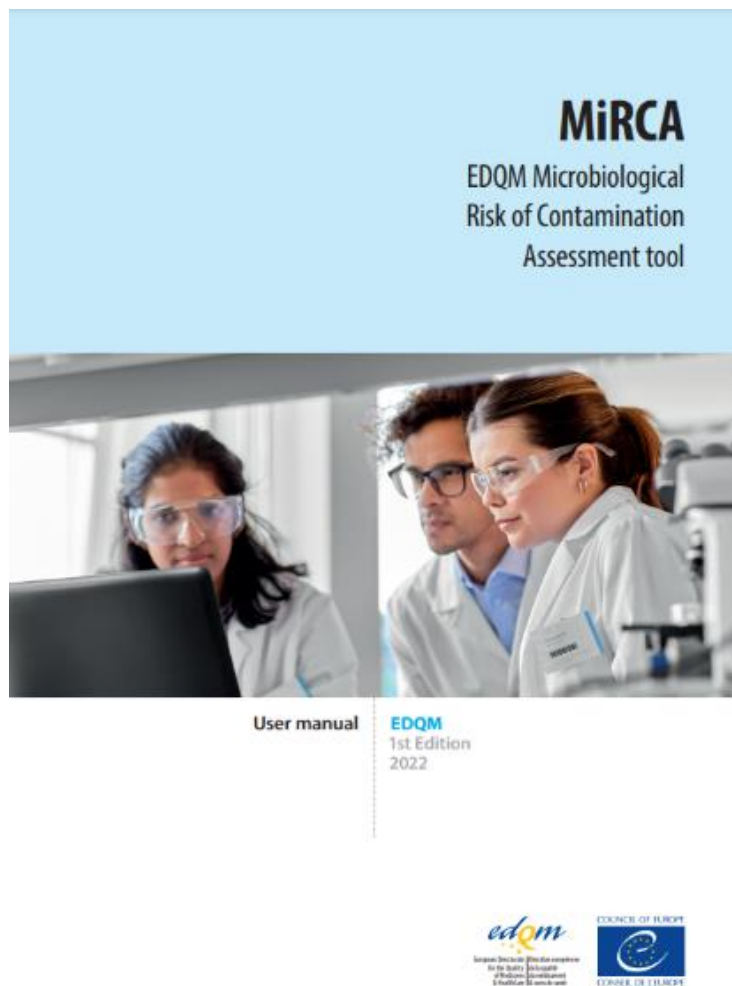
Statistics referring to the use of the MIRCA tool will be recorded and analysed by the EDQM and may be used for research purposes. In addition, the data may be used for research purposes and to inform guidance needs in future revisions of EDQM technical guides for *human application*.

[Legal disclaimer](#)

Applicable to identify risks over consolidated or new processes
Assess probability of generating contaminated products

Co-funded
by the European Union





A risk informed decision-making tool to assess the overall aseptic (microbiological) risk from procurement to distribution of tissues and cells for human application

What is the aim of the MiRCA tool?

- help users **identify potential risks** in novel, existing, or modified aseptic processes;
- **alert users** to the **degree of risk** of introducing microbiological contamination during the procurement or processing of tissues and cells;
- **support decisions** and changes to mitigate risks during aseptic processes.

