CASSS WCBP 2023

BioPhorum Plenshop

Best Practices for Lifecycle Management

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What is BioPhorum?

Why is the industry working on best practices for lifecycle management?

Simplification of the Requalification of Working Cell Banks

Best regulatory practices for the registration of raw materials

Best regulatory practices for the registration of process controls

Session Presenters and Pannelists

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Project Manager

What is BioPhorum?

10
Phorums

100+
industry changing initiatives

150+
member companies

7500+
active participants

1
voice for the industry

Unique **global** collaboration

Powerful vehicle for **change**

Industry leaders and experts working in concert

Delivers results by pooling knowledge, practices and ideas

Why is the biologics industry working on best practices for lifecycle management?

- **Our products are complex from a CMC point of view:**
  - Complex raw materials: APIs and others
  - Complex manufacturing processes
  - Complex controls: methods and specifications

- **There two ways of approaching complexity:**
  - Tight controls
  - Mature Quality Approach: Demonstration of product and process knowledge and understanding

- **Historic approach for life-saving medicines has been tight controls:** *we do the same thing every time and that ensures control of product quality, safety and efficacy*

In practical terms…

We are collecting the industry-wide product and process knowledge and understanding for biologics CMC

To date

Cell Banks

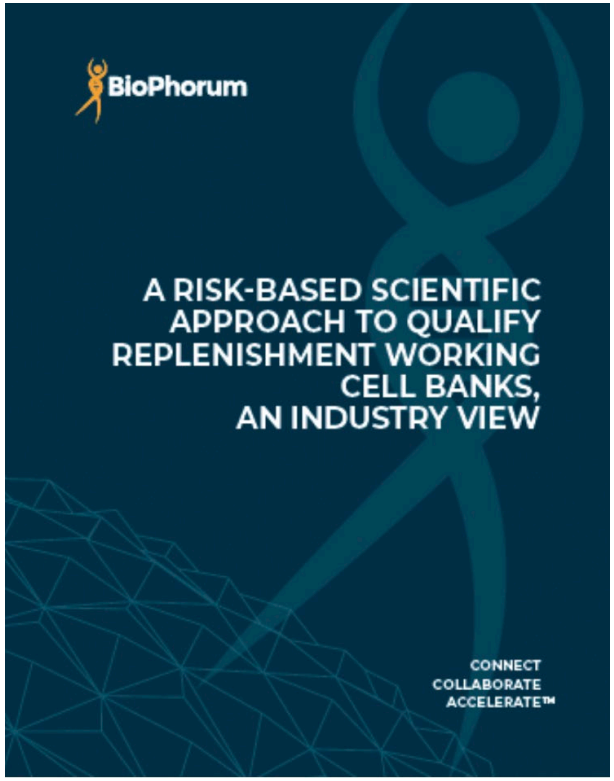
Raw Materials

Manufacturing processes

We are translating them into best practices for lifecycle management

The BioPhorum Approach

- For more information, see BioPhorum.com
  - All publications are the consensual output from the Biologics industry (more than 90% of biomanufacturers in the US and Europe are members)
  - All publications can be consulted free of charge from our website



BioPhorum

A risk-based scientific approach to qualify replenishment working cell banks – an industry view

Presented by

Pamela Pegman, Stephanie Robichaud

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Introduction

Cell banks represent the fundamental starting substrates for biological drug substance (DS)/drug substance intermediate (DSi) manufacturing. Streamlined technical and regulatory approaches to qualifying replenishment banks is imperative to lifecycle management and to ensure uninterrupted supply to patients in global markets

Availability of well-characterized cell banks capable of supporting manufacturing processes is imperative to ensure uninterrupted drug product (DP) supply to patients and to global markets.

Goal
Ensure a consistent cross-industry qualification strategy using a risk-based scientific approach, considering potential impact to cell bank growth and viability performance as well as impact to product quality.

Recommendations in this paper are intended to be globally applicable and relevant to WCBs for all biologics (including monoclonal antibodies (mAbs), therapeutic recombinant proteins, vaccines, and gene therapies).

