THE EUROPEAN DIRECTORATE FOR THE QUALITY OF MEDICINES & HEALTHCARE (EDQM)

edqm
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

Microbiological Risk of Contamination Assessment tool for tissues and cells

All you need to know about the MiRCA tool

EDQM Webinar, 19 January 2023

Introduction by the EDQM

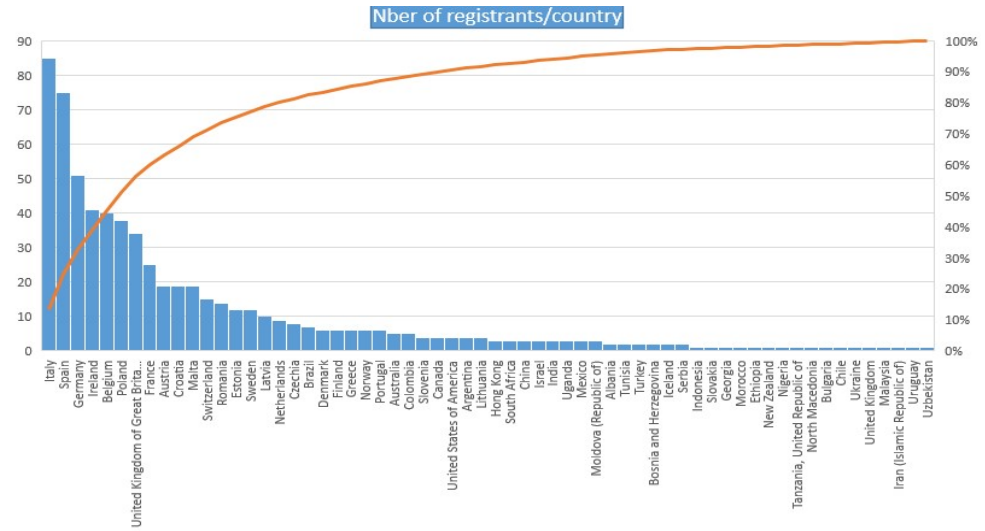
Dr Laurent Mallet

Head of Department of Biological Standardisation, OMCL Network & HealthCare,

EDQM, Council of Europe

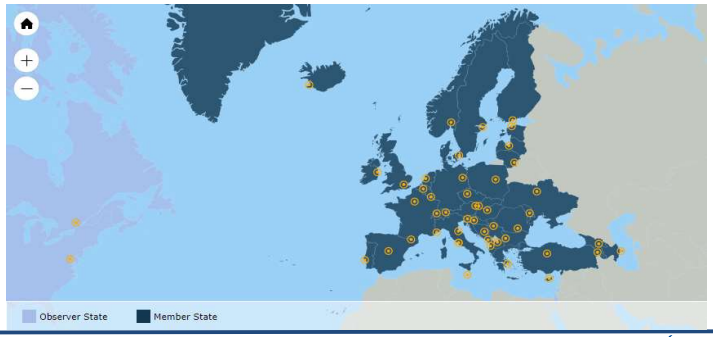
Registrants by country

N= 710



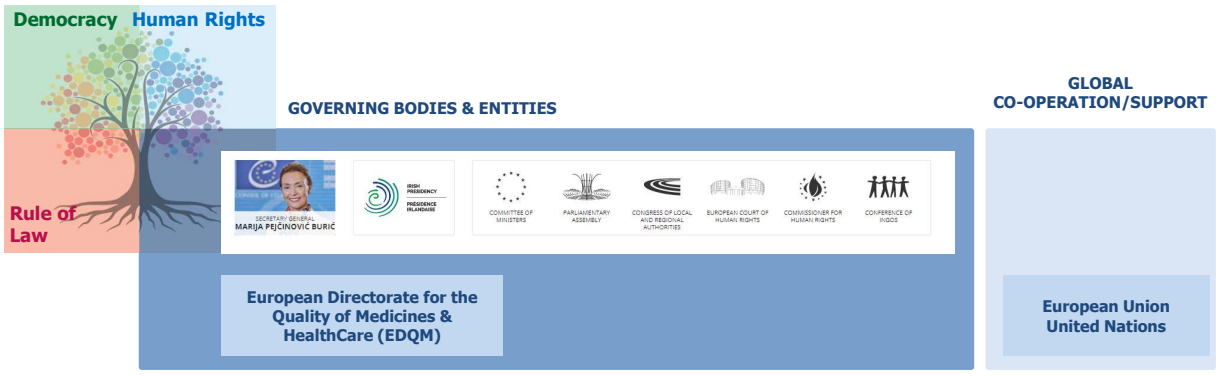
THE COUNCIL OF EUROPE: Who we are

- An intergovernmental organisation
- Founded in 1949
- Located in Strasbourg
- 46 Member States
- Population approximately 675 million



THE COUNCIL OF EUROPE: Governance & structure

COUNCIL OF EUROPE



THE COUNCIL OF EUROPE: Activity types

Standard-setting
Elaboration & adoption of standards and identification of best practices (*Conventions, recommendations, guidelines or policy recommendations)*

Technical co-operation
Activities aiming at raising awareness of standards and their implementation

Monitoring
Activities aimed at assessing compliance with standards

'Dynamic Triangle'

Structure types:
Intergovernmental Structures/Institutions/Independent mechanisms/Field presence/Partial Agreement

THE EDQM: Who we are

The **E**uropean **D**irectorate for the **Q**uality of **M**edicines & HealthCare (EDQM)

A Directorate of the **Council of Europe**

Work is based on the European Pharmacopoeia Partial Agreement -***Convention on the elaboration of a European Pharmacopoeia,*** adopted in 1964

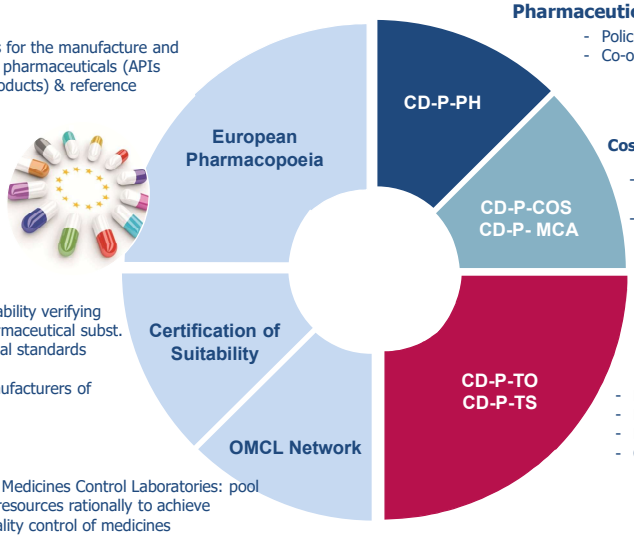
Contribute to the basic human right of access to good quality medicines and healthcare in Europe

THE EDQM: Mission & areas of work

EDQM contributes to the basic **human right of access to good quality medicines and healthcare**, and **promotes and protects human and animal health** by:

- establishing/providing official standards for the manufacture and quality control of medicines;
- granting Certificates of suitability which verify the compliance of pharmaceutical substances with European Pharmacopoeia standards
- co-ordinating a network of Official Medicines Control Laboratories (OMCL)
- **proposing ethical, safety and quality standards for transfusion and transplantation;**
- working with national, European and international organisations to combat falsification of medical products and similar crimes;
- providing policies and model approaches for the safe use of medicines, including guidelines on pharmaceutical care;
- establishing standards for cosmetics and food contact materials and co-ordinating the public control of cosmetics.

