

# PROACTIVE APPROACHES for QUALITY MANAGEMENT

Anabela Martins  
Micoteca da Universidade do Minho

Standard  
development  
procedure

Reference  
sources

Structure

Interpreting  
the  
provisions

Recognition  
scheme  
(foreseen)

Procedure  
for  
commenting

# ISO 20 387 standard Biobanks

Quality by Testing  
Approach

Quality by Design  
Approach

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# ISO 20 387

ISO TC 276

WG2

ISO TC 276

WG2

**DRAFT INTERNATIONAL STANDARD**  
**ISO/DIS 20387**

ISO/TC 276  
Voting begins on:  
2017-07-20

Secretariat: DIN  
Voting terminates on:  
2017-10-11

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**Biotechnology — Biobanking — General requirements for  
biobanking**

*Titre manque*

ICS: 07.080

Secretariat: **DIN**

Voting terminates on:  
**2017-10-11**

Titre manque

ICS: 07.080

# Method

## Standard development (general procedure)

Establishment of  
the scope

Recognition  
scheme and type  
of standard

Establishment of  
the type of S,  
structure and  
provisions

Commenting  
stages

Discussion  
inside the TC

Standard in DIS  
stage

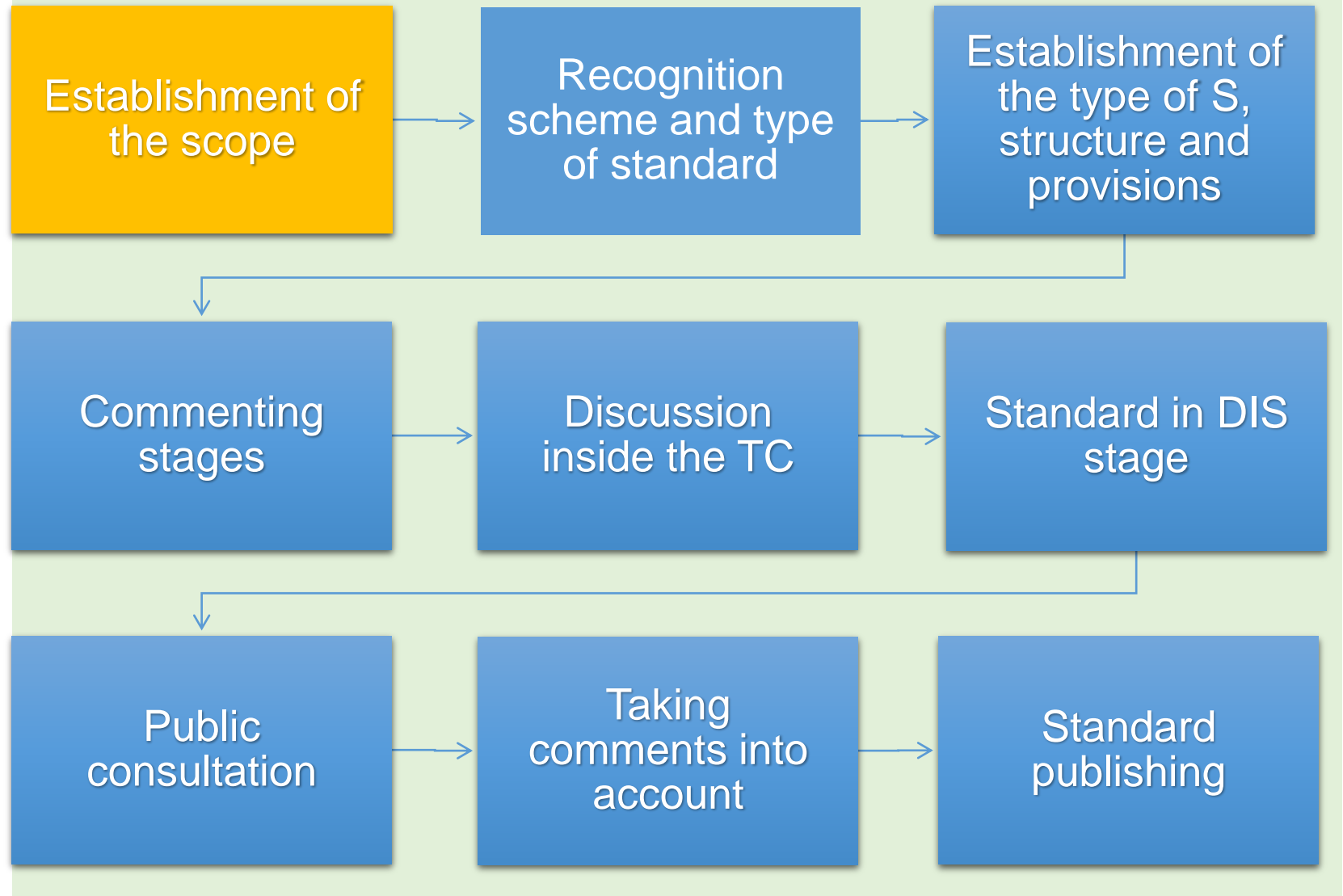
Public  
consultation

Taking  
comments into  
account

Standard  
publishing

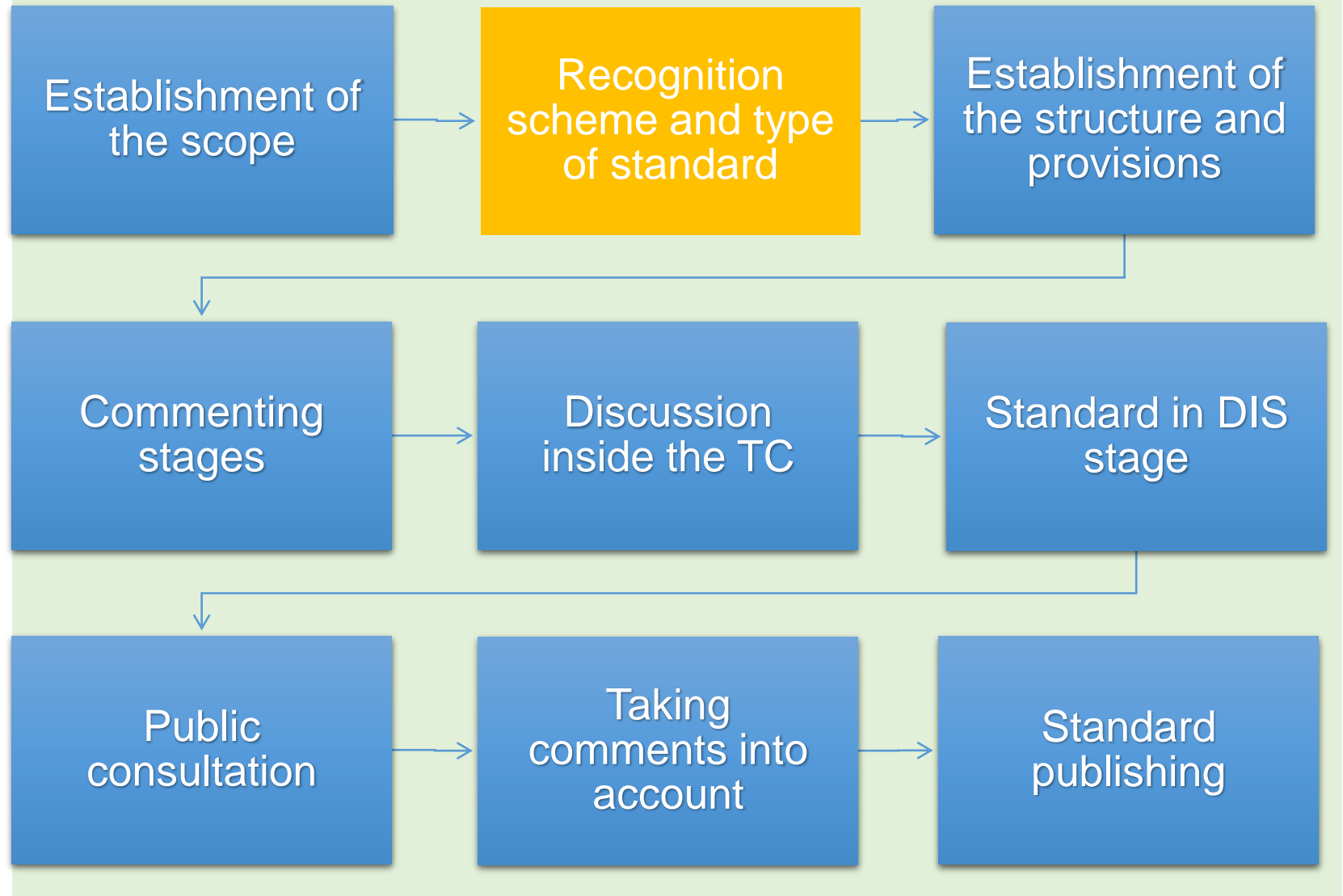
# Method

## Standard development (general procedure)



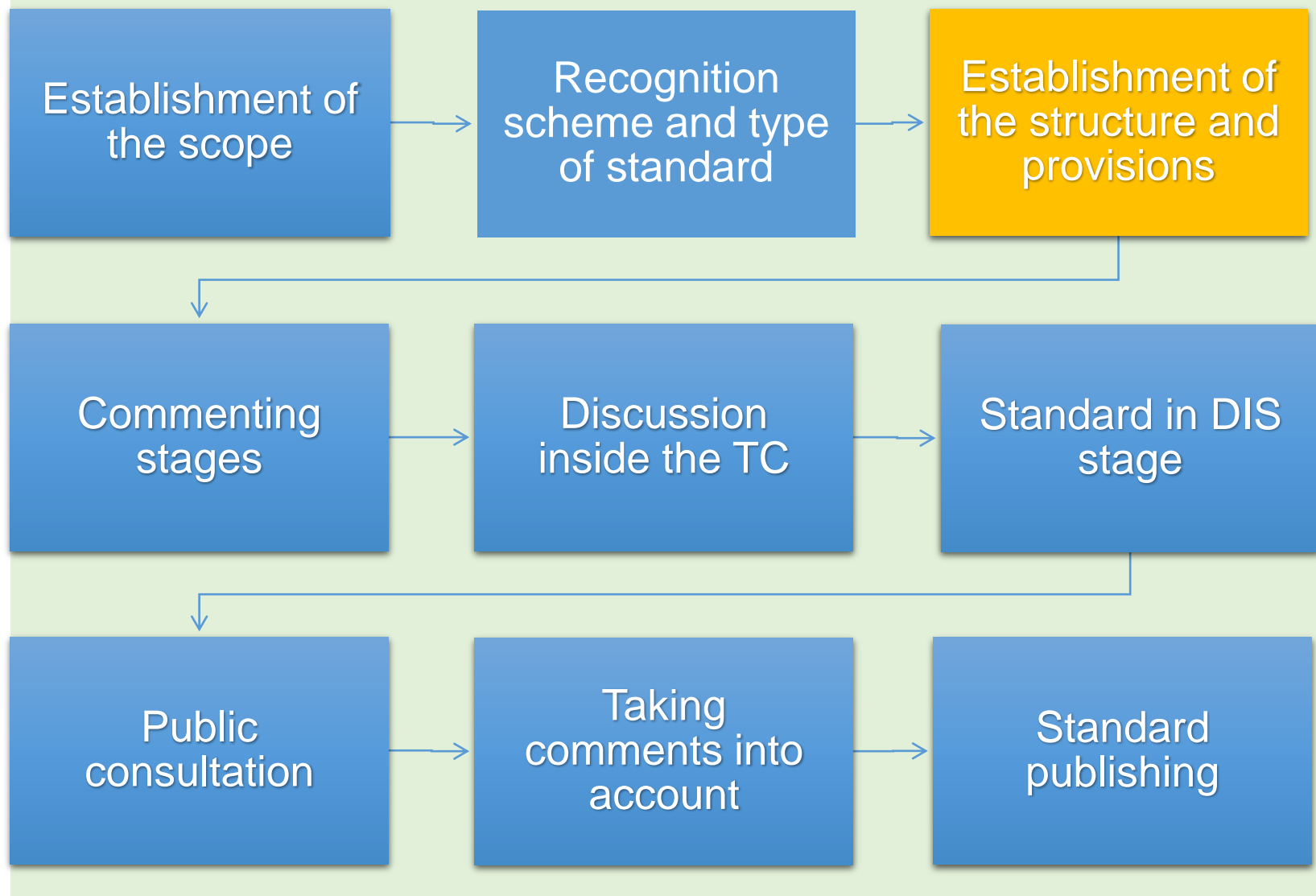
## Method

## Standard development (general procedure)



## Method

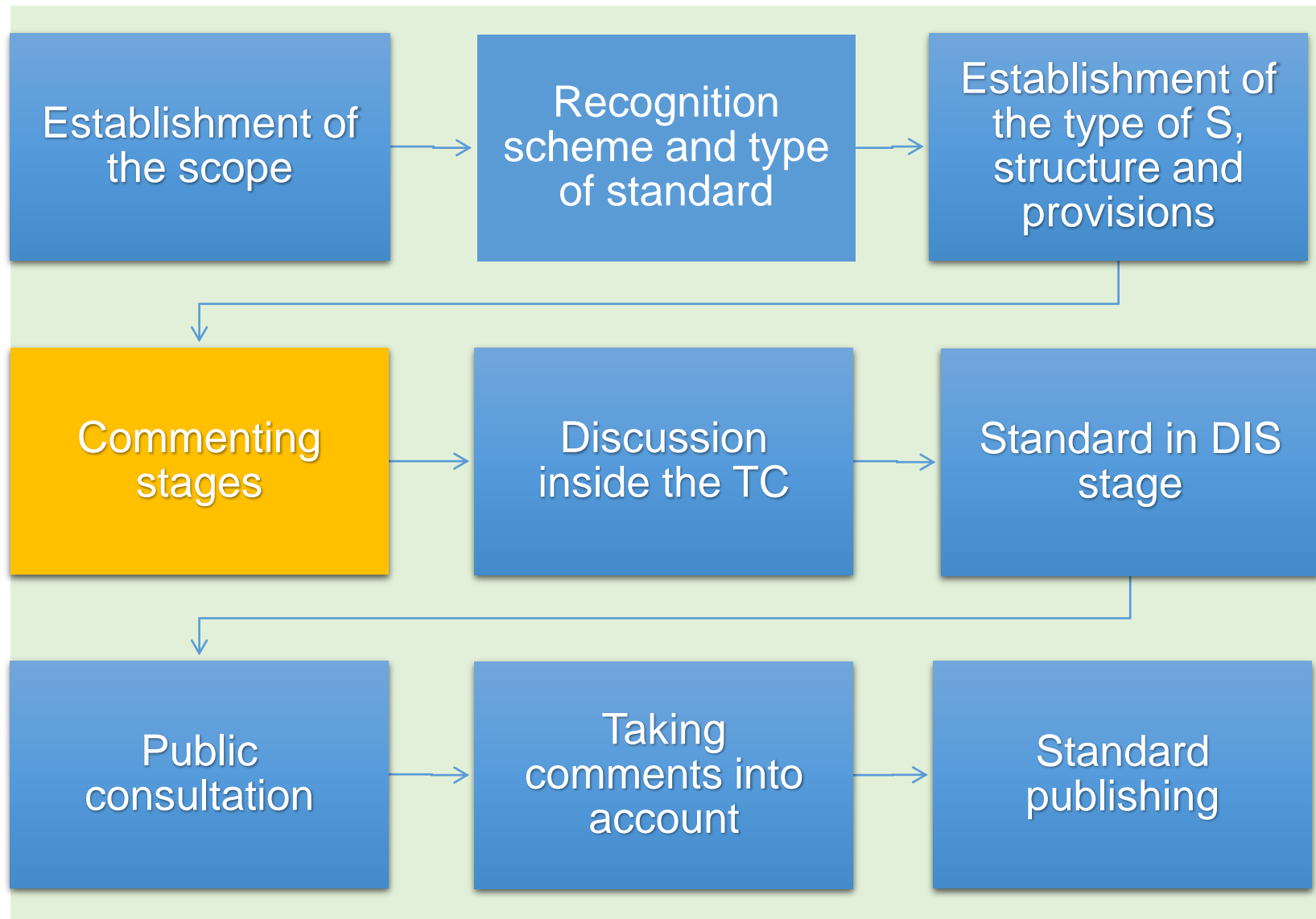
## Standard development (general procedure)





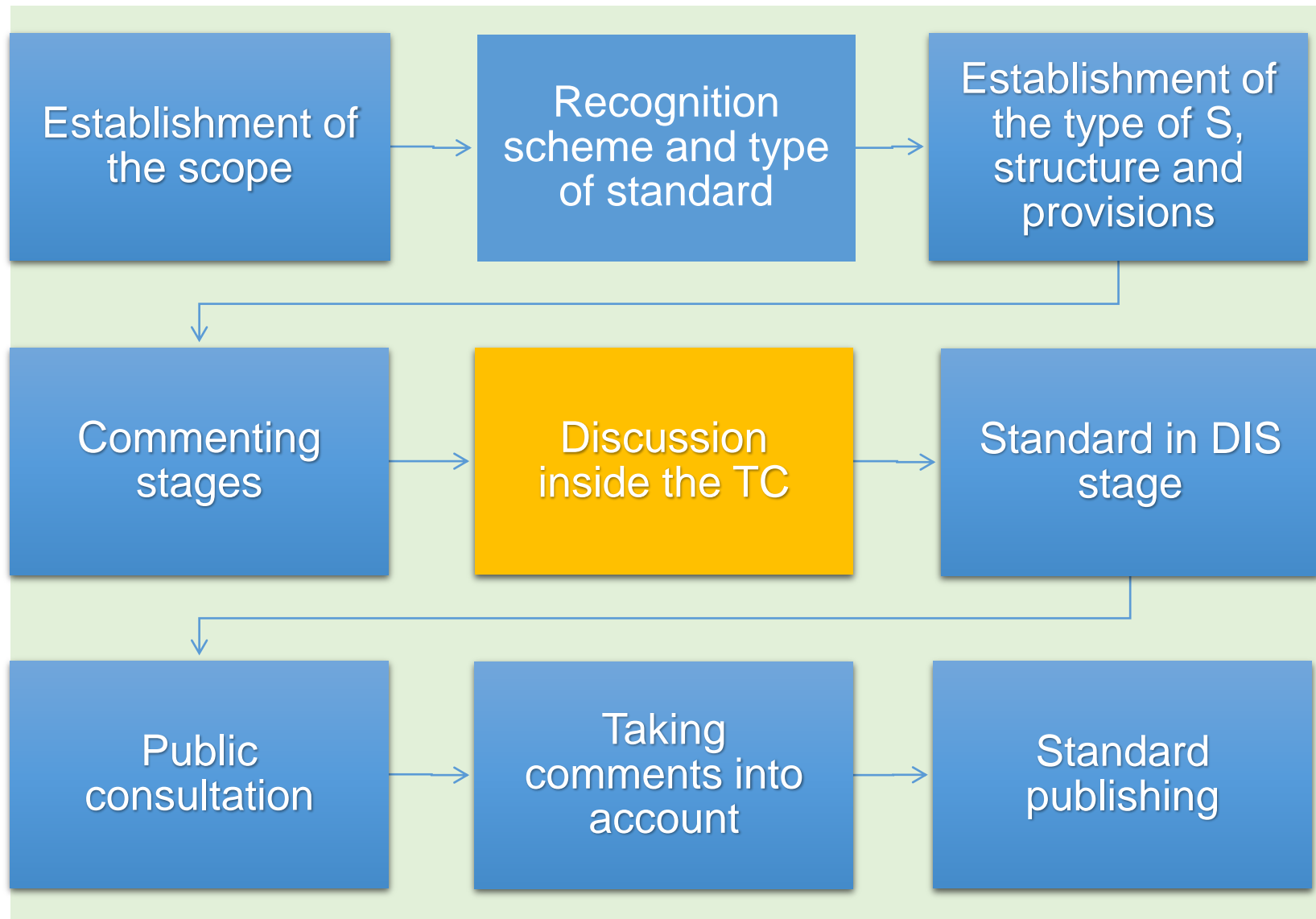
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## Standard development (general procedure)



