



Collaborating with suppliers to ensure the availability of high quality raw materials for AAV manufacturing


**European Biomanufacturing Summit
Düsseldorf, October 23, 2025**

**Dr. Frank Seibel
Roche Diagnostics GmbH**

Agenda

-  **1. Overview Regulatory Framework**
-  **2. Role of Quality Oversight for the QTA**
-  **3. Role of the QTA**
-  **4. Performance Evaluation**
-  **5. Summary**

Agenda

-  **1. Overview Regulatory Framework**
-  2. Role of Quality Oversight for the QTA
-  3. Role of the QTA
-  4. Performance Evaluation
-  5. Summary

Regulatory Framework



EudraLex
The Rules Governing Medicinal Products in the European Union
Volume 4
Good Manufacturing Practice

**Guidelines on Good Manufacturing Practice specific to Advanced
Therapy Medicinal Products**

Document History	
Adoption by the European Commission	22 November 2017
Date for coming into operation	ATMP manufacturers should comply with these Guidelines no later than 22 May 2018.

Regulatory Framework



EUROPEAN
COMMISSION

**DIRECTIVE 2002/98/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 27 January 2003**

setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC

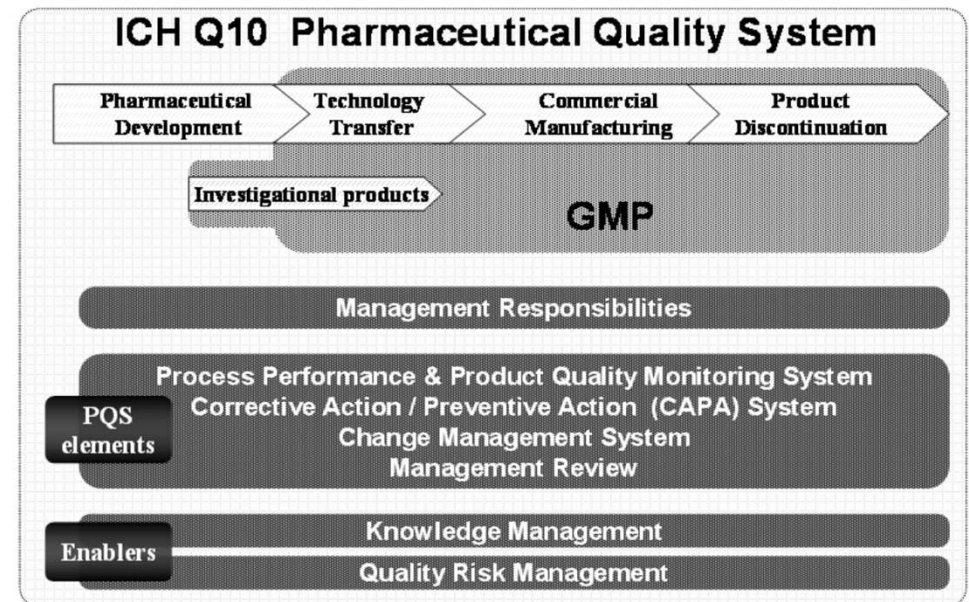
**DIRECTIVE 2004/23/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL
of 31 March 2004**

on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells

Regulatory Framework: EU GMP Volume 4

1.2. General Principles

Quality plays a major role in the safety and efficacy profile of ATPMPs. It is the responsibility of the ATMP manufacturer to ensure that appropriate measures are put in place to safeguard the quality of the product (so called „pharmaceutical quality system“).