THE EDQM: Mission & areas of work



- Official standards for the manufacture and quality control of pharmaceuticals (APIs and medicinal products) & reference standards (RS)

Pharmaceutical Care
- Policies & model approaches for the safe use of medicines
- Co-operation to combat falsification of medical products

Cosmetics & food contact materials
- Standards for cosmetics and food contact materials
- Coordinating control of cosmetics

- Certificates of Suitability verifying compliance of pharmaceutical subst. with pharmacopoeial standards
- Inspections of manufacturers of these substances

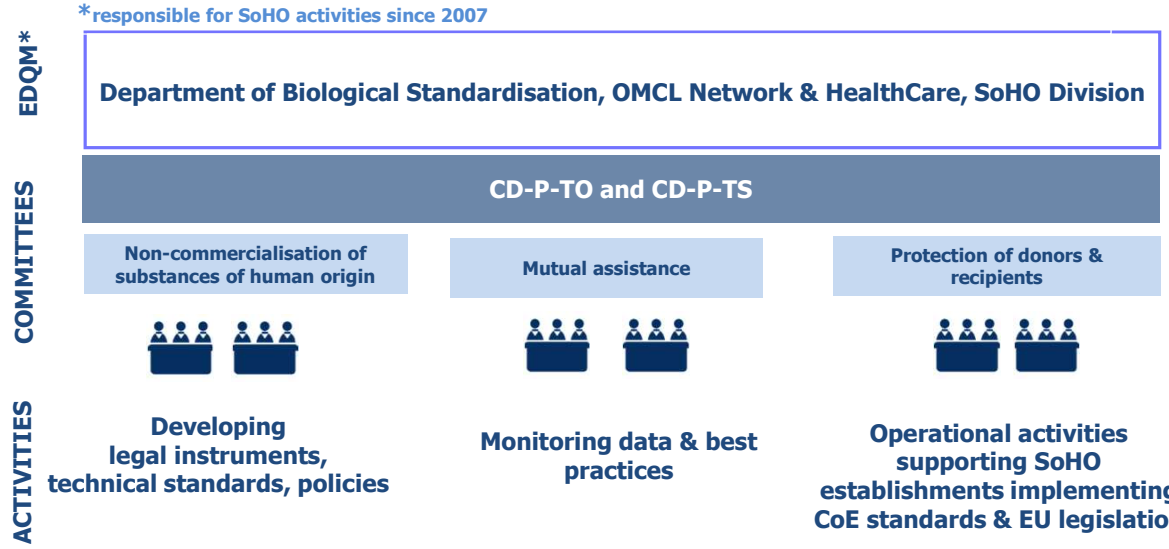
Substances of Human Origin (SoHO)
- Ethical, safety and quality standards
- Data collection
- Networks
- Co-operation and operational activities

- Network of Official Medicines Control Laboratories: pool expertise and use resources rationally to achieve effective public quality control of medicines

CD-P-X: Intergovernmental Structure

EDQM activities in the field of SoHO

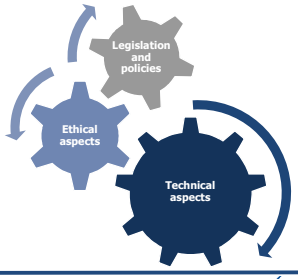
Governance of CoE SoHO activities



European Committee on Organ Transplantation (CD-P-TO)

Representatives *from 38 member states and 20 observer states and institutions (including the EC, WHO, CoE Committee on Bioethics and the main professional societies in the field)*

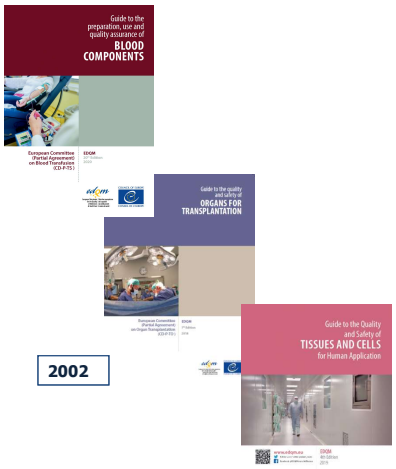
- **Development of quality, safety and ethical standards**
- **Promotion and non-commercialisation of organ, tissue and cell donation**
- **Fight against organ, tissue and cell trafficking**



Developing legal instruments, technical standards and policies

TECHNICAL STANDARDS (3 GUIDES)

- **Comprehensive guidelines** providing professionals with the most recent developments in the field
- Ensure high level of **quality and safety standards**
- Contribute to the **harmonisation** of these activities among European countries, facilitating uniform standards and practices
- **Continuous update** and maintenance
- **Consensus document** elaborated by experts nominated by member states and professional associations
- Addressed to the **46 CoE member states**



1992

2002

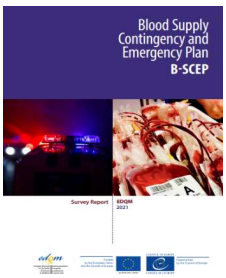
2013

Developing legal instruments, technical standards, policies

RECOMMENDATIONS/POSITION PAPERS/BEST PRACTICES

Blood:

- **Plasma supply:** recommendations on ways of increasing plasma collection, protecting donors
- **Blood Supply Contingency and Emergency Plan** (B-SCEP): recommendations and model preparedness plan



Tissues and cells:

- Understanding **post-mortem blood testing practices** for tissue donation
- **Illicit and unethical activities with human tissues and cells**

Non exhaustive list

Where to find our publications?

https://freepub.edqm.eu/publications

Monitoring data and best practices

DATA COLLECTION

Annual data collection & trend analysis

Analysis of biovigilance data (serious adverse reactions & events - SARE) on behalf of the European Commission – EU Member States

NETWORK- National Focal Points- Organ Trafficking

Annual data collection by National Focal Points (NFP) in co-operation with transplant programmes through dedicated IT platform **International database on travel for transplantation (RITTA)**

Microbiological Risk of Contamination Assessment (MiRCA) Tool

Why is MiRCA relevant?

- The aseptic procurement and processing of tissues and cells are some of the most difficult processes carried out by tissue establishments

- Failure in some of these process steps may lead to:
  - **microbiological contamination**
  - **loss** of tissues and cells, or even
  - **potential health hazards** if contamination is not detected before clinical application

Microbiological Risk of Contamination Assessment tool (MiRCA)

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.