Overview of regulatory requirements

ICH Q5D provides general regulatory guidance for cell banking requirements for initial marketing application

Including two tier master and working cell banks derived from a clonal population of cells, testing for adventitious agents, and demonstration of genetic stability

There are no specific guidelines for data requirements that apply when creating a replenishment WCB

HA expectations for qualification of replenishment WCBs have evolved to become more extensive

Small scale data alone is not adequate

Increase in requests to include manufacture of commercial scale DS lots, comparability, and stability information

Overview of regulatory requirements

Typically, the regulatory submission for a replenishment WCB would be:

- Prior approval supplement (US)
- Type IB/type II variation (EU)

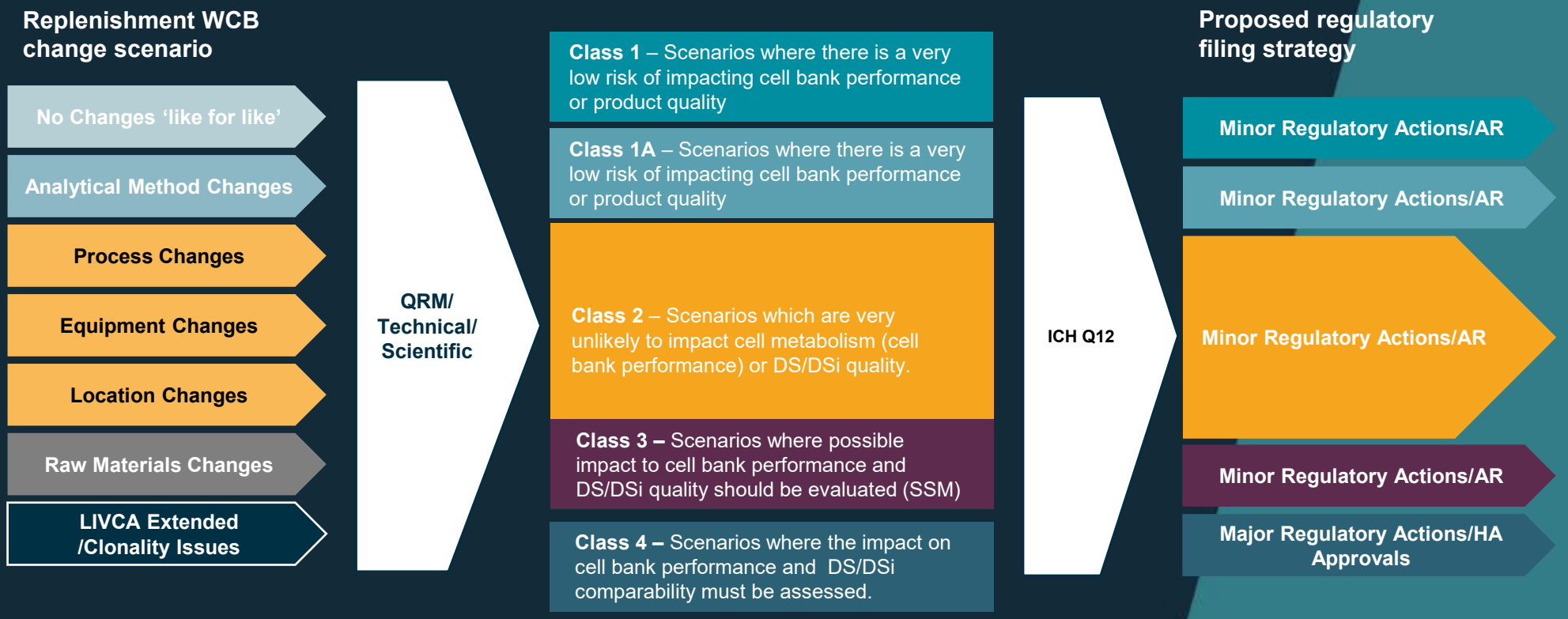
Use of a post approval change management protocol (PACMP) would allow for downgrade in reporting requirement:

- [illegible] (US)
- No variation submission (EU)

Consistent regulatory guidance with global alignment on regulatory requirements for manufacturing replenishment WCBs for marketed products, would streamline the post-approval process and help prevent delays, which can lead to drug shortages and regional supply-chain constraints.