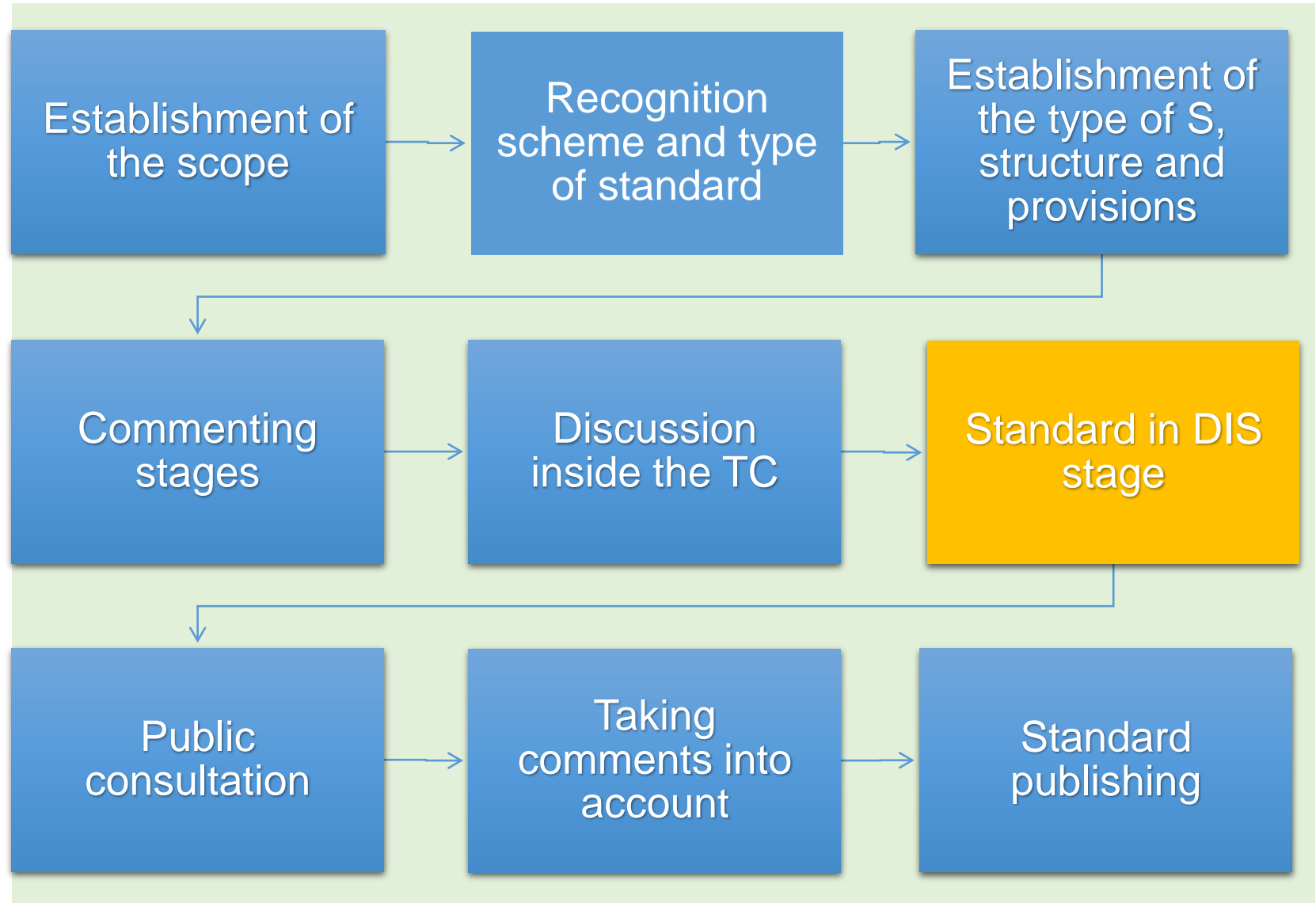
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## Standard development (general procedure)



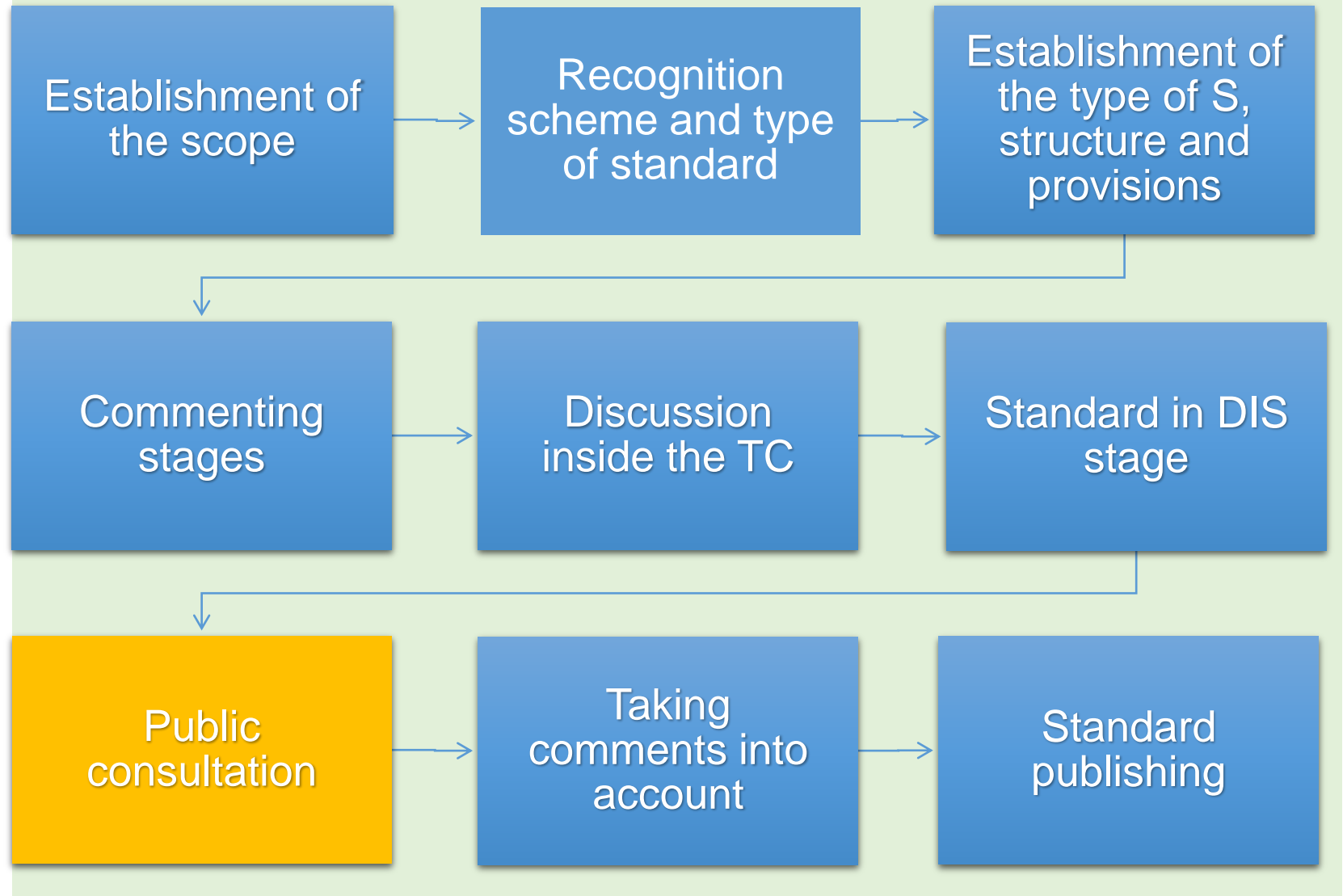
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publishing



## Method

## Reference sources

- OECD BPG 2007
- NFS 96-900 Quality management of BRCs and quality of biological resources
- NCI Best Practices
- UK Biobank Quality Standards
- MMI Guidelines for Standardized Biobanking
- ISO 9001
- ISO/IEC 17025



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# ISO/DIS 20387

## Structure

4. General requirements

5. Structural requirements

6. Resource requirements

7. Processes requirements

8. Management requirements - Option A | Option B

Annex A Documentation requirements



ISO TC 276

Standard's  
provisions

It conveys two main kinds of provisions:

Requirements

Recommendations

ISO TC 276

Standard's  
provisions

## RECOMMENDATION

"expression (...) conveying a suggested possible choice or course of action deemed to be particularly suitable without necessarily mentioning or excluding others."

“should”

ISO TC 276

Standard's  
provisions

## REQUIREMENT

"expression in the content of a document  
(...) from which no deviation is permitted  
if compliance with the document is to be  
claimed."

**"shall"**

# ISO 20 387

# Provisions

# REQUIREMENTS

clear, objective and verifiable

# REQUIREMENTS

clear, objective and verifiable

ISO 20 387

Provisions

## REQUIREMENTS

Must not block innovation and flexibility in  
biobanks -  
they should be expressed in terms of  
process management and performance  
criteria