A BIG THANK YOU TO THE WORKING GROUP

Introduction to the 5th Edition of the T&C Guide

Akila CHANDRASEKAR

Chair European Committee on Organ Transplantation
Co-Chair Guide to the Quality and Safety of Tissues and Cells

Jacinto SÁNCHEZ-IBÁÑEZ

Co-Chair Guide to the Quality and Safety of Tissues and Cells

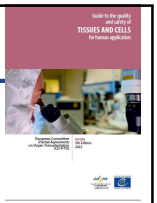
Guide to the Quality and Safety of Tissues and Cells for Human Application

Target audience

- Professionals involved in identifying potential donors
- Transplant coordinators managing the process of donation after death
- Testing laboratories
- Bone marrow and cord blood collection centres
- Tissue establishments processing and storing tissues and cells
- Fertility clinics
- Inspectors auditing the establishments and organisations responsible for human application
- Health authorities responsible for tissues and cells

In collaboration with:

Governance process



- **Co-ordination and Secretariat**: EDQM
- **Funding**: co-funded by EU and EDQM
- **Elaboration**: ad hoc working group (WG) composed of (40) official representatives (experts) nominated by member states and relevant professional associations.

The final composition of the WG is decided by the Secretariat, taking into account:

a) technical and scientific expertise in the field of the nominated experts (proven by a solid publication record, CV)

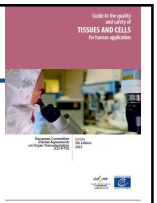
b) drafting needs (i.e. content for development and/or revision, as identified by the WG that elaborated the previous edition)

c) active participation in the elaboration of previous editions of the Guide (to ensure continuity and sustainability in the drafting process)

d) broad and balanced geographic representation

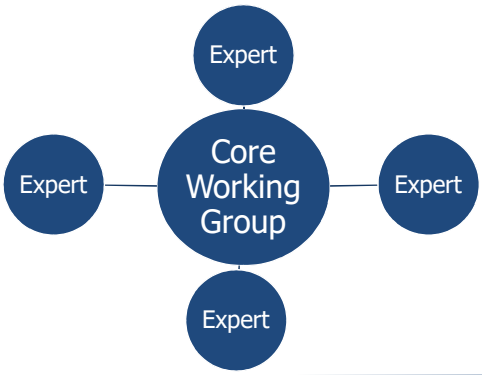
Experts complete a declaration of interest form (DoI) and confidentiality undertaking form.

Governance process

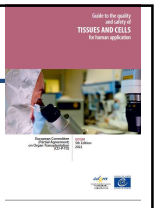


For those areas where the WG feels they lack specific expertise, it is possible to engage external experts. Group leaders of each chapter are responsible for co-ordinating these external contributions and submitting their work to the Secretariat within the established deadlines.

It is not a closed system for the working group only: if necessary "external" experts are contacted to improve and provide scientific knowledge and expertise in the field, participating in different chapters



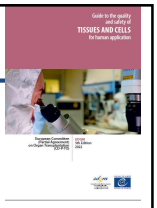
Structure and content

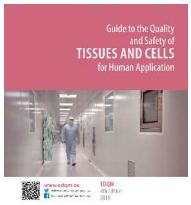


Must / Should

- In this edition the use of the word 'must' indicates mandatory compliance in alignment with Council of Europe recommendations and resolutions as well as with the current EU directives, but it also applies in those circumstances where an established good practice has been considered as essential by the working group
- With 'should', the aim is to indicate recommended compliance in accordance with commonly accepted good practice
- What the rule will be in the future is difficult to predict because some of the "musts" might change to should
- The main principles will be the same, based on published papers and on the experience of the working group and internal and external experts.

Structure and content





T&C guide 4th ed.

- Part A: General
- Part B: Tissue specific
- Part C: Developing applications

35 chapters

- Part D: T&C Monographs

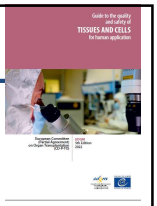
21 monographs

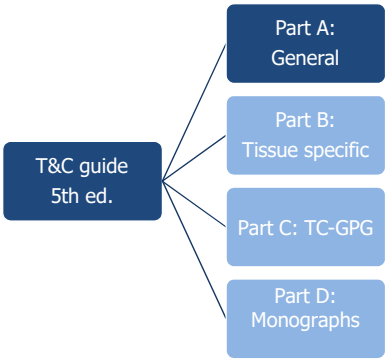
- Part E: GPG
- Appendices

34 appendices (sample qualification and validations, consent forms, etc.)

Funded by the European Union and the Council of Europe
Implemented by the Council of Europe

5th Edition updated contents



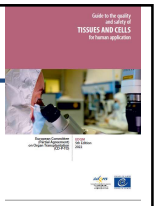


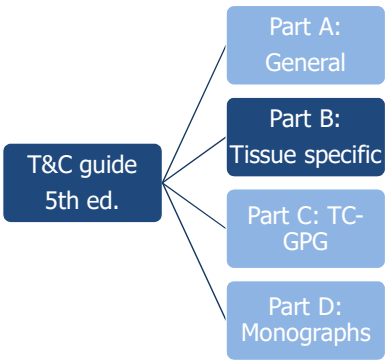
- Introduction
- Quality management and validation
- **Risk management**
- Recruitment of potential donors, identification and consent
- Donor evaluation
- Donor testing - markers for infectious diseases
- Procurement
- Premises
- Processing
- Storage
- Principles of microbiological testing
- Release, distribution and import/export
- Interaction between tissue establishments and Organisations responsible for human application
- Computerised systems
- Coding, packaging and labelling
- Traceability
- Biovigilance
- Introduction of novel processes and clinical application

New interactive tool

EDQM **Mi**crobiological **R**isk of **C**ontamination **A**ssessment tool (MiRCA)

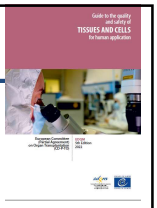
5th Edition Updated Contents





- Ocular
- Amniotic membrane
- Skin
- Cardiovascular
- Musculoskeletal
- Haematopoietic progenitor cells
- Umbilical cord blood progenitors
- Pancreatic islets
- Hepatocytes
- Adipose tissue
- Medically assisted reproduction
- Fertility preservation
- Human milk
- Intestinal microbiota
- Blood components for topical use or injection
- Tissues and cells as starting material

5th Edition Updated Contents



- T&C guide 5th ed.
  - Part A: General
  - Part B: Tissue specific
  - Part C:TC-GPG
  - Part D: Monographs

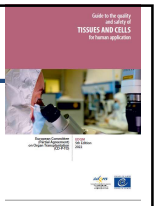
- ✓ TC-GPG describe the standards and specifications of quality systems to be implemented by TEs that want to comply with EU requirements
- ✓ Heavily based on Directives, GMP, EuroGTPs, JACIE and Blood Guide.
- ✓ The GPG for Tissue Establishments (TC-GPG) were elaborated following the example of the Blood Guide

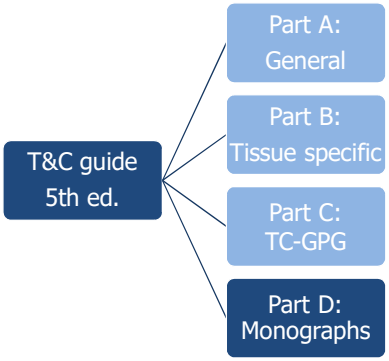
2016

Table of Contents (TC-GPG)

1. General principles
2. Quality management system
3. Management of outsourced activities (contractual agreements)
4. Personnel and organisation
5. Premises
6. Equipment and materials
7. Qualification, verification and validation
8. Donation
9. Donor testing
10. Procurement
11. Processing
12. Packaging, coding and labelling
13. Quality control (including microbiological control)
14. Distribution, import/export and recall
15. Documentation and records
16. Traceability
17. Biovigilance

5th Edition Updated Contents





- ✓ For well-characterised products with well-established clinical indications – as long as the established quality criteria are met and the product is used for the appropriate clinical indications. Thus, no need for heavy preparation process authorisation, clinical studies, etc.
- ✓ New processes/products would eventually move to having monographs once they become consolidated by evidence and a consensus was reached on the release criteria and appropriate clinical indications.