Regulatory Framework: EU GMP Volume 4

2.2 Application of the Risk-based approach by ATMP manufacturers

2.15 The quality risks... are...dependant on

- Characteristics and origin of cells / tissues
- Vectors (e.g. replication competence or reverse transcription)
- Transgenes
- Expressed protein
- **Raw materials**, matrixes
- Manufacturing process



23 January 2025
EMA/CHMP/ICH/24235/2006 Corr.2
Committee for Medicinal Products for Human Use



[ICH guideline Q9 \(R1\) on quality risk management](#)

Regulatory Framework: EU GMP Volume 4

2.3.1 RBA in connection with raw materials

- Understanding of the role of the raw material in the manufacturing process
- Understanding of the properties
- Risk of raw materials to intrinsic properties
 - growth factor vs. basic media
 - media with or w/o cytokines
 - raw material from animal origin vs. autologous plasma
- Potential contact of raw material with starting material

- Sufficient control strategy
 - Supplier qualification
 - Performance of suitable functional testing

Regulatory Framework: EU GMP Volume 4

7.2. Raw Materials

7.13. Reference to PhEur 5.2.12

General chapter on raw materials of biological origin for the production of cell based and gene therapy medicinal products

7.14. Specifications – Focus on critical raw materials

- Establishing quality requirements to ensure suitability for the intended use
- Acceptance criteria
- Establishing „agreed specifications“ with suppliers
- Documenting rationale if and why a raw material is assessed as „critical raw material“

Regulatory Framework: EU GMP Volume 4

7.2. Raw Materials – Special focus areas

- Use of a Supplier CoA (not needed for raw materials authorized as medicinal products in the EU (i.e. Human Serum Albumin, recombinant proteins))
- Contamination risk for raw materials of biological origin during their passage
 - TSE
 - Mycoplasma
 - Other products being in contact with raw materials
- Traceability of raw materials in case of product recalls

Regulatory Framework: EU GMP Volume 4

9.5.3. Sterilization

- Sterilization ... is effective in terms of removing the contaminants while preserving the activity of ... raw materials

12.2.2. Retention of samples

- Reference samples of critical raw materials (e.g. cytokines, growth factors, enzymes, sera) should be retained during the shelf- life of the relevant raw materials.


Agenda

-  1. Overview Regulatory Framework
-  **2. Role of Quality Oversight for the QTA**
-  3. Role of the QTA
-  4. Performance Evaluation
-  5. Summary

How to define Quality Oversight

„State of control“ has to be achieved and maintained

„... develop and use effective monitoring and control systems for process performance and product quality, providing assurance of continued suitability and capability of processes...”

A graphic element featuring a dark blue rectangular box with white text. To the left of the box is a decorative pattern of overlapping squares in various shades of blue and grey. The text inside the box reads "ICH Q10 Pharmaceutical Quality System (PQS)".

ICH Q10
Pharmaceutical
Quality System (PQS)

What is Quality Oversight

ENSURING	CONTROLLING
<ul style="list-style-type: none">• Assure• Guarantee	<ul style="list-style-type: none">• Checking• Surveilling



Oversight Responsibilities

Patient

- Quality, Safety, Efficacy
- Availability




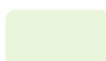
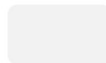
Authorities