Replenishment WCB qualification approach

QRM approach – potential risks associated with change, the impact on the cell bank performance and DS/DSi quality are all assessed to develop an appropriate cell bank qualification strategy.



Proposed qualification approach for replenishment WCB – – Class 1/1A

Change scenario	Proposed replenishment WCB qualification approach
No change to cell bank Process, RM, PDL, equipment, facility, analytical methods	• Proceed to change control to intro cell bank • No formal thaw & growth assessment, (may be done as business risk mitigation) • No small or commercial scale confirmation required
Changes to the analytical method for release	• Proceed to change control and risk assessment to Intro analytical change, and intro cell bank • No formal thaw & growth assessment, (may be done as business risk mitigation) • No small or commercial scale confirmation required

Qualification approach process/equipment/ manufacturing location changes – Class 2

Change scenario

Process changes

Passage scheme; #Viable cells per vial; cell concentration method; change to gas mix (microbial); CFR settings; WCB process-scale changes, vial/container change. Freezing media: cryoprotectant (DMSO/glycerol) concentration, conditioned medium vs fresh medium, alternative cryoprotectant

Equipment changes

Vessel; agitation; centrifugation equipment; basic lab equipment (incubator); dispensing device; cell counting device; implementation of CRF vs static -80°C

Facility location changes

WCB manufacturing site CMO vs internal; change in WCB manufacturing suite but at the same site

Proposed replenishment WCB qualification approach

- Proceed to change control and risk assessment
- Thaw & growth/viability assessment
- No small or commercial-scale process/PQ confirmation required

Qualification approach raw material changes

– Class 3

Change scenario

Raw material change

Chemical RM: supplier (like for like); grade improvement;
RM manufacturing site (like for like);
Biological RM (serum, plant extract, BSA): supplier;
RM manufacturing site; country of origin; animal origin to recombinant/animal-free (specific to freezing media)

Proposed replenishment WCB qualification approach

- Proceed to change control and risk assessment
- Apply SSM to demonstrate acceptable product quality on DS^/Dsi+
- No commercial-scale process/PQ confirmation required

Qualification approach LIVCA changes or clonality questions – Class 4

Change scenario

Expected PDL change beyond what is demonstrated MCB clonality in question

Proposed replenishment WCB qualification approach

Proceed to change control and risk assessment
Conduct commercial-scale process/PQ confirmation
Conduct DP DS Stability
Repeat genetic stability if appropriate

Conclusion

Replenishment Cell Bank Qualification is a key component in Life cycle management.

To minimize product continuity risk and account for the lack of technical drivers, the Consortium recommends a class-based approach to replenishment WCB qualification, that accounts for:

- Like-for like scenarios
- Changes in analytical methods
- Changes to process, equipment, or facility location
- Raw material changes
- Impacts to LIVCA or MCB clonality

Harmonization toward a risk-based system for categorization of post-approval changes is an important step to achieving objective of ICH Q12, which would provide:

- Flexibility in the regulatory approach
- Framework for lowering regulatory submission requirements
- Uninterrupted drug substance (DS) and drug product (DP) supply to patients and to global markets

Questions for feedback

Is the agency/ies working on this topic?

Does the agency/ies agree with the proposed approach?

Can the Agencies speak to specific concerns relating to replenishment WCB qualification and help us understand the rationale

What would the next steps towards adoption be?