23 Monographs 4th edition

43 Monographs 5th edition

Format and content of monographs

- Definition of product
- List of established clinical indications
- Critical properties
- Quality control requirements
- Storage and transport
- Labelling and information for users
- Specific warnings

19.3: Glycerol-preserved skin allograft

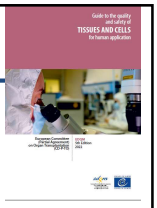
Tissue/cell product	Glycerol-preserved skin allograft
Definition	Human split-thickness, glycerol-preserved, de-vitalised skin grafts, with epidermis and upper dermis components for the treatment of skin loss.
Established clinical indications	• Temporary biological dressing: – in partial-thickness burns, – on meshed autografts (sandwich technique), – on donor site, – after application of *in vitro* cultured keratinocytes. • Temporary wound coverage after excision in full-thickness burns. • Temporary coverage in toxic epidermolytic necrolysis. • Temporary biological dressing for difficult, non-healing wounds, to protect and preserve the viable granulation tissue from desiccation and necrosis (antalgic and antibacterial effect). • Wound-bed preparation (promoting wound healing).
Critical properties	• Graft thickness ranging 0.2-0.8 mm. • Plain or meshed. • No evidence of microbial growth.
Quality control requirements	• Intact epidermis and upper dermis (normal morphological structure). • Microbiological testing (aerobic and anaerobic bacteria, fungi).
Storage and transport	• The graft is stored in glycerol 85 % solution to keep the tissue preserved before use. • The graft is stored at refrigerator temperature (2-8 °C); storage at room temperature (15-25 °C) during transportation is possible. • Maximum time: storage at 2-8 °C for 5 years.
Special labelling and accompanying information	• In the EU, the grafts must be labelled with the Single European Code (SEC), as applicable. • Specific information not coded in the SEC must be included in accompanying documentation or on the label: – Size of graft, width and length – Graft thickness – Plain or meshed.
Special warnings	• Rinse out glycerol before use (incubation in a large volume of sterile 0.9 % NaCl solution for 10 min at room temperature). • Not to be used if the storage medium is opaque.

Tissue and cell monographs

Benefits and uses:

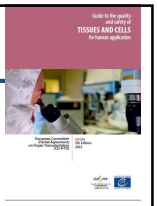
- ✓ **TEs**: will be able to compare their processes (and the information they have regarding clinical indications for which their products are used) with these monographs to:
  - ➢ implement correct quality checks
  - ➢ confirm to their HA that their product complies with an EDQM T&C Guide monograph
- ✓ **HAs**: for these products, will only need to check that the quality parameters and intended clinical uses are being appropriately verified by the TE (impact on Preparation Process Authorisation)
- ✓ **Both**: will know that products that do not have a matching monograph need more attention – risk assessment, validation, possibly clinical studies, etc. before they are authorised and supplied for routine use.
- ✓ The number of monographs will increase over the years

Revision process & consultation



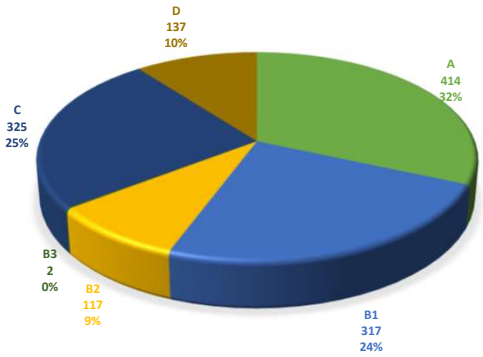
- **Stakeholder consultation**: invitations sent to national health authorities (via CD-P-TO members, participants and observers, and the EC NCA mailing list); relevant scientific associations, and others designated by any of the above. typically lasts 6 weeks.
- Comments are revised one by one and all decisions (why a suggestion is or is not accepted) must be explained
- Transparent procedure

Stakeholder consultation



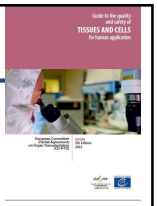
3 May to 1 June

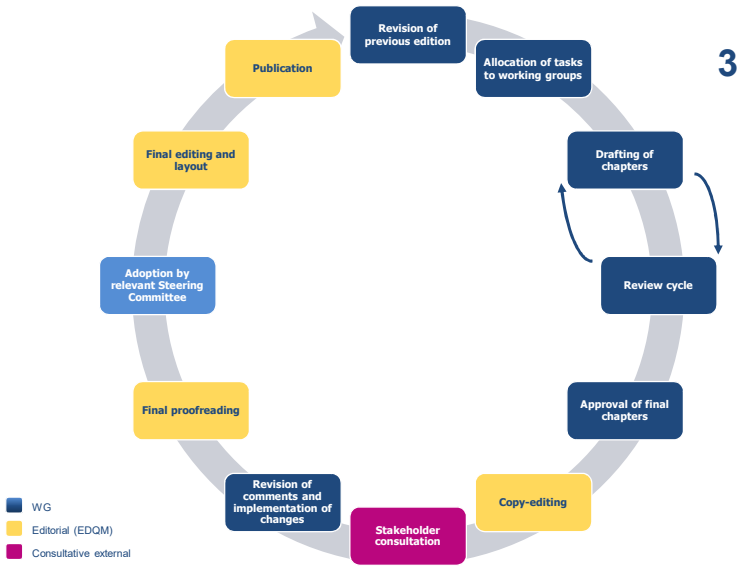
253 experts participated
1314 comments



56% of them were accepted either directly or after slight modification

Council of Europe Technical Guidance





3-yr cycle

With professional associations

With EU-funded projects

- The Guides compile the best available knowledge, including that produced thanks to EU-funded projects, to elaborate their recommendations
  - **Dissemination**
  - **Sustainability**
  - Ensures **future and continuous update** and maintenance
- The Guides themselves provide source material for EU-funded projects
  - Best available and up-to-date information to **build on**
  - **Training** material (e.g. T&C Guide used in EUSTITE Training for inspectors)

Summary

- Each chapter ends with a list of bibliographic references related to the topic
- It is not only a list of requirements decided by the experts
- At least for professionals in the field and for some CA/HA, inspectors, etc., it is the only reference guide that covers all aspects of tissues and cells
- Finally, the purpose of the Guide is to help ensure the safety and quality of tissues and cells for human application, while also ensuring the protection of donors, recipients and their offspring and respect for fundamental human rights.