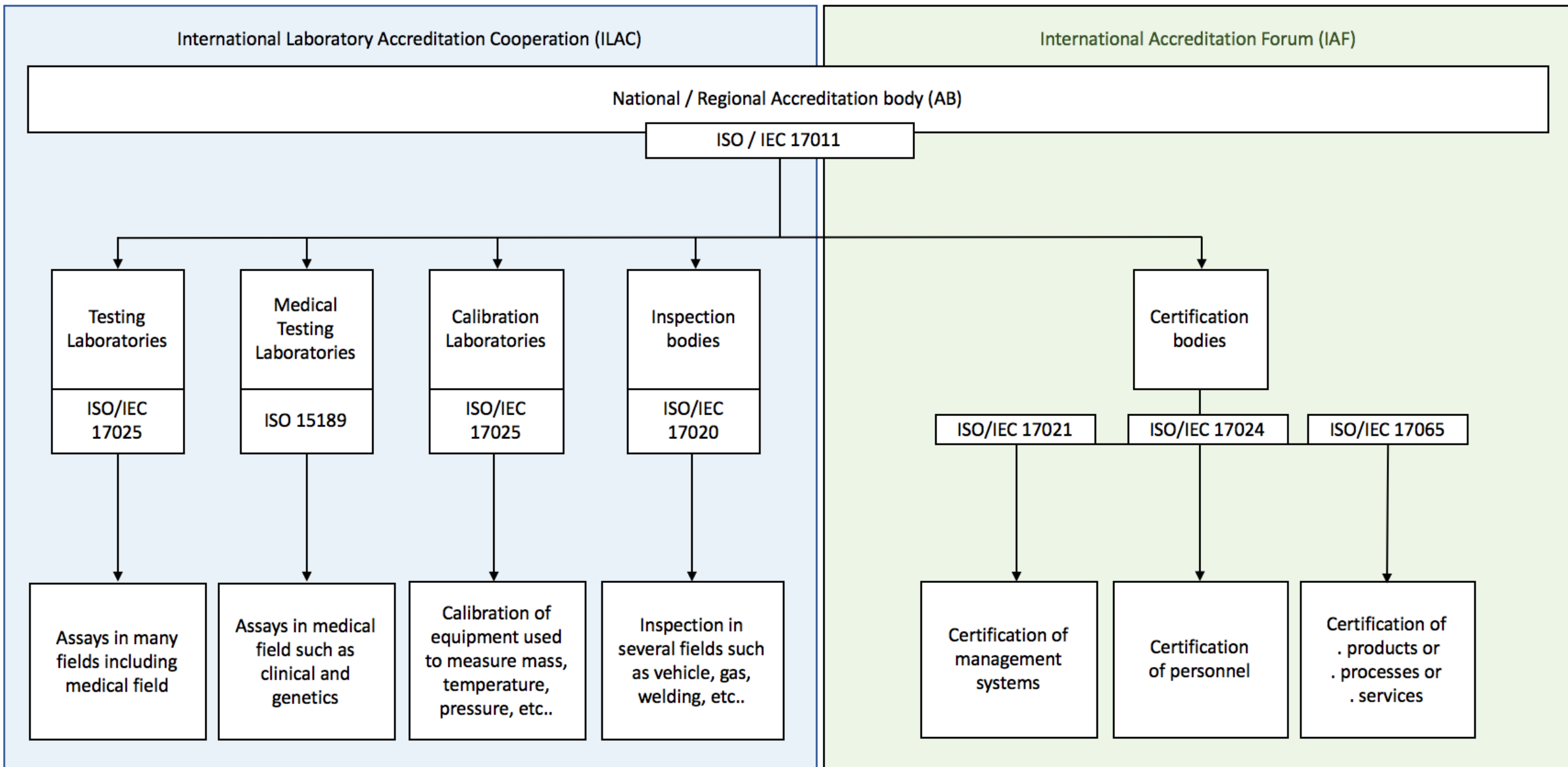
ISO/DIS 20387

Accreditation

## Accreditation of Biobanks



Recognition of the technical competence  
of biobanks to perform testing on  
biological material



International Laboratory Accreditation Cooperation (ILAC)

International Accreditation Forum (IAF)

National / Regional Accreditation body (AB)

ISO / IEC 17011

Biobanking

Testing  
Laboratories

Medical  
Testing  
Laboratories

Calibration  
Laboratories

Inspection  
bodies

Certification  
bodies

ISO 20387

ISO/IEC  
17025

ISO 15189

ISO/IEC  
17025

ISO/IEC  
17020

ISO/IEC  
17021

BM testing

Assays in many  
fields including  
medical field

Assays in medical  
field such as  
clinical and  
genetics

Calibration of  
equipment used  
to measure mass,  
temperature,  
pressure, etc..

Inspection in  
several fields such  
as vehicle, gas,  
welding, etc..

Management  
systems  
certification

Personnel  
certification

Product / service  
certification

International Laboratory Accreditation Cooperation (ILAC)

International Accreditation Forum (IAF)

National / Regional Accreditation body (AB)

ISO / IEC 17011

Testing  
Laboratories

ISO/IEC  
17025

Assays in many  
fields including  
medical field

Medical  
Testing  
Laboratories

ISO 15189

Assays in medical  
field such as  
clinical and  
genetics

Calibration  
Laboratories

ISO/IEC  
17025

Calibration of  
equipment used  
to measure mass,  
temperature,  
pressure, etc..

Inspection  
bodies

ISO/IEC  
17020

Inspection in  
several fields such  
as vehicle, gas,  
welding, etc..

Certification  
bodies

ISO/IEC 17021

Certification of  
management  
systems

ISO/IEC 17024

Certification  
of personnel

ISO/IEC 17065

Certification of  
. products or  
. processes or  
. services

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Quality by Design  
Approach



ISO TC 276

Public  
consultation

National Standard  
Body

Deadline:  
???

Deadline:  
Oct 11

Comments

ISO



# ISO 20 387

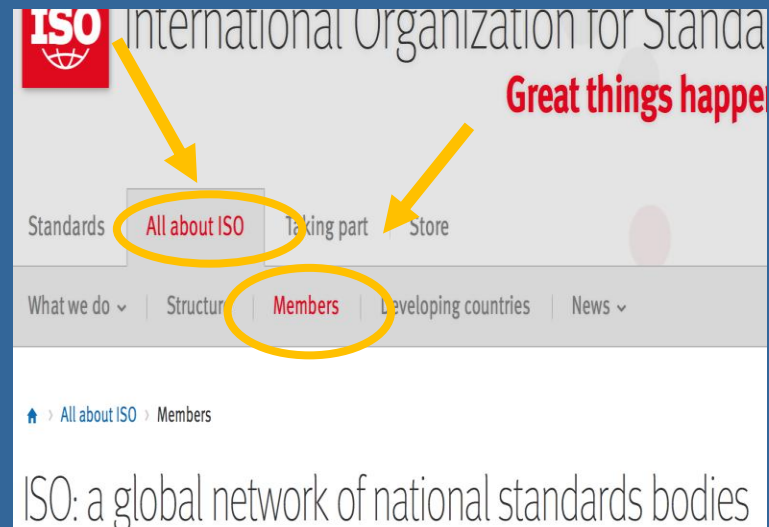
## Public consultation

# How to find the National Standard Body contact

# ISO TC 276

Public  
consultation

*National  
standard body*



Cuba	NC
Cyprus	CYS
Czech Republic	UNMZ
Côte d'Ivoire	CODINORM
Denmark	DS

## UNMZ

Czech Republic

Membership: Member body

The work of technical standardization in the country was started by the Czechoslovak Electrotechnical Association, established in 1919, and by the Czechoslovak Association of Standardization, established in 1922. In 1951, the activities of the two organizations were combined, and the Office for Standardization and Measurements was set up. The Federal Office for Standards, Metrology and Testing was established in 1968.

Since January 1993, after the splitting of Czechoslovakia into two independent states, the

Czech Office for Standards, Metrology and  
Testing

Biskupský dvůr 1148/5  
110 00 Praha 1  
Czech Republic

Tel: +420 2 21 80 21 11 / +420 224 907 175  
Fax: +420 221802300  
E-mail: [unmz@unmz.cz](mailto:unmz@unmz.cz)

[UNMZ Website](#)

## Template for comments and secretariat observations

Date:	Document:
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1	2	(3)	4	5	(6)	(7)
MB <sup>1</sup>	Clause No./ Subclause No./ Annex (e.g. 3.1)	Paragraph/ Figure/Table/ Note (e.g. Table 1)	Type of com- ment <sup>2</sup>	Comment (justification for change) by the MB	Proposed change by the MB	Secretariat observations on each comment submitted
PT	5.1	note	●	Justification	Provision re-written	

ge / te / ed

- general
- technical
- editorial

Standard development procedure	Reference sources	Structure	Interpreting the provisions	Recognition scheme (foreseen)	Procedure for commenting
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# ISO 20 387 standard Biobanks