For more information, contact your company's BioPhorum representative or **Karan.middleton@biophorum.com**

catherine.wyatt@biophorum.com

We encourage continued citation of the White paper in regulatory submissions. Please provide any feedback.

www.biophorum.com

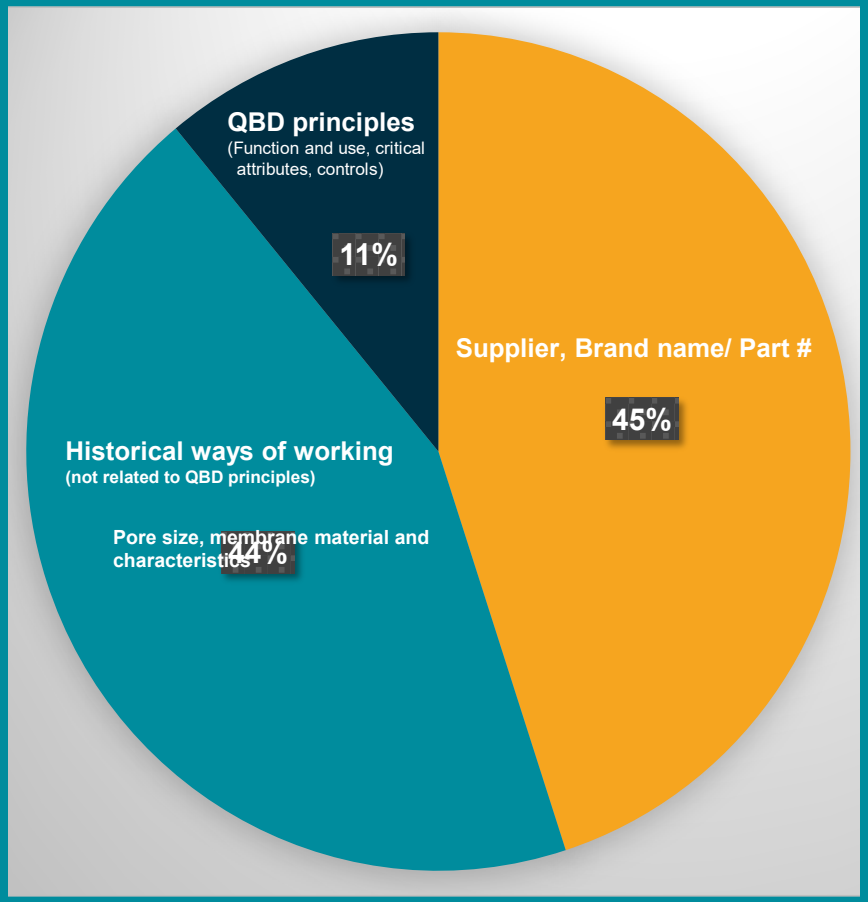
Best regulatory practices for the registration of raw materials

Kavita Ayier

Seagen
Senior Director and Portfolio Head for Commercial Biologics, Global Regulatory Affairs - CMC