Introduction to the MiRCA tool-setting the scene

EDQM **Mi**crobiological **R**isk of **C**ontamination **A**ssessment tool for tissues and cells for human application

Johan GUNS

Quality Coordinator of Medical Laboratories and Tissue Banks
Universitair Ziekenhuis Brussel (Belgium)

Universitair Ziekenhuis Brussel

Moving from Compliance to Risk-based Systems

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;

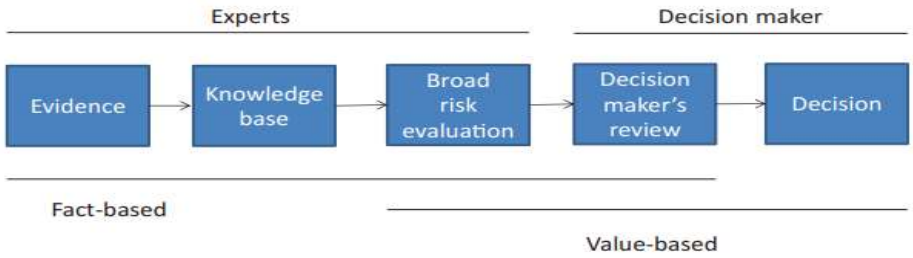
(b) specifying, based on a structured and documented risk assessment for each SoHO preparation, validating and maintaining a defined air quality in processing areas;

(c) specifying, procuring and decontaminating equipment, materials and solutions such that their sterility is ensured.

Challenges of risk assessment

- Which is the most appropriate risk assessment technique or tool for the process I want to assess?
- Have I identified all the risk factors for my specific process?
- Is the right expertise around the table?
- Which probability and likelihood scales should I select?
- How can I calculate the overall risk?
- How should I interpret the risk outcome? Which risk matrix should I use? Which risk needs my attention?

Risk informed decision-making



There are known knowns. These are things we know that we know.

There are known unknowns. There are things that we know we don't know.

But there are also unknown unknowns. There are things we don't know that we don't know.

Challenges of risk assessment

EDQM 3th ed., 2017
1 general risk matrix
Defining the type of procurement area (operating theatre, morgue, etc.)

Table 6.1. Factors and criteria to be considered in risk assessment of the procurement procedure

Factor	Low	Risk			High
Duration of exposure of procured tissues/cells during procurement	no exposure (closed system)	→			≥ 3 h
No. of personnel present while tissues/cells are exposed to the environment	1-2 persons	→			≥ 6 persons
Reduction of bioburden during or after procurement	closed system	validated antibiotic/substances treatment	only substances intended to reduce microbiological contamination (e.g. glycerol)	only washing intended to reduce microbiological contamination	no reduction
Reduction of bioburden during processing	validated sterilisation	substantial microbial reduction	limited microbial reduction (e.g. antibiotics)	only washing intended to reduce microbiological contamination	no reduction
Risk that contaminants will not be detected in the tissue due to the limitations of the sampling method	tissues preserved in culture medium (contamination is visible or revealed during microbiological testing of the medium)	culture of transport media and/or washing solution	a biopsy of tissue tested from each individual tissue	swabbing	no detection method
Route of application	superficial coverage (e.g. corneas, skin, amniotic membrane) or application in intra-uterine cavity	durable implant in a poorly vascularised site	small durable implant in a well vascularised site	large durable implant in a well vascularised site	direct application into the blood stream (infusion)

EDQM 4th ed., 2019
1 general risk matrix and 6 tissue specific risk matrixes
Defining the type of procurement area (operating theatre, morgue, etc.)
Outcome is vague and subject of debate for several years

Table 6.2. Example of musculoskeletal tissue recovery procedure with the specified characteristics

Factor	Low	Risk			High
Duration of exposure of procured tissues/cells during procurement [2]	no exposure (closed system)	≤ 1h	1-2 h	2-3 h	≥ 3 h
No. of personnel present while tissues/cells are exposed to the environment [3]	1 persons	2-3 persons	4 persons	5 persons	≥ 6 persons
Reduction of bioburden during or after procurement	closed system	validated antibiotic/substances treatment	only substances intended to reduce microbiological contamination (e.g. glycerol)	washing intended to reduce microbiological contamination	no reduction
Reduction of bioburden during processing	validated sterilisation	substantial microbial reduction	limited microbial reduction (e.g. antibiotics)	washing intended to reduce microbiological contamination	no reduction
Risk that contaminants will not be detected in the tissue or cell due to the limitations of the sampling method	tissues or cells preserved in culture medium (contamination is visible or revealed during microbiological testing of the medium)	culture of transport media and/or washing solution	a biopsy of tissue tested from each individual tissue	swabbing	no detection method
Route of application	superficial coverage (e.g. corneas, skin, amniotic membrane) or application in intra-uterine cavity	durable implant in a poorly vascularised site	small durable clinical application in a well-vascularised site	large durable clinical application in a well-vascularised site	direct application into the blood-stream (infusion)

Risk assessment tools

- **Cause and effect analysis**: (Ishikawa Diagram, also referred to as fishbone diagram, herringbone diagram or Fishikawa diagram). Causes are grouped in broad categories to cover all possible origins of the issue.
- **The Five Why's**. The aim is to uncover the root cause of a problem or defect, investigating the issue by asking 'why' five times.
- **Fault Tree Analysis**. To explore the causes of system-level failures.
- **Failure Mode Effect Analysis (FMEA).** Failures are prioritized according to how serious their consequences are, how frequently they occur, and how easily they can be detected.
- **Risk ranking**. identified risks are assessed either quantitatively or qualitatively, to ascertain which ones have the highest likelihood of occurrence and which ones, if they occur, have the greatest consequences; this ranks the risks in overall order of importance.

Approach of MiRCA

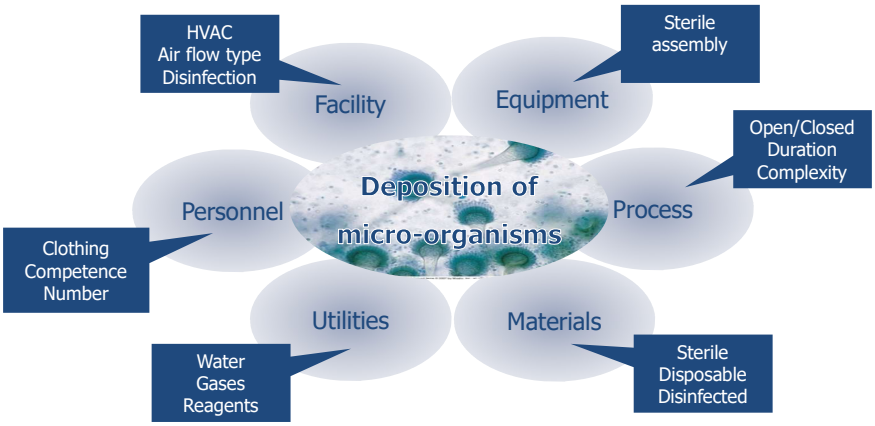
A risk informed decision-making tool to assess the overall aseptic (microbiological) risk from procurement to distribution of tissues and cells for human application

Definition of aseptic technique:

"Procedures designed to prevent contamination from micro-organisms and spread of infection"

Approach of MiRCA

Prevent the loss of T&C due to microbial contamination during aseptic procurement and processing and to reduce the risk of infection being transmitted to recipients