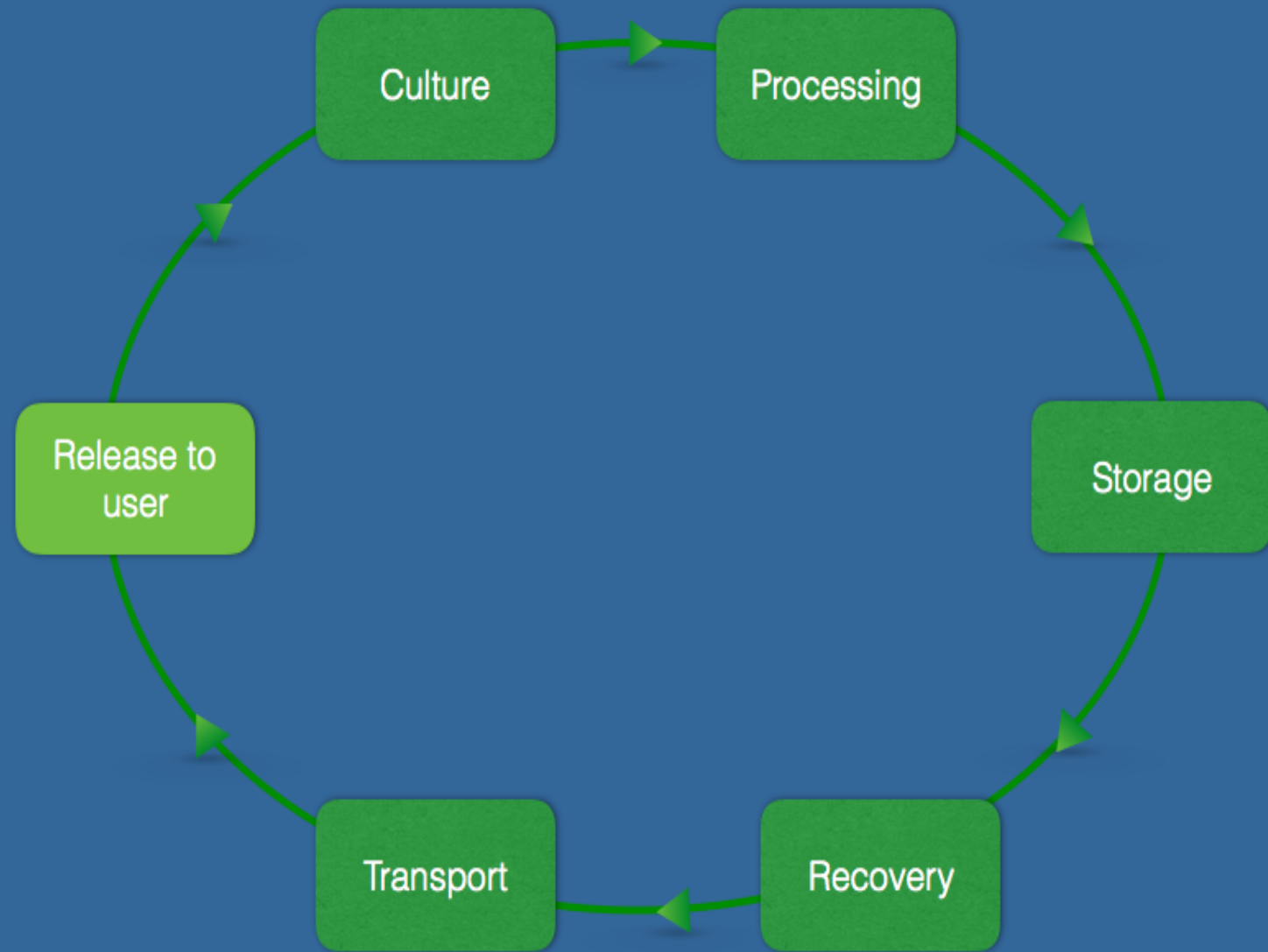
7

Quality by Testing  
Approach

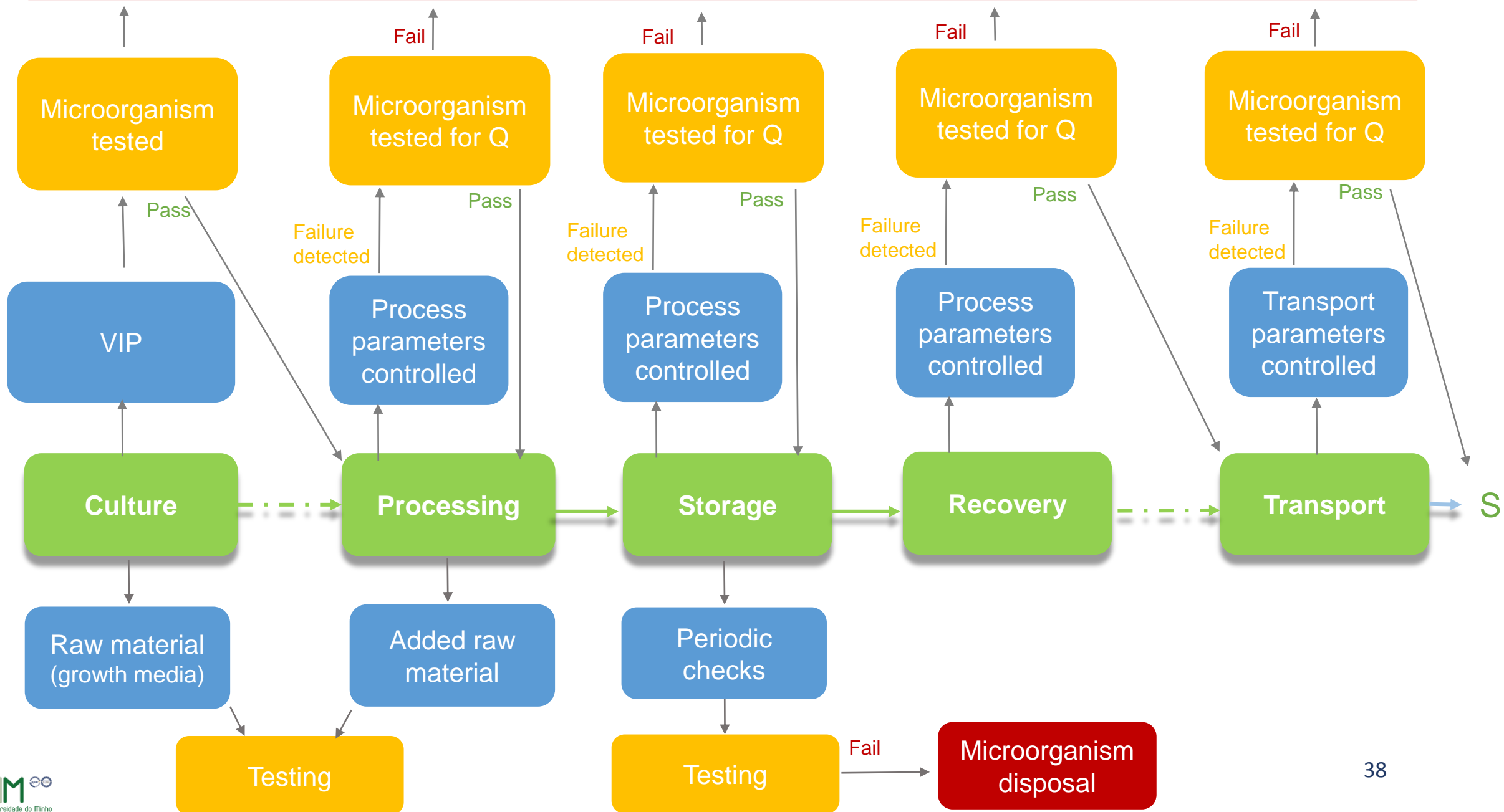
Quality by Design  
Approach

QbT

The  
microorganism  
preservation  
lifecycle

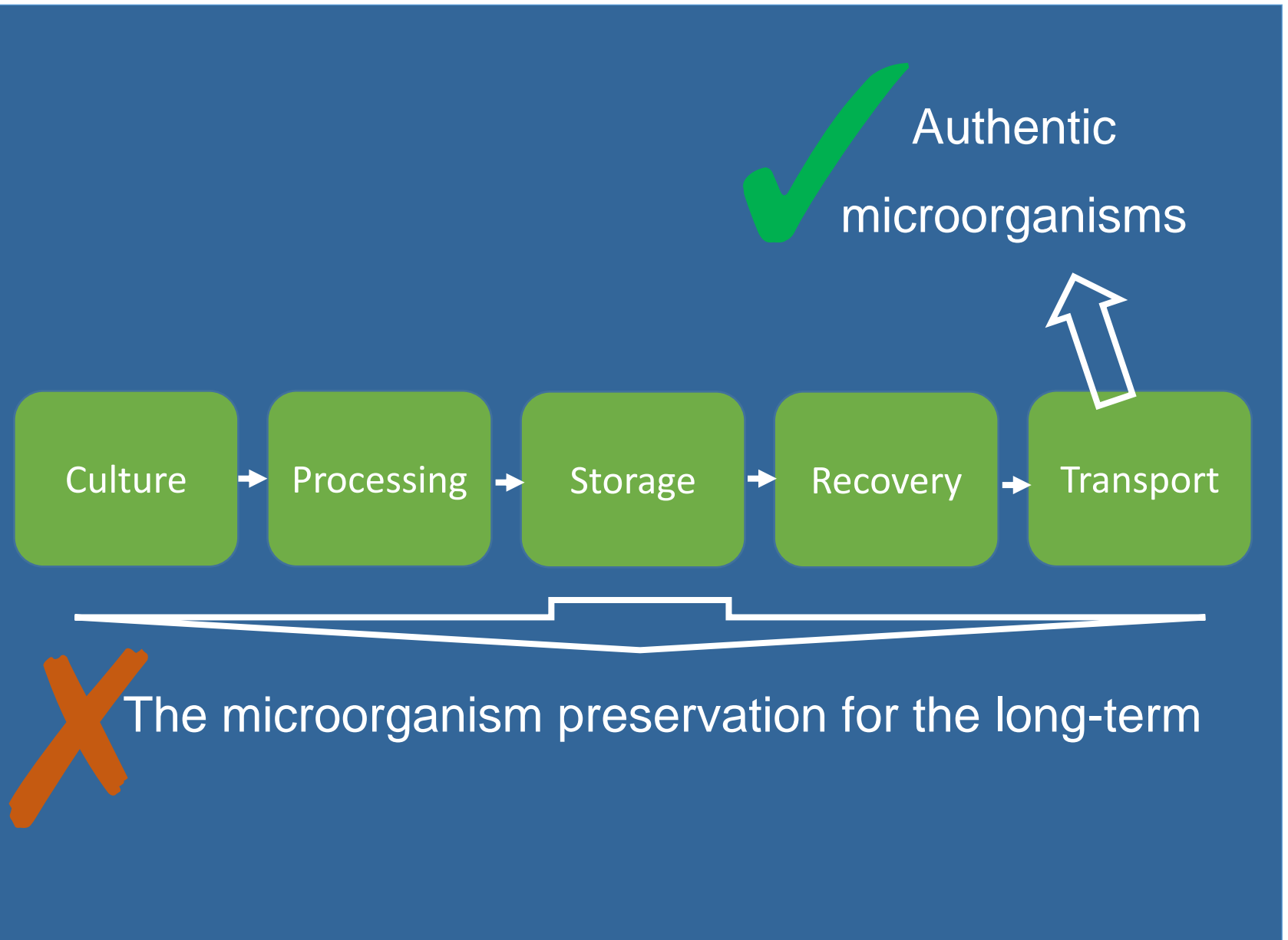


# Microorganism disposal



# Approaches to Q

Results from QbT



Standard development procedure	Reference sources	Structure	Interpreting the provisions	Recognition scheme (foreseen)	Procedure for commenting
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# ISO 20 387 standard Biobanks

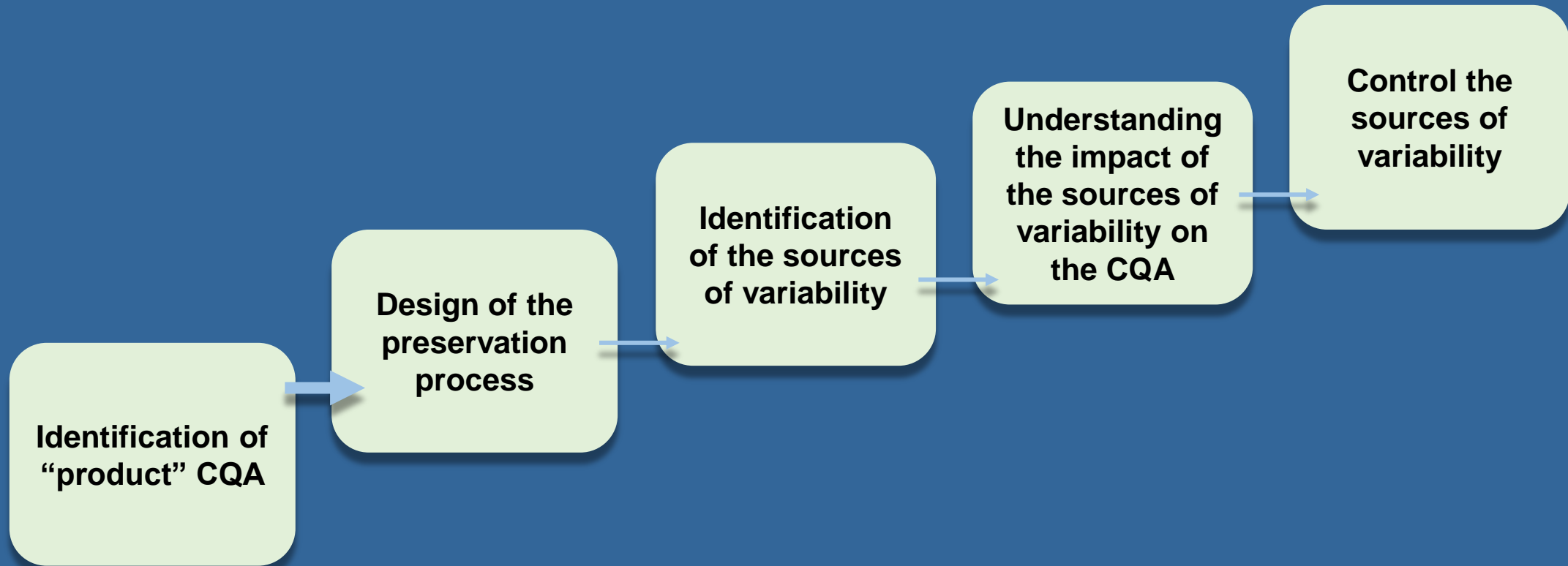
Quality by Testing  
Approach

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Quality by Design  
Approach