Industry Survey Indicates Diversity in Raw Material Registration Practices

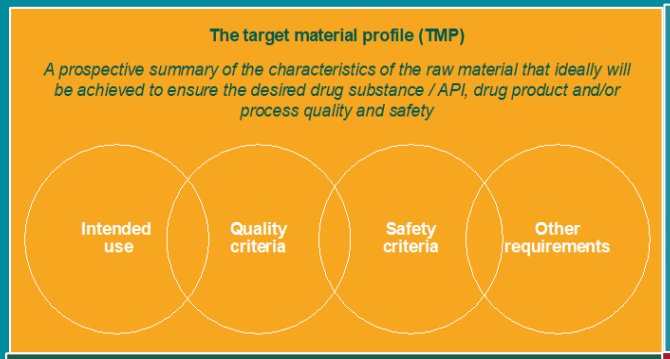
Virus Retentive Filter

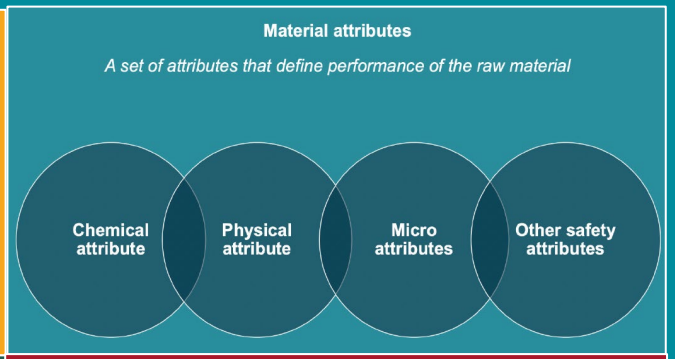


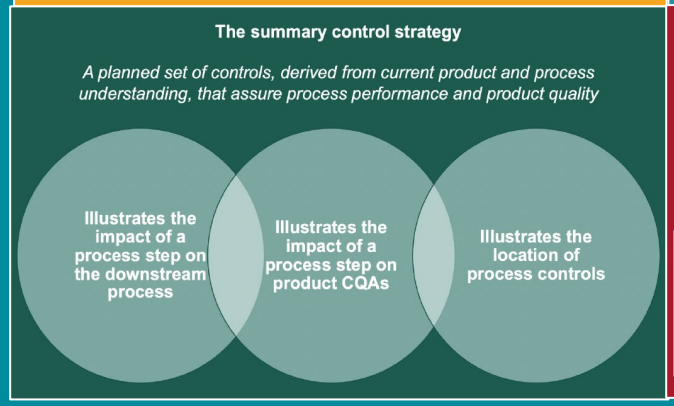
- Raw materials primarily registered using non QBD principles
- Limits the ability to introduce alternate supplier sources as,
  - *Tight controls for materials do not support demonstration of equivalency*
  - *Global regulatory approvals can be prolonged*
- Information in regulatory dossier might not be reflective of the understanding of raw material impact on product quality
- Team proposes a "Scientific Risk-Based Approach" for raw material control and registration practices leveraging Quality by Design (QBD) and/ or ICH Q12 principles

A Systematic And Mature Quality Approach for the Registration of Raw Materials

A 4-Step Process To Identify Critical Material Attributes (CMAs)







Definition of the CMAs and controls

Review of impact of Material Attributes on TMP and/ or Control strategy helps determine impact of material on process step performance and product quality

QBD

Registration of materials based on CMA and function
- Utilize knowledge and understanding of raw material impact on process and product quality
- Evaluate the impact by scoring

ICH Q12

- Define CMA as established conditions
- Secure health agency concurrence on approach for management of future change and the acceptability criteria
- Allows use of PACMP

Benefits

- Increased flexibility of supply and continuity
- Improved process robustness
- Enhanced quality of regulatory submissions
- Regulatory filing relief (PQS or a reduced filing category)

Making second sourcing easier: Risk-based registration of complex and innovative raw materials

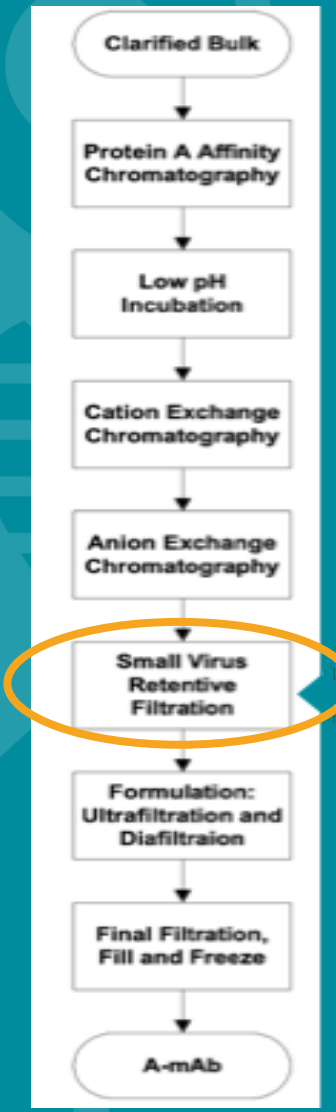
Example of the virus removal filter

- Approach based on Demonstration of Product and Process Knowledge and Understanding