Individual risk value (IRV)

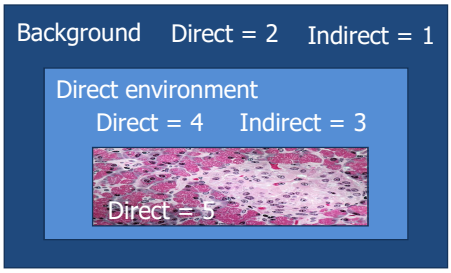
2 dimensions of identified risks

Probability of Occurrence (0-5) X Impact of Occurrence (1-5)

0 = Negligible or not applicable
1 = Very low
2 = Low
3 = Moderate
4 = High
5 = Very High

X Temporal distribution (0-5)

Time-dependent max. 5 hours
Intervention-dependent (1)



55 Individual risk factors

MiRCA tool

Procurement T&C
22
Individual risk factors

Processing and distribution T&C
33
Individual risk factors

Individual risk value (IRV) = Probability x Impact x Temporal distribution

↓

Total risk score = sum of individual risk factor scores

↓

Risk reduction factor (validated decontamination/sterilisation methods)

Risk reduction factor

- A 99% reduction is applied for a validated sterilisation process achieving an SAL of at least 10^{-6}, for example gamma irradiation.
- A 90% reduction is applied for any validated method that achieves (SAL ≤ 10^{-5} or ≤ 10^{-4}), for example a chemical treatment.
- A 50% reduction is applied for any validated method that achieves (SAL ≤ 10^{-3}), for example a validated antibiotic cocktail at 22 to 37 °C.
- A 20% reduction is applied for any validated method that achieves (SAL ≤ 10^{-3} and ≤ 10^{-2}), for example a validated antibiotic cocktail at 2 to 8 °C.
- If no validated decontamination or sterilisation method is used, no risk reduction factor is applied.

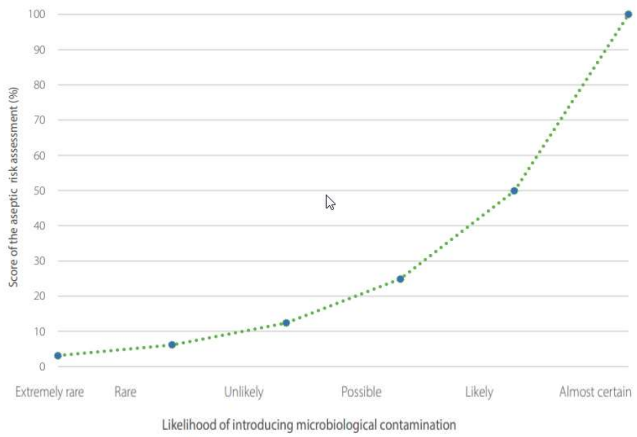
MiRCA user manual

Method/Process

Risk Factor	*IRV*	*Rationale*
Warm ischaemia time before procurement	P	Deceased donors can be transferred from the site of death to the hospital within hours after cardiac arrest, with a prolonged warm ischaemic time that might favour the growth and migration of micro-organisms in the blood prior to body refrigeration in the morgues of the referring hospital or inside the hospital. Warm ischaemia time is not only detrimental to tissue and cell viability but has also an impact on the potential contamination of TC due to translocation and proliferation of microflora present in some organs and tissues [6, 11, 18, 19, 22, 23, 24, 25, 26]. Warm ischaemia time is defined as the time from death until the start of procurement of organs, tissues or cells [27]. 0 – Living donor 1 – < 1 hour 2 – 1-3 hours 3 – 3-6 hours 4 – 6-12 hours 5 – > 12 hours The time of warm ischaemia is indicated as the average time of warm ischaemia observed during the last year.
	I	The warm ischaemia time has an impact on the translocation of micro-organisms and is conducive to the proliferation of micro-organisms which indirectly affects the deposition of micro-organisms on TC. Weight correction factor = 4.
	T	The risk factor is intervention-dependent and will be assessed as implemented (expressed by one) or not implemented (expressed by zero). The duration of warm ischaemia time is incorporated in the probability factor.

Interpretation of outcomes

Figure 1. **Risk scores translated to a risk profile by an exponential algorithm**



Risk profile	Proposed improvements
Possible	A profile of 'possible' indicates that the risks of a graft harbouring contamination at the point of distribution are rising, and that there may be opportunities to reduce this risk. Individual risk scores could be considered to help indicate where improvements could be made to reduce the risk profile even further.
Likely	A profile of 'likely' indicates that the risks of a graft harbouring contamination at the point of distribution is significant, and that there may be opportunities to reduce this risk. Individual risk scores could be considered to help indicate where improvements could be made to reduce the risk profile. Where feasible, it may be worth considering use of a decontamination or sterilisation protocol if one is not already used, or the use of a more powerful protocol if one is already used.

Thanks!

MiRCA working group	MiRCA app development
Akila Chandrasekar	Mar Lomero
Johan Guns	Bao-Thanh Nguyenvan
Richard Lomas	Elisabeth Poirier
Mar Lomero	
Marta López Fraga	
Jacinto Sánchez Ibáñez	
Jaime Tabera Fernández	

Let's get to the point: how does MiRCA work?

https://soho-guides.edqm.eu/home/

What it the goal of a mock assessment? Procurement

Richard LOMAS

Senior Clinical Development Scientist
NHS Blood and Transplant Tissue Services (UK)

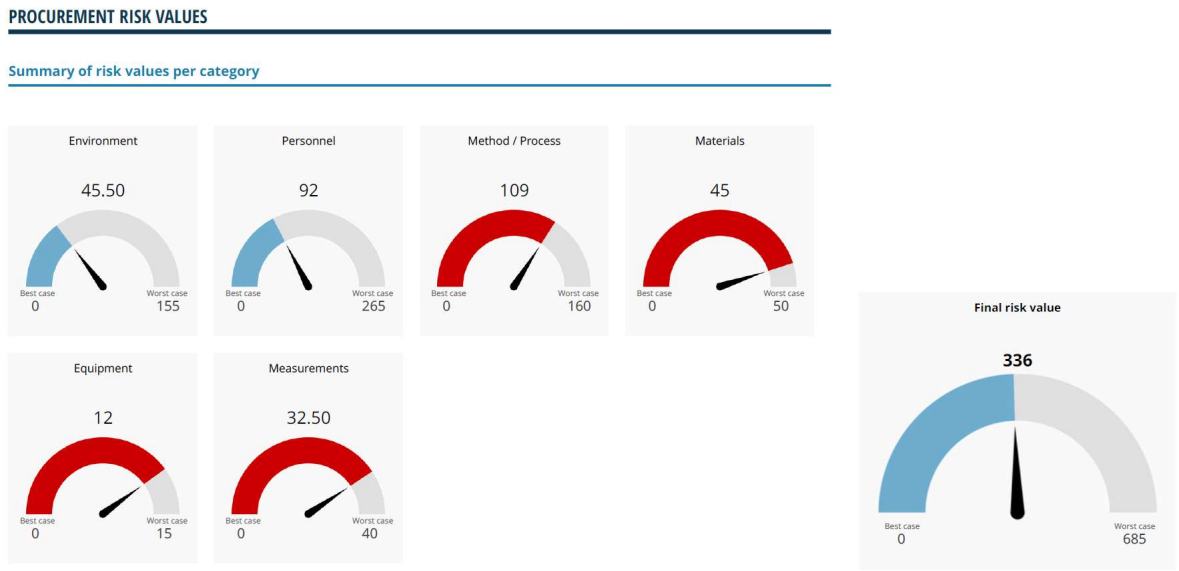
NHS
Blood and Transplant

Current procurement process

Assumes a 'worst case' procurement process, comprising:

- Procurement from deceased donors in a mortuary environment, up to 48 hours post mortem and permitting up to 12 hours warm ischaemia time.
- Procurement is performed by inexperienced operators, wearing non-sterile protective equipment, in a busy, uncontrolled environment.
- A low level decontamination is used to clean the cadaver prior to procurement, and no attempt is made to decontaminate the heart prior to or during transport to the processing facility
- The heart is transported in a drawstring bag container
- Consumables used during the procurement are re-useable, and reagents are prepared in-house and are multiple use
- Microbial control is based on a single sample of wash solution

MiRCA evaluation of the current procurement process



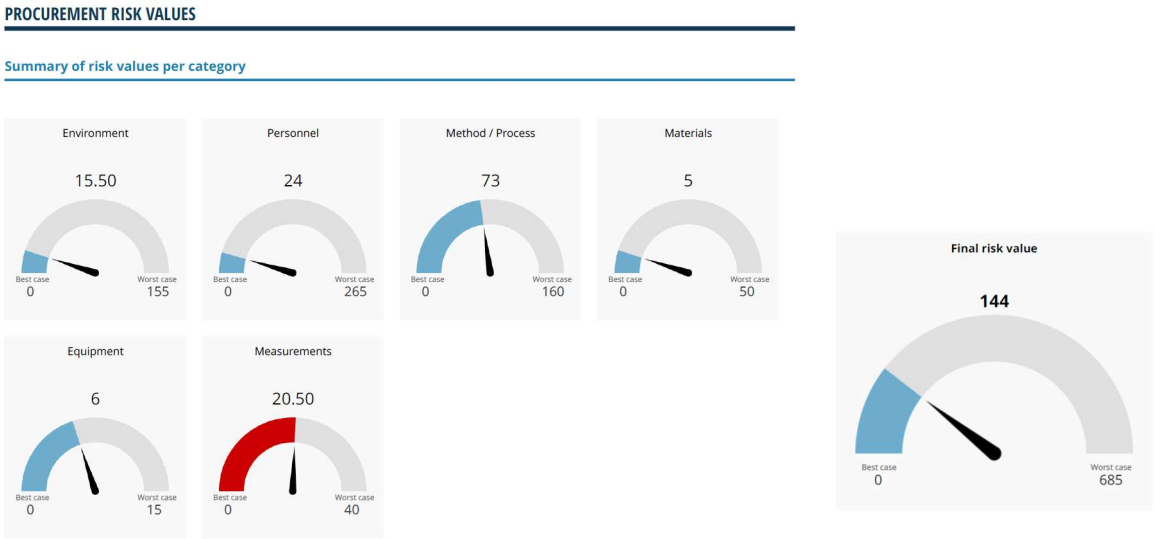
Options for procurement process improvement (1) - A major change

Procure immediately post mortem in an operating theatre, during organ procurement

- Leads to multiple process improvements, including:
  - Improves the quality and sanitisation of the procurement environment
  - Utilises more experienced personnel, wearing better quality equipment, working more efficiently in smaller numbers
  - Minimises warm and cold ischaemia time
  - Surgical standard pre-decontamination cleaning
  - Utilises pre-prepared 'off the shelf' consumables and reagents
  - Utilises sterile equipment

https://soho-guides.edqm.eu/home/

Revised MiRCA evaluation of the procurement process following change (1)



Change 1 (Major change)

This change (comprising multiple process improvements) has reduced our overall procurement risk score from 336 to 144, a risk reduction of **67%**

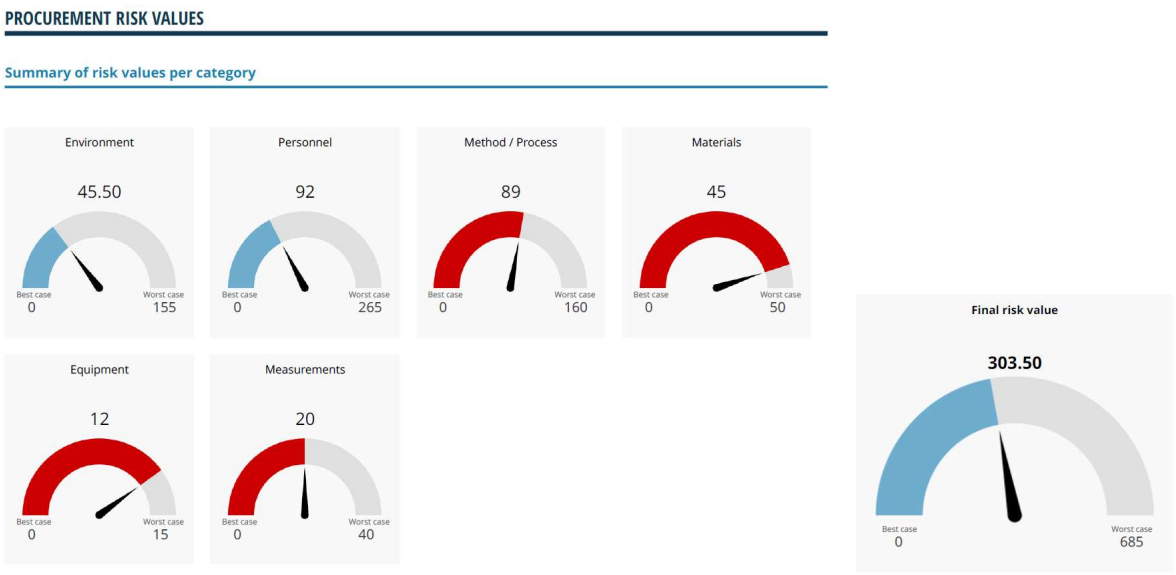
Options for procurement process improvement (2) - A minor change

Implement decontamination of the heart following procurement, and improve pre-processing microbiology testing

- Process improvements comprise:
  - Decontaminating the surface of the heart with povidone iodine/chlorhexidine post-procurement
  - Addition of antibiotics to the transport solution
  - Testing multiple tissue samples pre-processing

https://soho-guides.edqm.eu/home/

Revised MiRCA evaluation of the procurement process following change (2)



Change 2 (Minor change)

This change (comprising 2-3 process improvements) has reduced our overall procurement risk score from 336 to 303, a risk reduction of **10%**

Mock processing assessment

Jaime TABERA

Operations and Quality manager
Barcelona Tissue Bank (Spain)

BANC DE SANG I TEIXITS

Current Preparation Process

- Assumes a 'worst case' preparation process, comprising:
  - Processing in grade A with grade D background
  - Weak sanitisation program
  - Processing is performed using non sterile gloves or garments
  - Tissues of different donors are processed in the same direct environment
  - Weak microbiological control over tissue and environment
  - The decontamination method is not validated