- Approval granted
- Commitment to comply
- Commitment to deliver

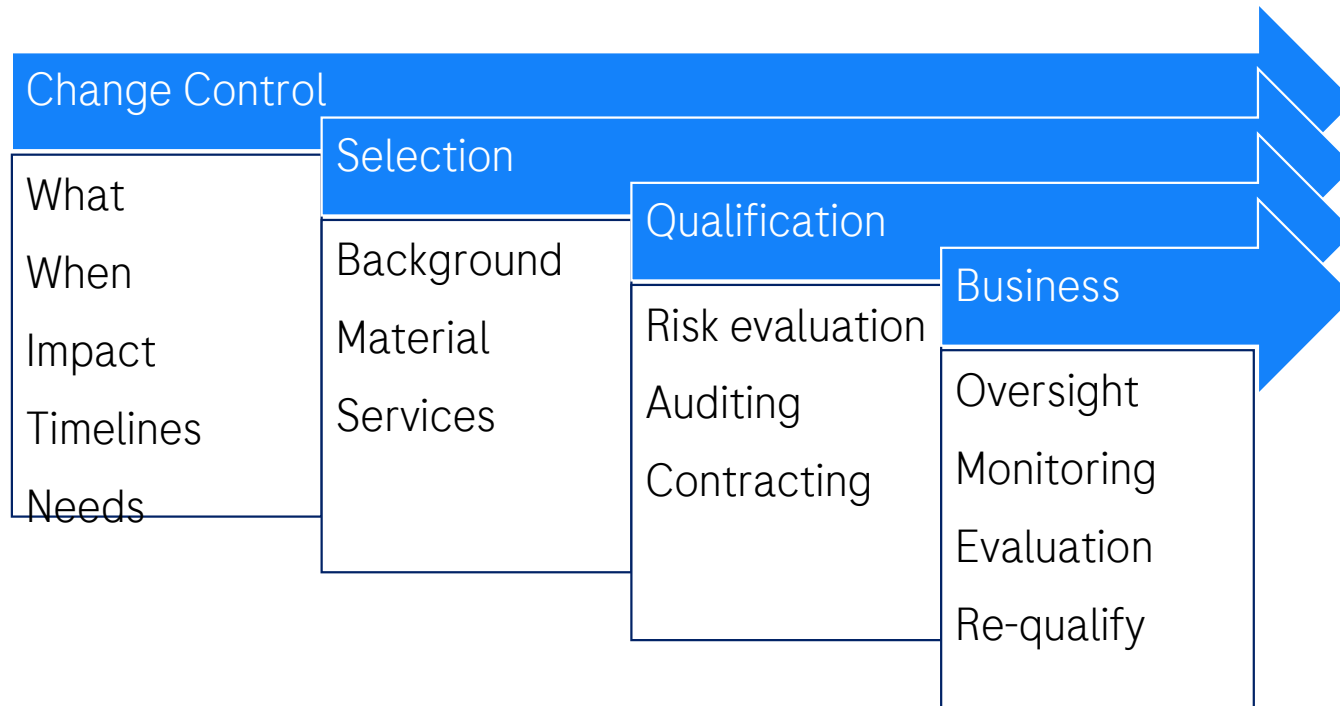
Your company

- Reputation
- Resources

Agenda

-  1. Overview Regulatory Framework
-  2. Role of Quality Oversight for the QTA
-  **3. Role of the QTA**
-  4. Performance Evaluation
-  5. Summary