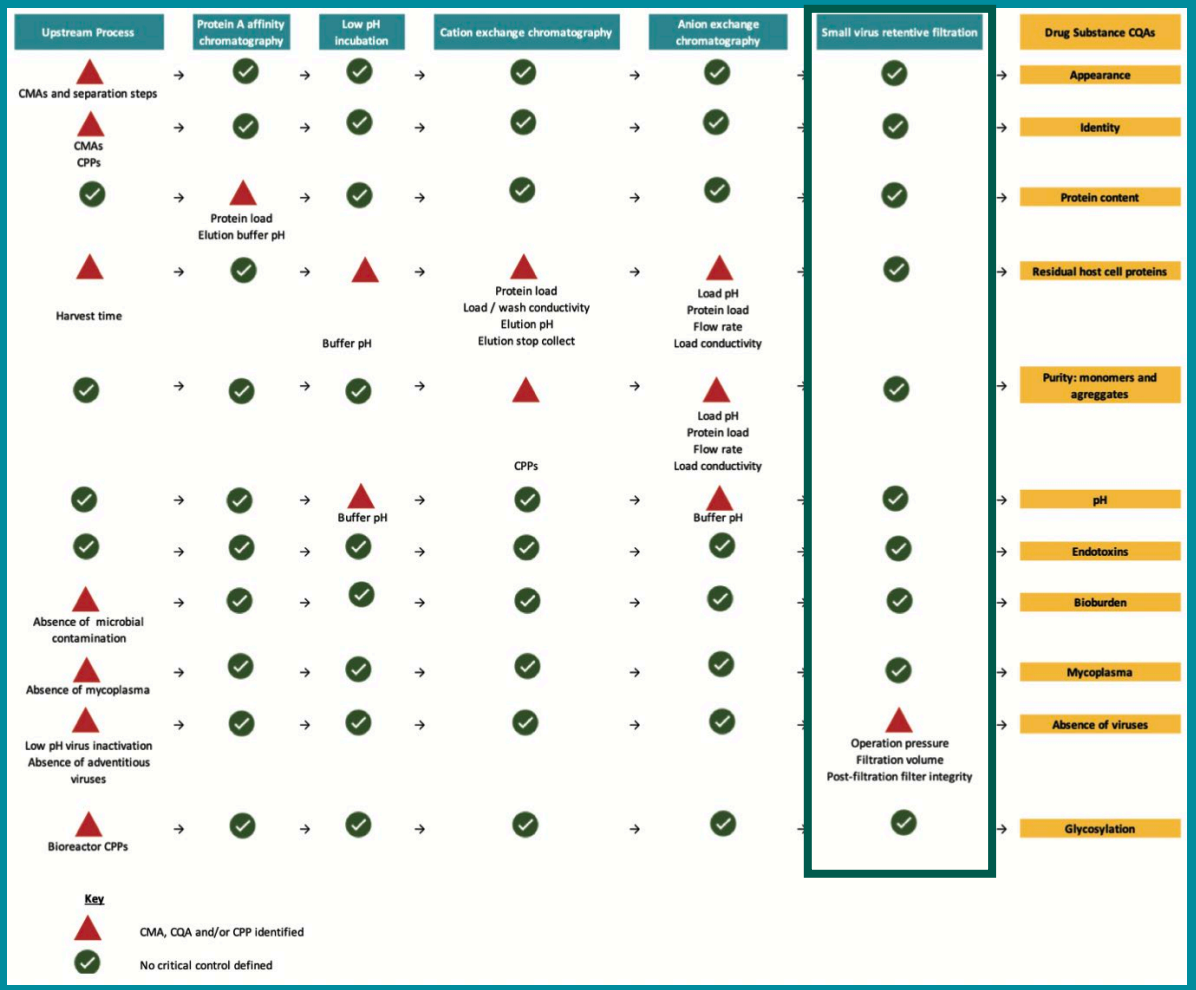
  - Identification of viral filter CMAs & controls via 4 Step process,
    - Definition of TMP
    - Review of product summary control strategy
    - Description of material attributes
    - Identification of the CMAs required to ensure product quality and safety