# Quality by Design \_ capturing process knowledge



# Quality by Design

Risk Assessment (RA)

Design of experiments (DOE)

Design space (DS)

# Risk assessment \_ Check-list

## Identification of all the process factors

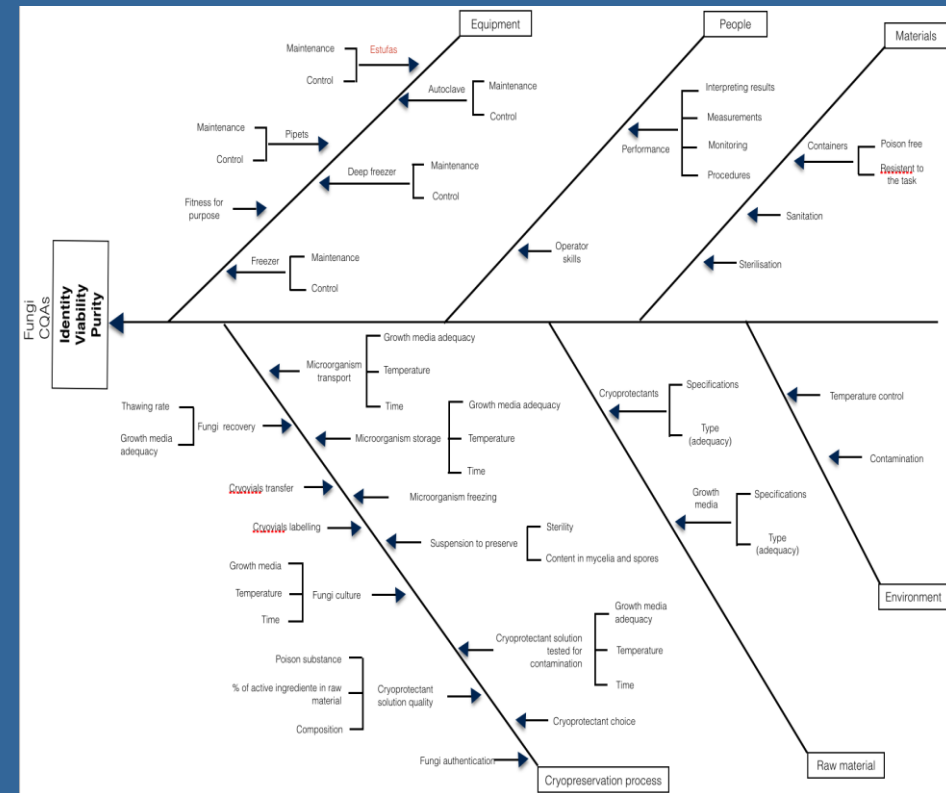
FACTORS	PP	AA	RM	WEC	O	M	E	U	P	Mth
Cryoprotectant temperature	✓									
Cryoprotectant components mass	✓									
Cryoprotectant suspension aliquots mass	✓									
Sterilisation temperature	✓									
Sterilisation time	✓									
Incubation temperature	✓									
Incubation time	✓									
Temperature decreasing rate in the freezing container	✓									
Time for freezing (freezing container)	✓									
Time for transfer	✓									
Transfer temperature conditions	✓									
Storage temperature	✓									
Temperature increasing rate	✓									
Cryoprotectant			✓							
Temperature				✓						
Humidity				✓						
Sterility				✓		✓				
Sanitation				✓		✓		✓		
Microorganism authenticity		✓								
Microorganism purity		✓								
Microorganism viability		✓								
Calibration							✓			
Maintenance							✓			
Fitness for purpose			✓				✓		✓	✓
Effectiveness					✓		✓		✓	✓
Consistency					✓				✓	✓
Competence	✓				✓					
Specification			✓			✓		✓		

Process parameters	PP	M	Material
Authentication attributes	AA	E	Equipment
Raw material	RM	U	Utilities
Work environment conditions	WEC	P	Procedures
Operator	O	Mth	Methods

# Risk assessment \_ Ishikawa diagram

Identification of  
potential risks and  
their causes



# Risk assessment \_ Failure Mode and Effect Analysis

## Scoring the factors in terms of Risk Priority Number

(arithmetic product of the I, L and A)

Stage in cryopreservation process	Potential failure	Potential effect of failure	Impact	Potential cause of failure	Likelihood	Existing control for prevention	Existing control for detection	Ability to detect	RPN
Microorganism culture	Absence of microorganism growth	Loss of microorganism	5	Operator lacking skills	1	---	---	2	10
				Type of growth media not adequate	1	---	---	2	10
				Growth media lacking quality due to components low quality	1	---	---	2	10
				Growth media lacking quality due to fail in preparation	1	---	---	2	10
				Growth media out of date	2	Growth media labelling	---	1	10
Suspension to preserve (quality)	Lack of sterilisation	Failure in purity	5	Failure in sterilisation procedure	2	---	Sample incubation	1	10
	Absence of spores and mycelia in the suspension	Microorganism not preserved	5	Operator lacking skills	1	Operator training	---	2	10
Cryovials labelling	Failure in shelf life record	Loss of microorganism	5	Operator failure	1	---	---	3	15
	Wrong name	Loss of microorganism	5	Operator failure	1	---	---	3	15
Microorganism freezing	Decreasing temperature rate not adequate	Cell damage	5	Freezing container does not provide the necessary freezing rate	2	---	---	2	20
				Wrong setting	2	---	---	3	30
	Temperature failure in the freezing container	Cell damage	5	Equipment failure	2	---	---	3	30
				Equipment failure	2	---	---	3	30
	Time failure in the freezing container	Cell damage	5	Operator failure	2	---	---	3	30

# Design of Experiments (DOE)

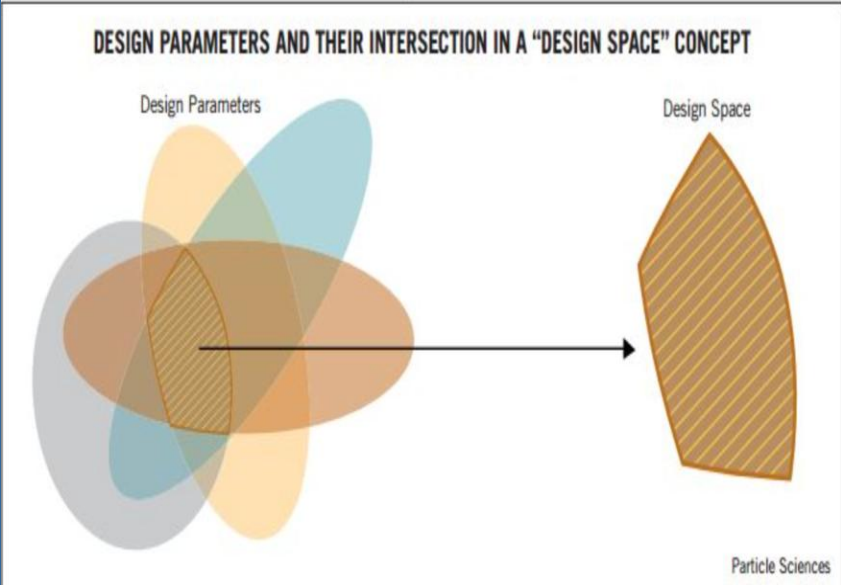
Screening  
significant factors  
influencing CQA

Run	A	B	C	Shrinkage
1	-1	-1	-1	2.22, 2.11, 2.14
2	+1	-1	-1	1.42, 1.54, 1.05
3	-1	+1	-1	2.25, 2.31, 2.21
4	+1	+1	-1	1.00, 1.38, 1.19
5	-1	-1	+1	1.73, 1.86, 1.79
6	+1	-1	+1	2.71, 2.45, 2.46
7	-1	+1	+1	1.84, 1.76, 1.70
8	+1	+1	+1	2.27, 2.69, 2.71

Source: Jiju Antony; Design of Experiments for Engineers and Scientists

## Design Space

# Multidimensional combination and interaction of factors that have been demonstrated to provide quality assurance

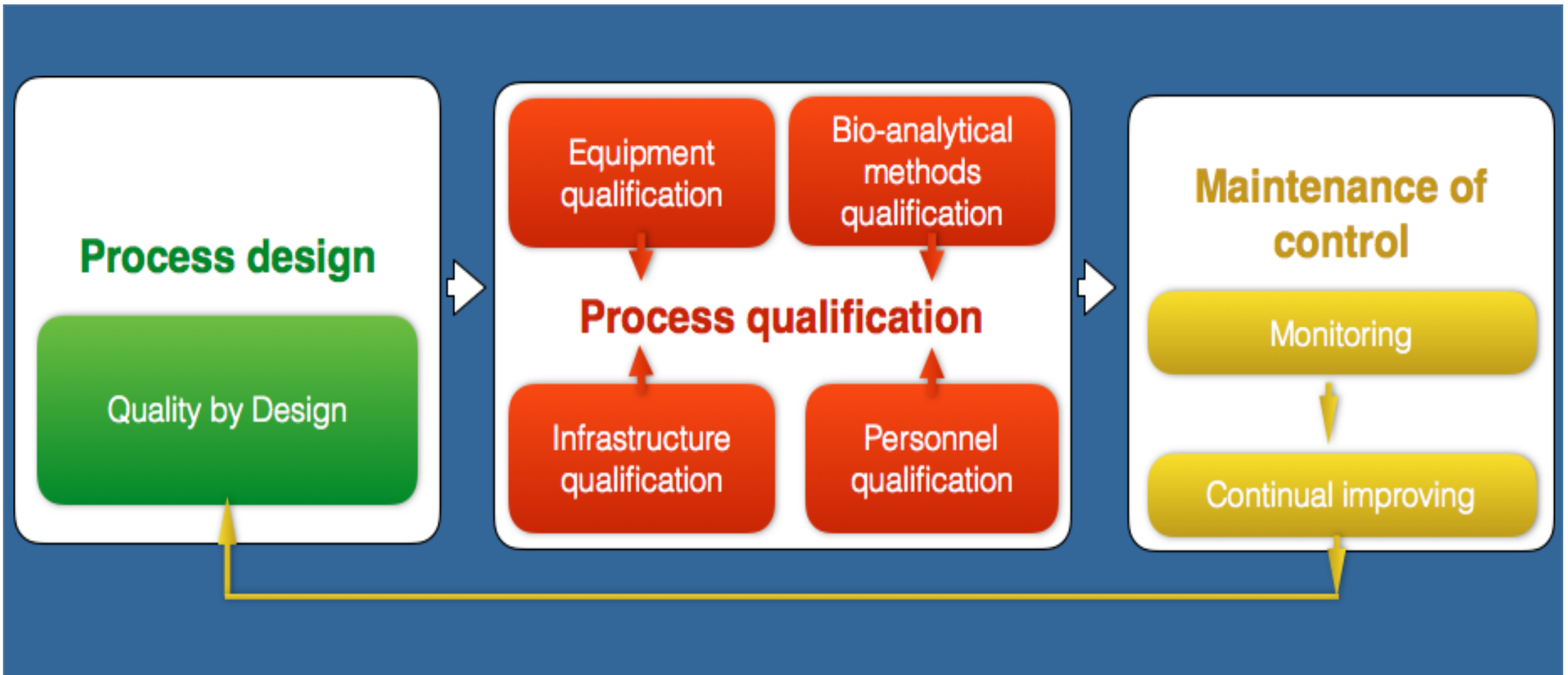


# Design Space

How to integrate QbD in a standard?