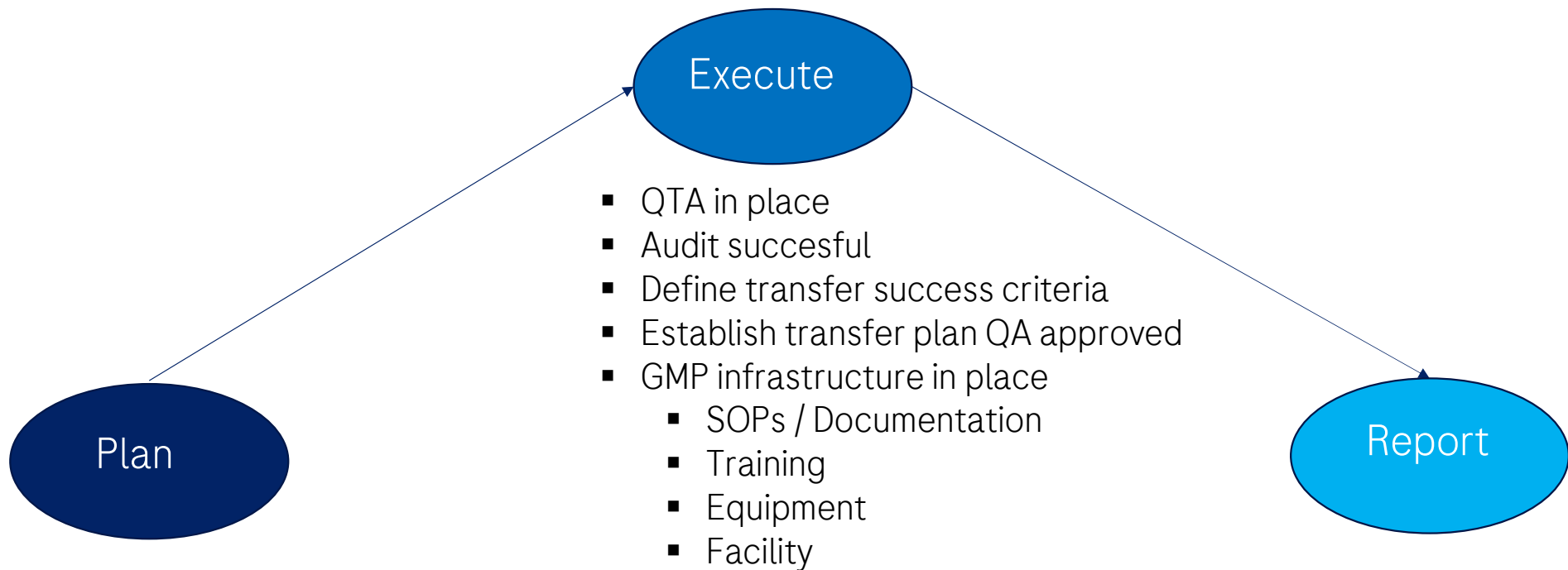
Steps to start supplier business



Impact of Non-GMP aspects

- Single source ?
- Delivery reliability ?
- Company history / reputation ?
- How important are you for your partner regarding production and financial volume ?

Technology Transfer



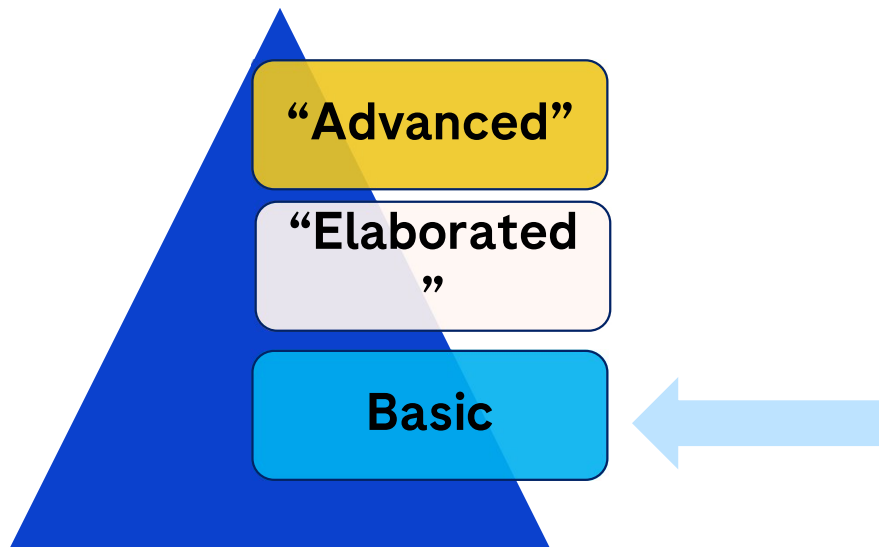
The QTA as key success factor

Scope of the Quality Technical Agreement (QTA): Definition of the minimum key requirements / determination of responsibilities

- Regulatory Compliance
- Deviation / Investigation handling
- Change Control (Approval)
- Subcontracting
- Escalation rules / Notification timelines
- Inspection notification
- Auditing right (periodic & for cause)

The QTA and the „Business contract“ should not be mixed – there might be an overlap, but they have a different scope

How to deal with different standards



- Compliance = „Ensuring Quality Oversight“
- Not negotiable
- PQS in place including all elements:
 - Deviation management
 - Complaint management
 - Supplier qualification
 - Qualification / Validation
 - Documentation
 - Training
 - ...

How to agree on the QTA

Nice to have

- Fulfills a “want”, not a need
- = “Luxury”

Good to have

- Fulfills a “want”, not a need
- Is a helpful addition to ease circumstances

Must have

- Fulfills an elemental need / non negotiable
- Limited options to deviate from there


How to agree on the QTA

The easier the implementation – the higher the acceptance

- Support for improvements
- Offer / accept a Person in the Plant (PiP)
- Offer additional simplification over time
- Offer perspectives for more business in the future
- @ Contract Giver: Offer bonuses for excellent performance

Make it attractive for your contract partner

Agenda

-  1. Overview Regulatory Framework
-  2. Role of Quality Oversight for the QTA
-  3. Role of the QTA
-  **4. Performance Evaluation**
-  5. Summary