Step 1: Definition of Virus Retentive Filter TMP

- Intended use
  - Filter must remove viruses still present in the API in a robust and consistent manner
  - After polishing chromatography step and prior to UF/DF formulation step
- Quality criteria
  - Filter system integrity performance– pre-use (supplier check as part of release) and post use
  - Allow for continuous flow and volume to be processed until defined end point is reached
  - Removal of >99.99% of viruses and particle-like viruses present prior to filtration (at least with a log-factor of 4)
  - Should not allow non- specific binding like protein load and availability of qualified scale down model (ICH Q5A)
- Safety criteria
  - Extractable and leachable risk-assessment and interaction with API
  - Filter compatibility with sanitization process, microbial, viral and endotoxin quality consistent with bioburden management
  - Absence of biological reactivity (USP <88> Class VI / USP <87> / ISO 10993 Parts 5, 6, 10, and 11)
- Manufacturability criteria
  - Filter must withstand process pressure
  - Highly secured connections for system integrity
  - Step yield



Step 2: Review Product Control Strategy for a mAB



- Where does the raw material fit into the process?
  - Small virus retentive filtration is the final virus-removal step
- How does the raw material impact the overall control strategy?
  - Critical contributor to viral safety of the product through control of,
    - Two CPPs, operating pressure and filtration volume
    - One CQA, post filtration filter integrity

Steps 3 and 4: Virus Retentive Filter Material Attributes and CMA Determination

Attribute	Impact	Variability	Detection
Chemical attributes			
Composition	Medium	Medium	Low
Physical attributes			
Filter dimensions	Medium	Medium	Low
Maximum load volume	Medium	Medium	Low
Maximum/ Minimum protein concentration	Medium	Medium	Low
Membrane architecture	Medium	Medium	Low
Pore size	Medium	Medium	Low
Membrane type	Low	N/A	N/A
Shedding	Low	N/A	N/A
Clearance of small viruses	High	Low	Low
Filter integrity	High	Low	Low
Microbial attributes			
Bioburden	Medium	Low	Low
Absence of viruses	Low	N/A	N/A
Absence of endotoxins	Low	N/A	N/A
Other attributes			
Dominant filtration mechanism during model virus testing	High	Medium	Low

- Systematic review of all material attributes and scoring on impact on process performance and product quality (as defined through TMP and control strategy)
  - High impact is a CMA
  - Medium impact requires control and verification
- For control strategy associated with virus retentive filters, three CMAs were identified,
  - Viral clearance achieved by filter for small viruses
  - Dominant mechanism of retention during model virus testing
  - Post filtration filter integrity
- An equivalent filter may be used that meets the acceptance criteria for the filter CMAs
  - Filter verification informed by scoring must be performed via manufacturability study, viral control strategy validation, extractable and leachable risk assessment and chemical compatibility

Traditional Versus Mature Quality Approach

Elements of the control strategy	Traditional controls	Mature quality approach – controls based on QbD principles
Virus removal	Name and part ID of the filter CPPs: filtration volume and flow/pressure	**Filter CMA:** log 4 reduction factor for small viruses For **Name and part ID of the filter, PPs:** filtration volume and flow/pressure Equivalent filters may be used and appropriate ranges of process parameters defined
Dominant mechanism	–	**Filter CMA:** the dominant mechanism of retention when tested for model viruses is size exclusion
Filter was able to perform its function, i.e. virus removal	**CQA:** filter integrity after filtration	

➢ *All details in the BioPhorum paper (Free Access):*
https://www.biophorum.com/download/biophorum-approach-to-the-registration-of-innovative-raw-materials-using-quality-by-design-principles/