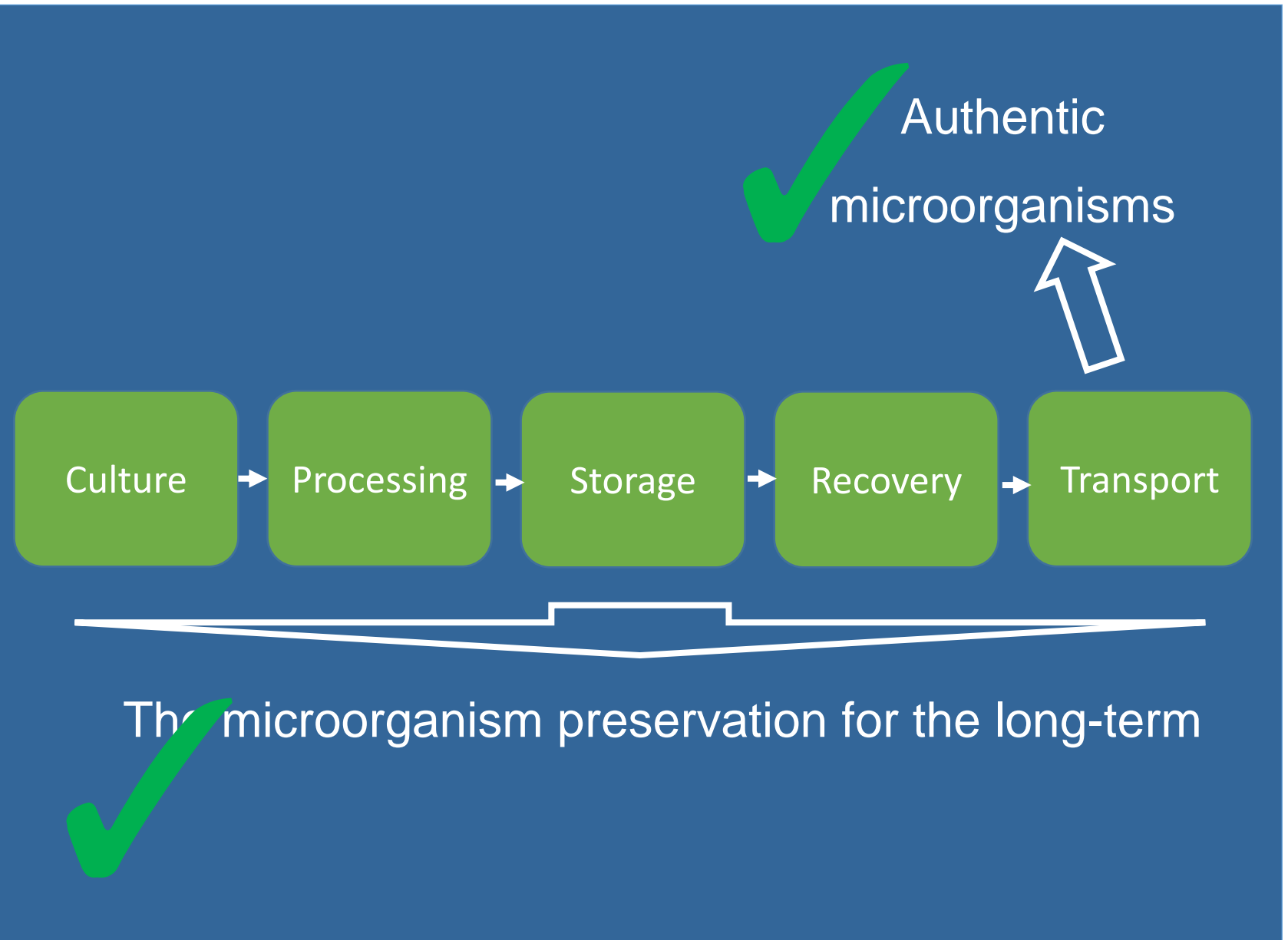


# Integration of QbD in standards

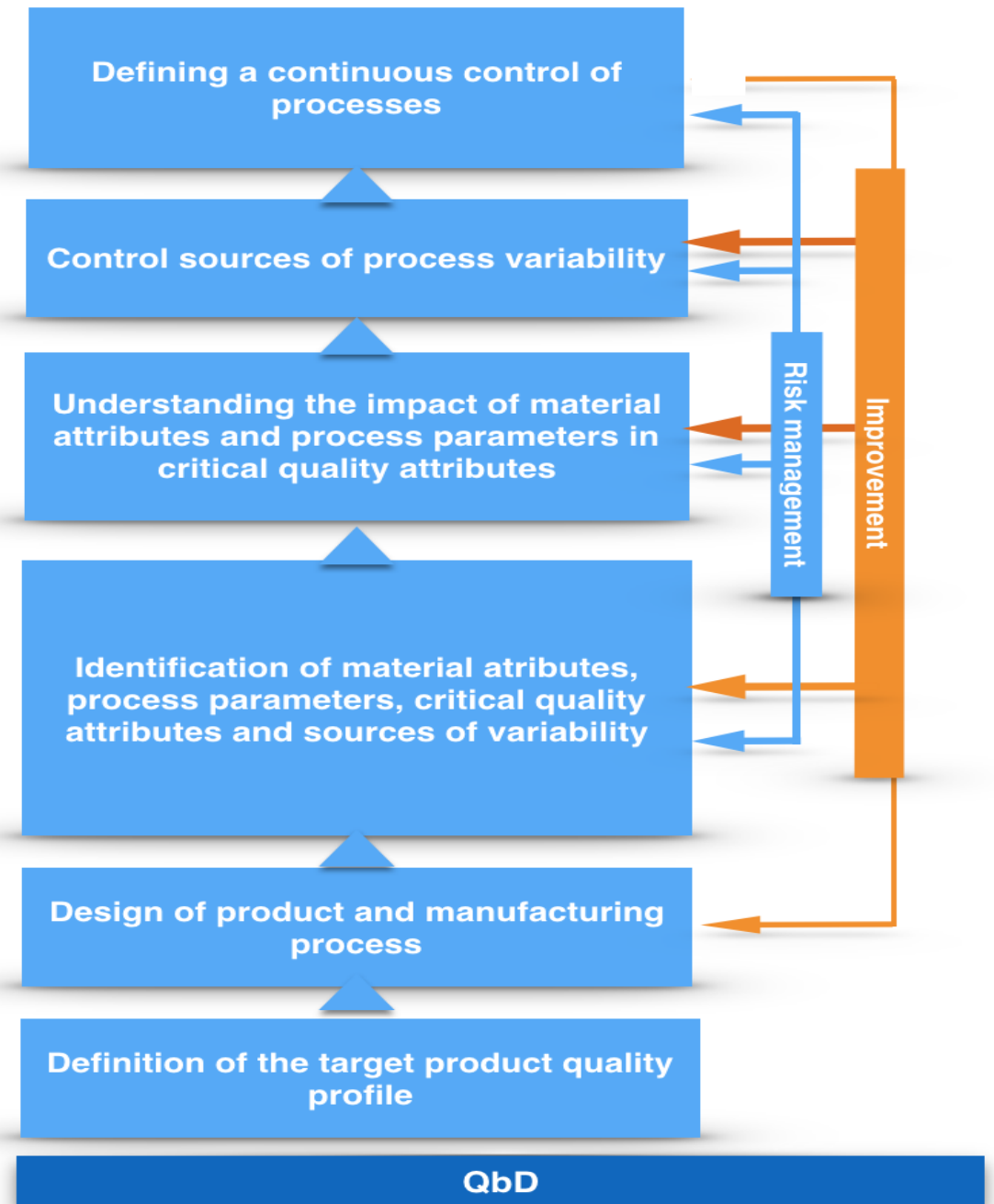
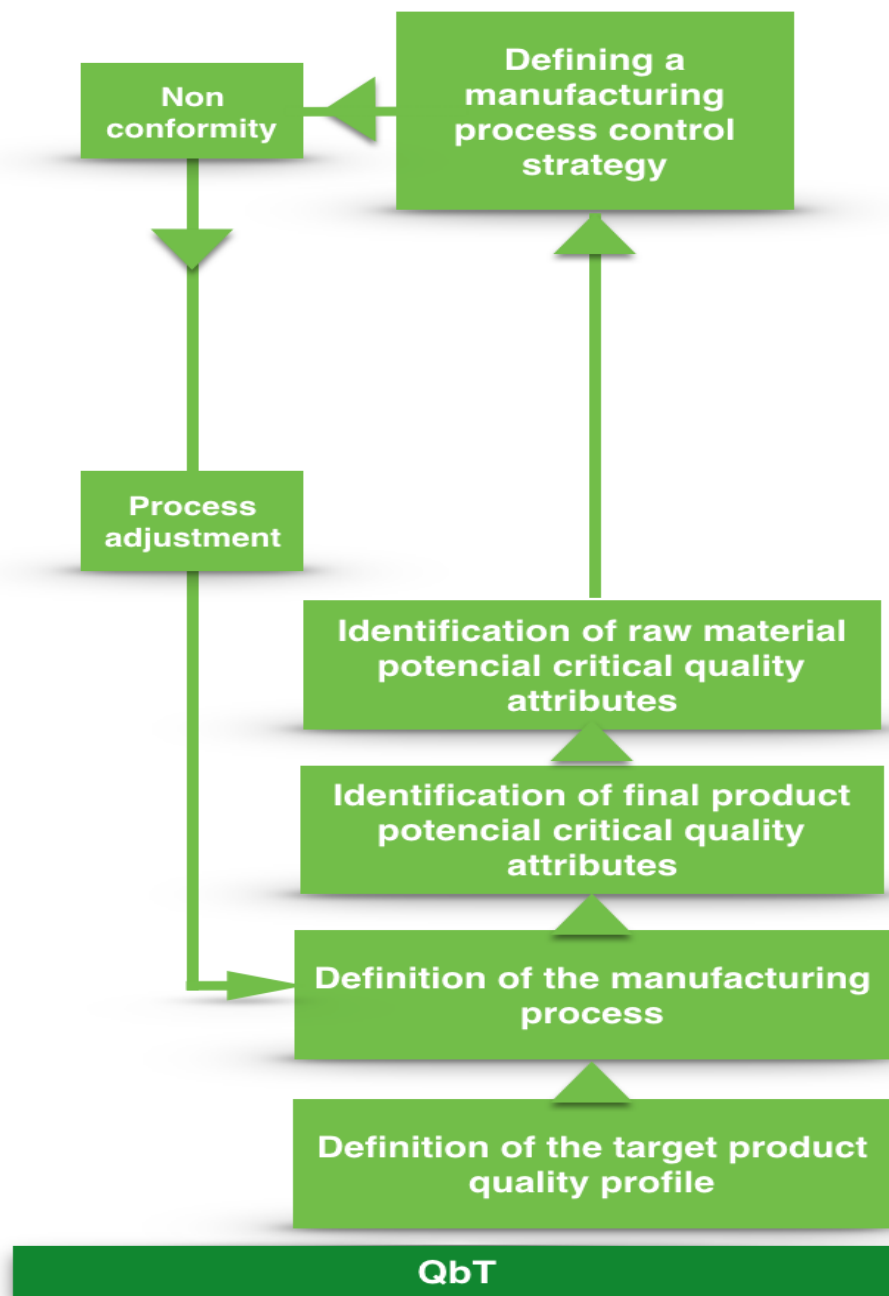