Risk Assessment approach

EDQM Standards

SoHO Supply Chain

Risk Assessment approach

EDQM Standards

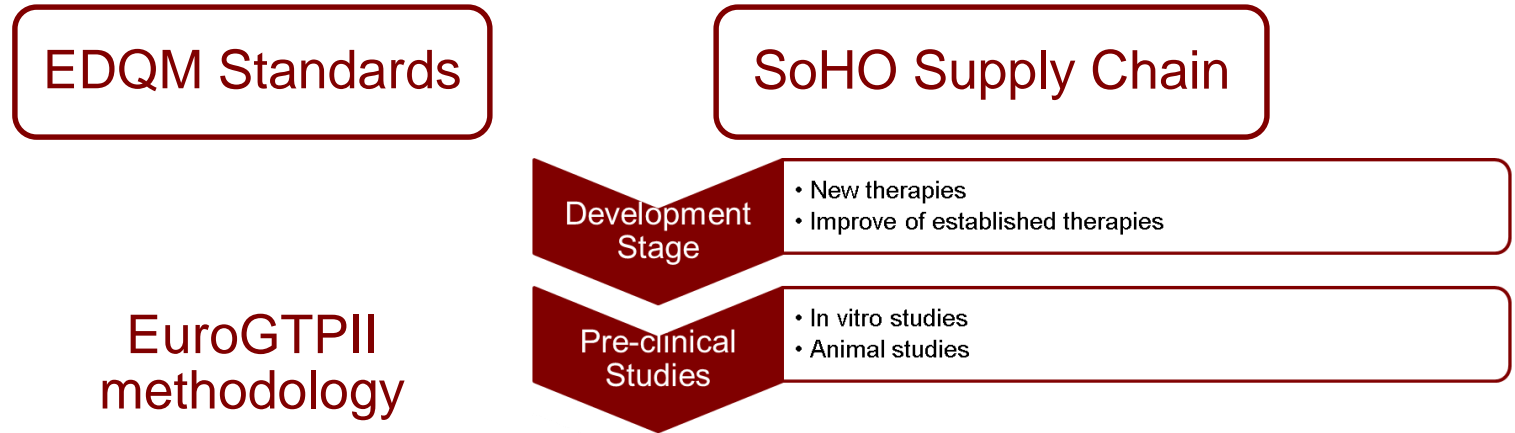
SoHO Supply Chain

Development
Stage

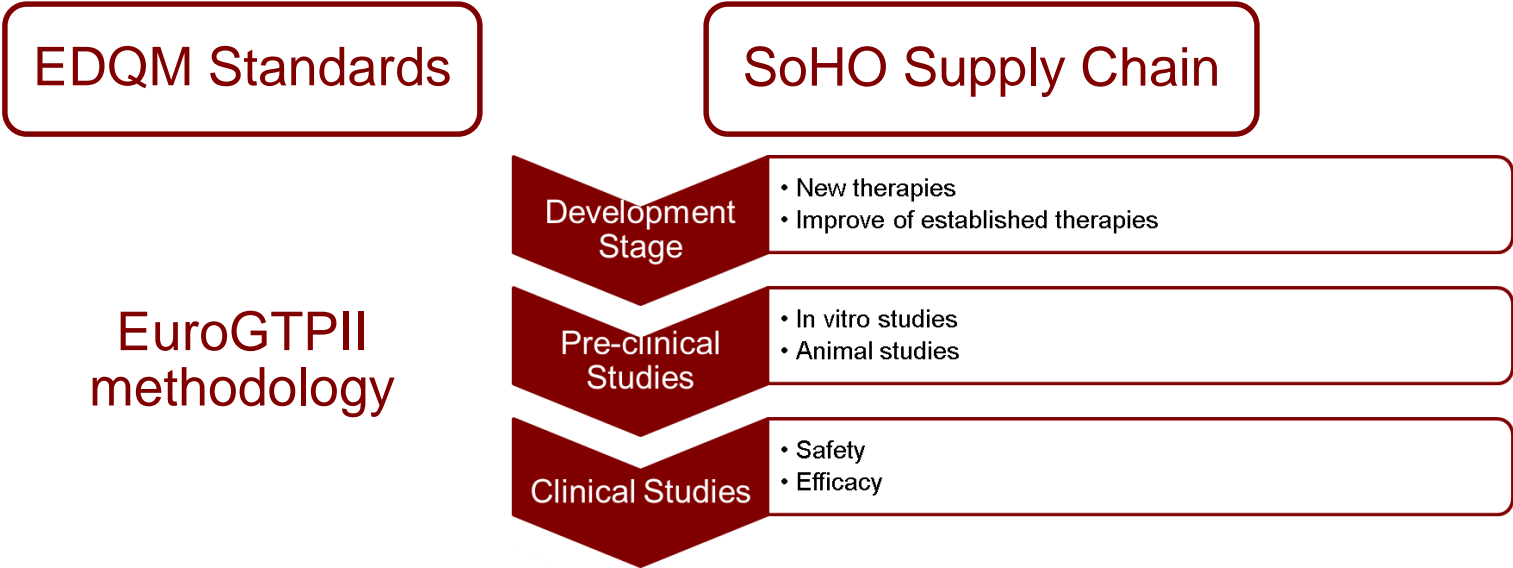
- New therapies
- Improve of established therapies