MiRCA evaluation of the current preparation process

- Several improvement opportunities
- Two strategies
  1. Quick improvements
  2. Extensive improvements

Options for preparation process improvement (1) - A quick improvement

Validated decontamination method that achieves (SAL ≤ 10-3)

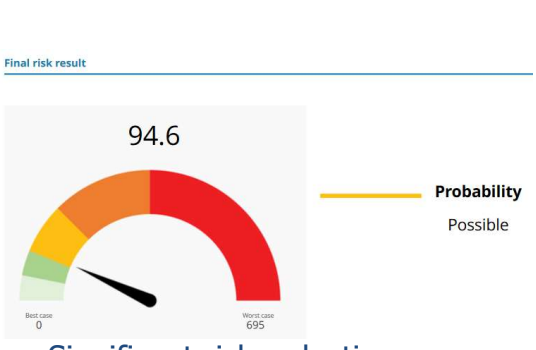
Revised MiRCA evaluation of the preparation process following improvement (1)

- Significant risk reduction
- Still several improvement opportunities

Options for preparation process improvement (2) - Extensive improvements

- Processing in grade A with grade C background
- Intensive sanitisation program
- Processing is performed using sterile gloves or garments
- Tissues from different donors are not processed in the same direct environment
- Intensive microbiological control over tissue and environment
- The decontamination method is validated

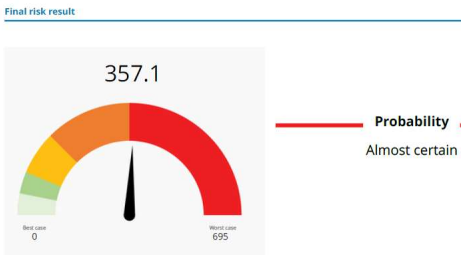
Revised MiRCA evaluation of the preparation process following improvement (2)



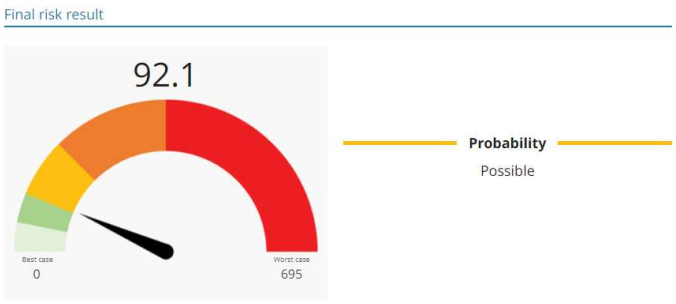
- Significant risk reduction
- Accumulative small residual risks can make it 'possible'
- Still some improvement opportunities

If we add the best improvement of procurement and processing to the initial example

Starting point



After applying improvements in procurement and processing steps



Relevance of MiRCA to tissue establishments and health authorities

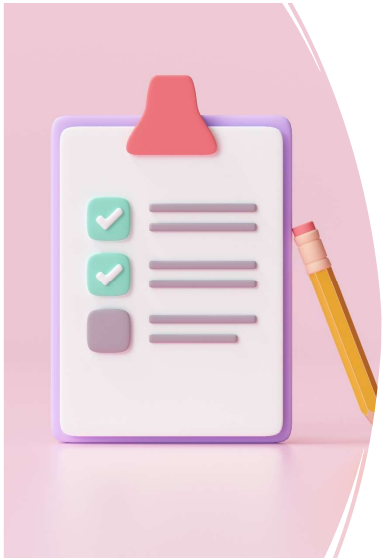
Akila CHANDRASEKAR

Chair European Committee on Organ Transplantation
Co-Chair Guide to the Quality and Safety of Tissues and Cells

Relevance to tissue establishments and/or procurement organisations

- A tool specifically developed for tissue establishments and/or procurement organisations
- Systematic method for evaluation of the risk of contamination throughout the process
- Easy to access and use, online format and possibility of storing the assessments
- Transparent and quantitative method for demonstrating the impact of process improvements
- Internal benchmarking and potentially external benchmarking
- Can be complementary to other risk assessment tools, such as EuroGTP2
- Generates evidence that can be presented to health/competent authorities as part of Preparation Process Dossiers (PPDs)
- Suggests most cost effective solutions to improve quality and safety

Advantages for competent/health authorities



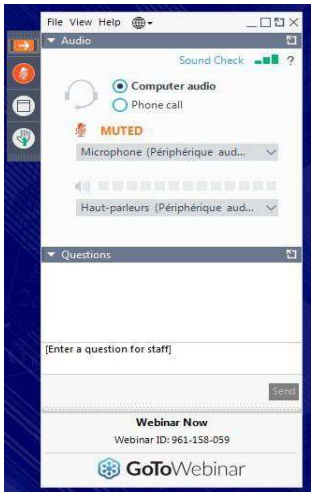
- Specifically developed for tissue establishments and/or procurement organisations
- Recognises the effort of tissue establishments to improve quality and safety
- Provides a standardised assessment report
- Transparent and objective methodology
- Realistic evaluation of risk; recognises that zero risk is not achievable
- Potential possibility of external benchmarking
- Allows the legal requirements established by the EU Directives to be checked objectively

General Advantages

- The report results in a complete and clear picture of the real situation as regards the risk of contamination.
- Improved processes may result in decreased risks and enhanced outcomes
- Flags quick and easy wins to improve quality and safety of tissues and cells
- Safer transplants and/or clinical applications

The floor is yours!

Type your question in the question panel and then click on 'Send'



Take home messages

Jacinto SÁNCHEZ-IBÁÑEZ

Co-Chair Guide to the Quality and Safety of Tissues and Cells

Take-home messages

- The MiRCA tool models the impact of any change in the procurement or processing protocols on the overall risk of a graft being contaminated
- It includes multiple independent and interconnecting risk factors
- No single risk factor (with the exception of terminal decontamination) is a 'game changer'
- To reduce the risk of contamination, and thus improve the safety of grafts, the whole process should be considered and optimised

Take-home messages

- There are other risk assessment tools that can be used effectively in the evaluation of risk contamination, with good results
- The added value of MiRCA is that you do not need to think about the risk factors, these are pre-defined in the tool
- MiRCA can be used to document and record the decisions made and rationales used in the different stages of the risk assessment process, and the outcome can be printed

Take-home messages

- The report can be used as evidence for health authorities to show that an appropriate risk assessment process has been undertaken, as required by the legislation, with respect to novel and modified aseptic processes and an evaluation of the potential reduction of risk contamination has been performed
- Permits mock evaluations, simple to use and provides rapid feedback on where to reduce risks
- The owner of each report is the person that performs the evaluation, guaranteeing data protection and confidentiality
- Please help us to improve the tool: share your feedback and your microbiological results during your assessments
- The tool will be revised periodically

Have you created your account in MiRCA?????

https://soho-guides.edqm.eu/register/account/

Thank you for your attention

Stay connected with the EDQM

EDQM Newsletter: **https://go.edqm.eu/Newsletter**
LinkedIn: **https://www.linkedin.com/company/edqm/**
Twitter: **@edqm_news**
Facebook: **@EDQMCouncilofEurope**