# Microbial BRC

Result

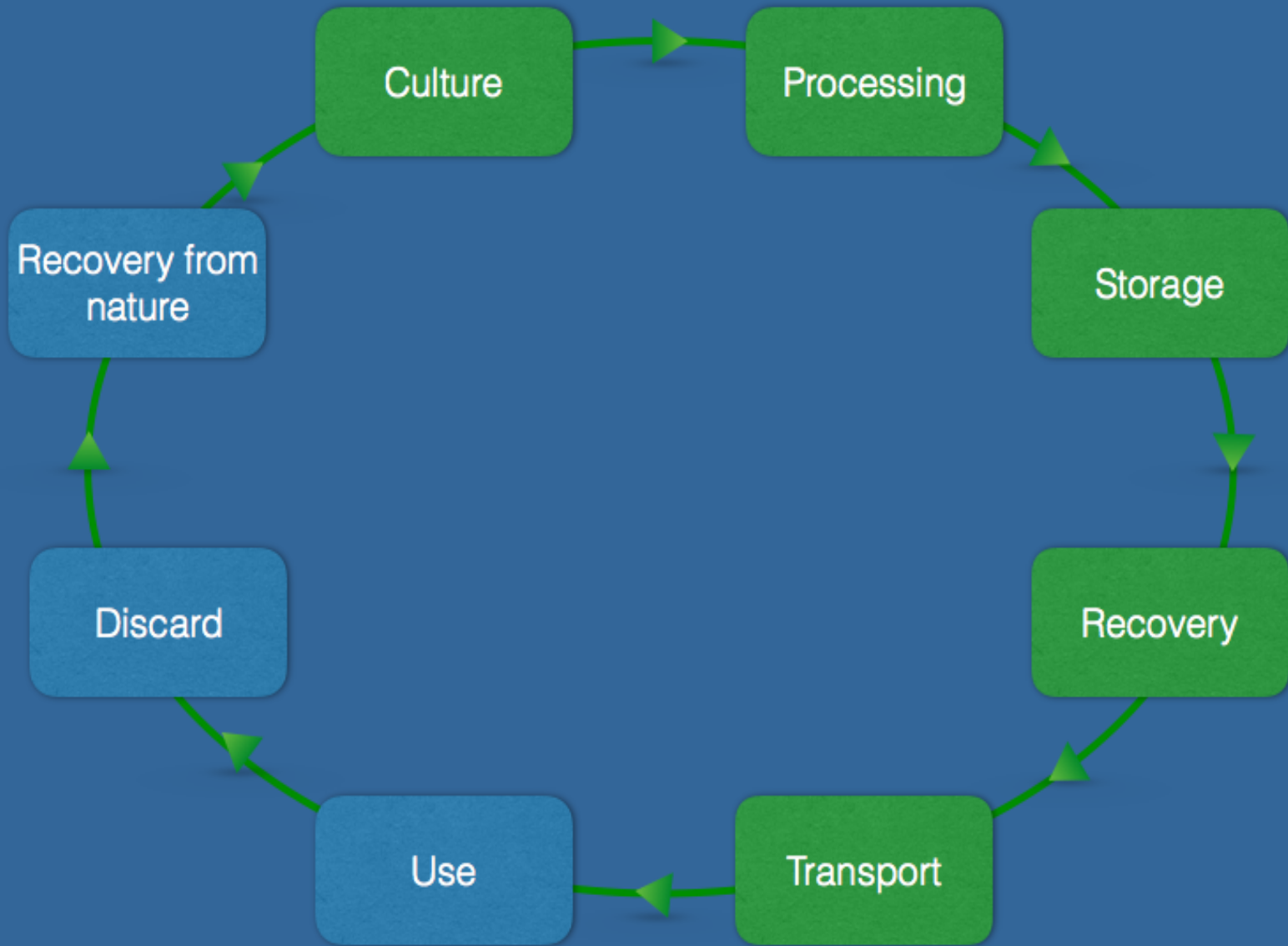


Thank you  
for your kind attention



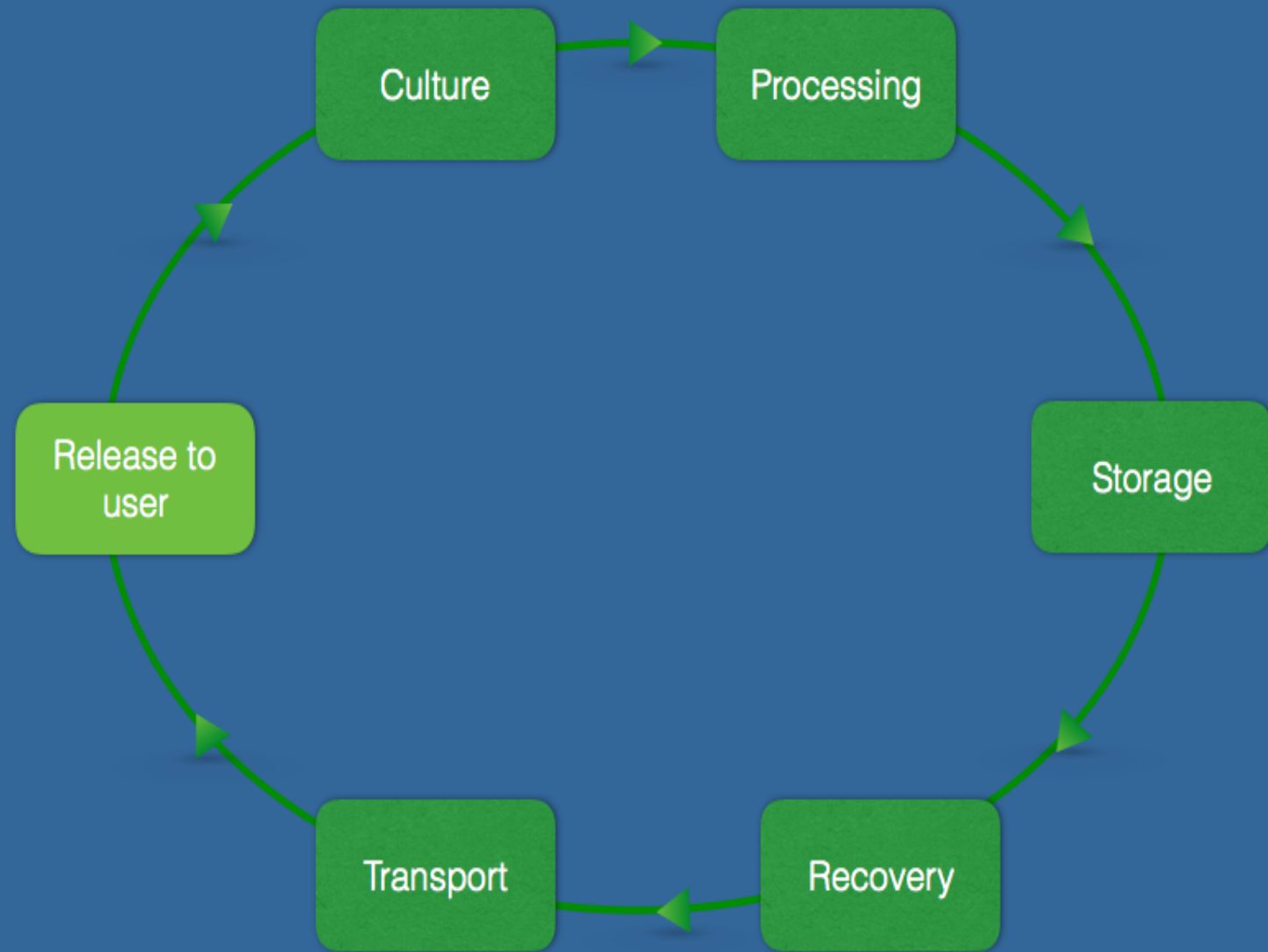
QbT

The  
microorganism  
technological  
lifecycle



QbT

The  
microorganism  
preservation  
lifecycle



QbT

The  
microorganism  
preservation  
lifecycle



ISO/DIS 20387

Accreditation

## Accreditation



Recognition of the technical competence  
to perform conformity assessment



ISO/DIS 20387

Accreditation

## Conformity assessment

- Testing
- Calibration
- Inspection
- Certification

ISO/DIS 20387

Certification

Certification



Confirmation that certain (specified) characteristics of a product, process, person or organization conform with the requirements