EuroGTPII
methodology

Risk Assessment approach



Risk Assessment approach



Risk Assessment approach

EDQM Standards

SoHO Supply Chain

ICH Q9 RM tools

EuroGTPII
methodology

Development
Stage

- New therapies
- Improve of established therapies

Pre-clinical
Studies

- In vitro studies
- Animal studies

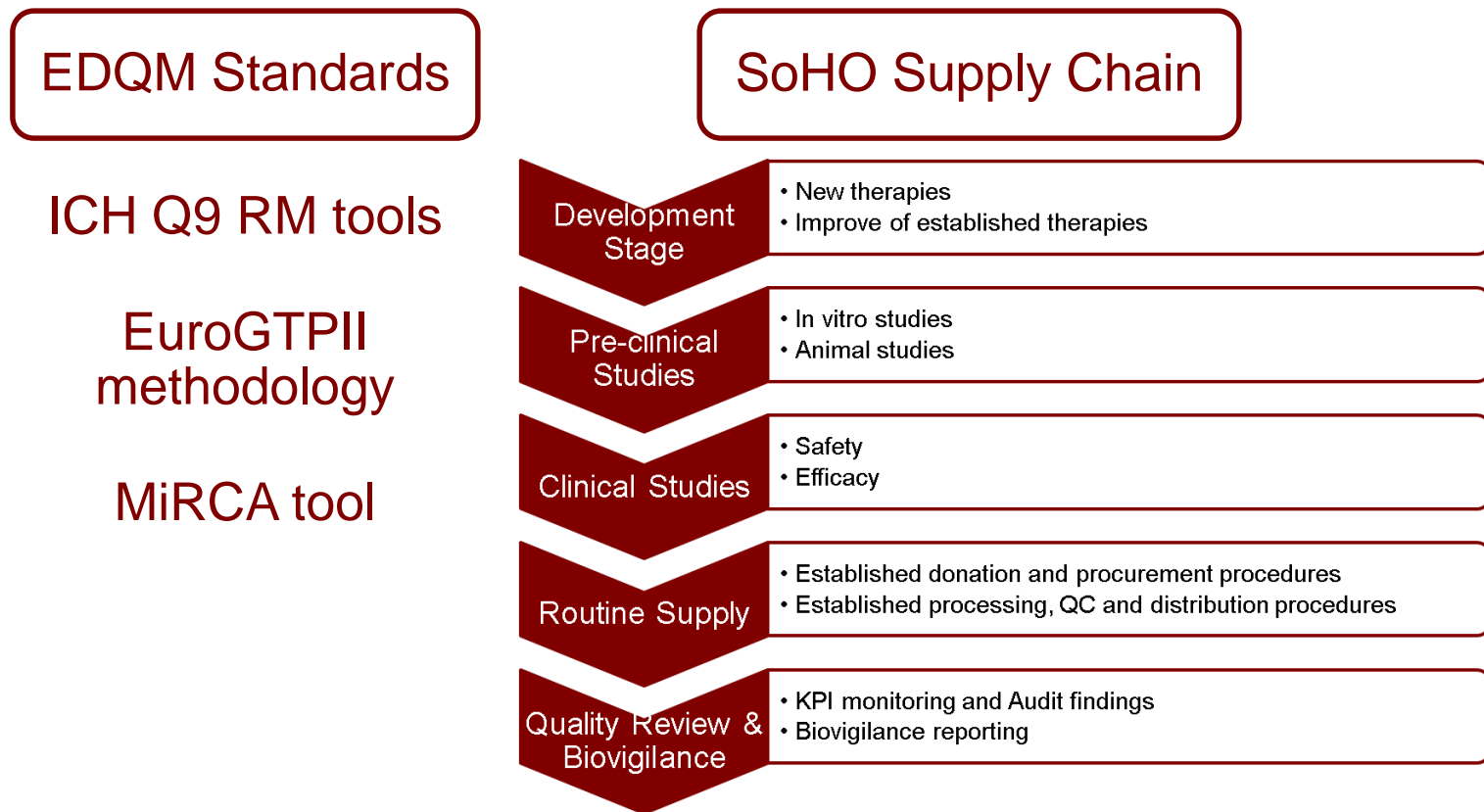
Clinical Studies

- Safety
- Efficacy

Routine Supply

- Established donation and procurement procedures
- Established processing, QC and distribution procedures