Performance Evaluation



Quality
Oversight Level



Quality vs.
Reliability



Frequency of
Evaluation



Other

Performance Evaluation

Quality Oversight

Apply the same level of Oversight as for your „own / internal“ activities, because it is

- YOUR product
- YOUR responsibility
- YOUR monitoring & evaluation accountability

Performance Evaluation

**Quality vs.
Reliability**

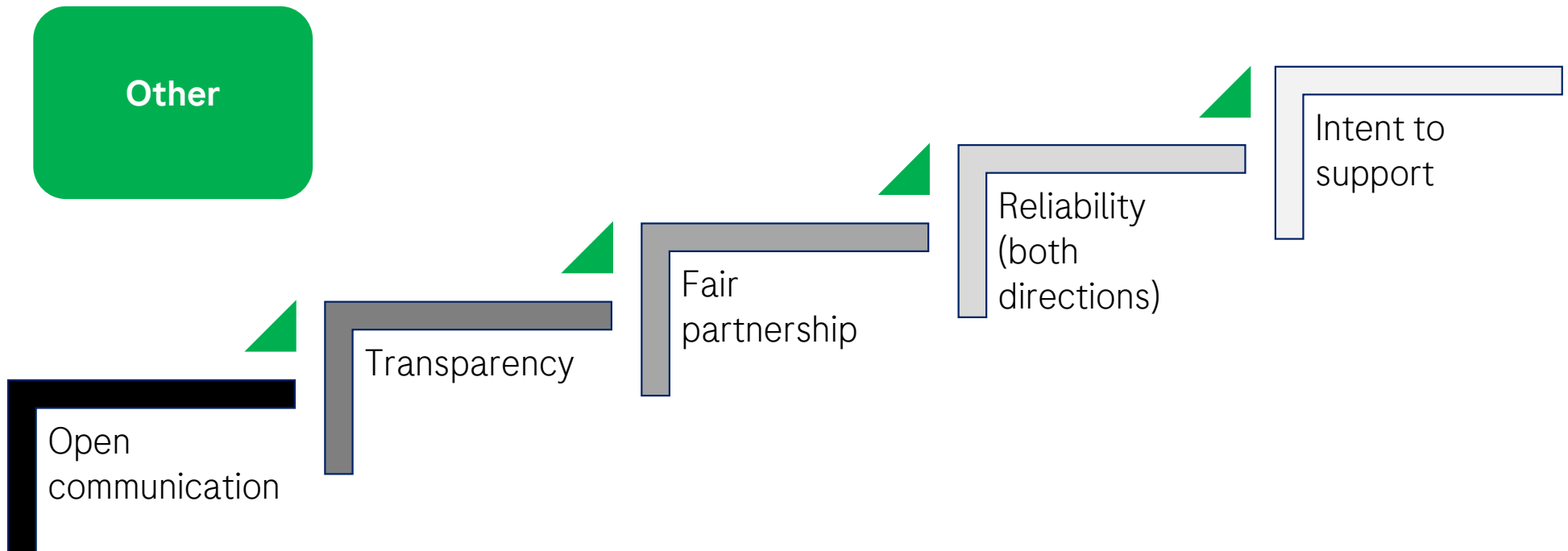
Quality Performance	Reliability Performance
Exceptions per volume	OTIF
Repeat events	Timeliness of production
Audit history	Timeliness of information
	Timeliness of escalation

Performance Evaluation




**Frequency
of
Evaluation**

Continuously	Periodically
Supplier score card	Formal re-qualification (2 y)
Metrics	Management review
Trending	Sharing Supplier Score card

Performance Evaluation



Agenda

-  1. Overview Regulatory Framework
-  2. Role of Quality Oversight for the QTA
-  3. Role of the QTA
-  4. Performance Evaluation
-  **5. Summary**

Summary

- AAV manufacturing is focusing on specific aspects while still following general basic principles
- Build structure around the basics first, then specify the different aspects
- A good QTA is the core of a sustainably good supplier partnership
- Keep it simple!

Questions

?