Risk Assessment approach



Risk Assessment approach

EDQM Standards

ICH Q9 RM tools

EuroGTPII
methodology

MiRCA tool

**Harmonized Authorization
and Inspection Procedure**

SoHO Supply Chain

Development
Stage

- New therapies
- Improve of established therapies

Pre-clinical
Studies

- In vitro studies
- Animal studies

Clinical Studies

- Safety
- Efficacy

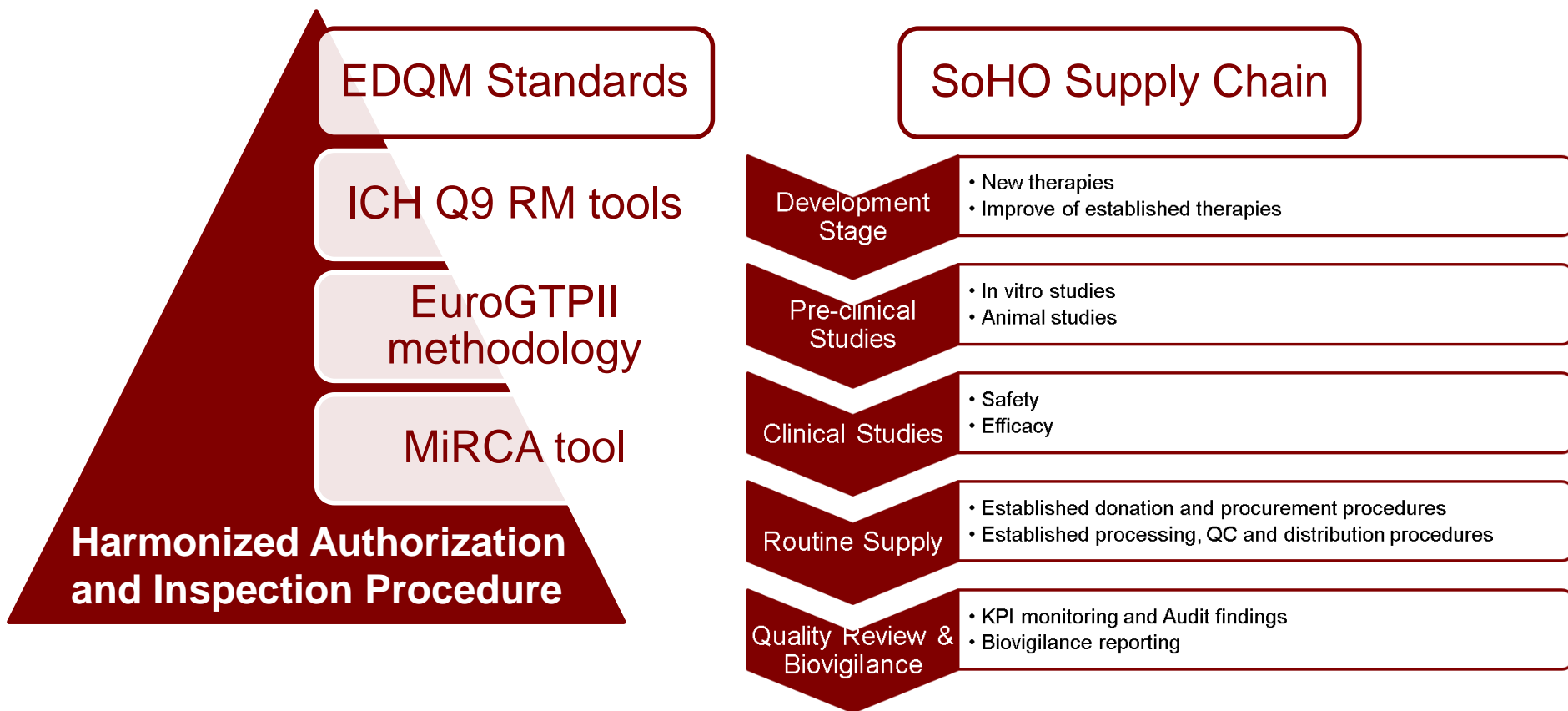
Routine Supply

- Established donation and procurement procedures
- Established processing, QC and distribution procedures

Quality Review &
Biovigilance

- KPI monitoring and Audit findings
- Biovigilance reporting

Risk Assessment approach



We can use RM tools to authorize and inspect, in a harmonized manner, the full process

Take home messages

- The Risk Management exercises help to harmonize legislation and Good Practices across the EU
- The Risk Management exercises allow the Legislation to be closer to the scientific advance
- The Risk Management exercises ease the CAs and professionals to enlarge the knowledge



BANC DE SANG
I TEIXITS

*Moltes
gràcies*

Salut/

bancsang.net