Best regulatory practices for the registration of process controls

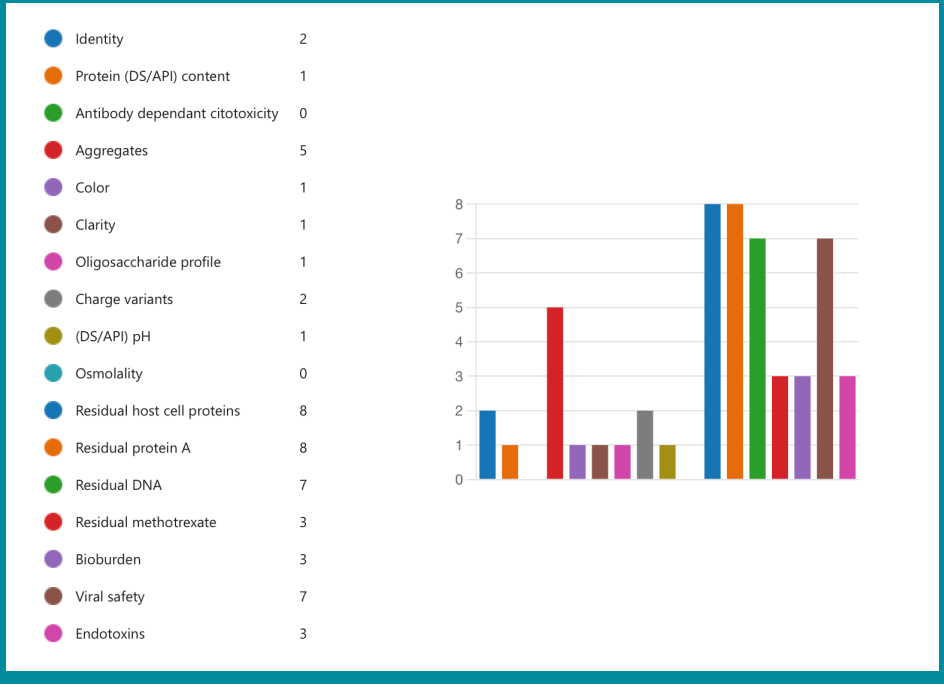
Linda Iemieux

Merck & Co, Inc., Rahway, NJ
Director/Principal Scientist, Biologics – Regulatory Affairs CMC

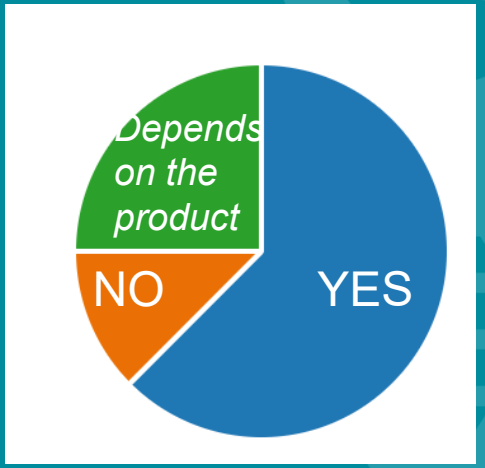
Industry Survey Indicates Diversity in Process Controls Registration Practices

Protein A Purification

Question 1: What product CQAs does your organization associate with protein A purification?



Question 2: Is Protein A purification typically associated with CPPs?

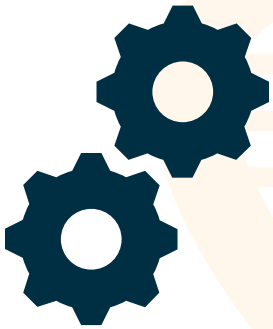


Question 3: What are the CPPs that would typically be registered for the protein A purification step?

No CPPs	
1	Elution buffer pH
4	Linear velocity, load ratio, start/end collection, wash volume
4	Load ratio, temperature, elution buffer concentration, wash to buffer concentration
5	Load ratio, elution buffer pH, column bed height, flow rates, number of re-use cycles

The BioPhorum Approach

How can we build regulatory dossiers that allow acceptable operational flexibility whilst upholding product quality and thereby patient safety?

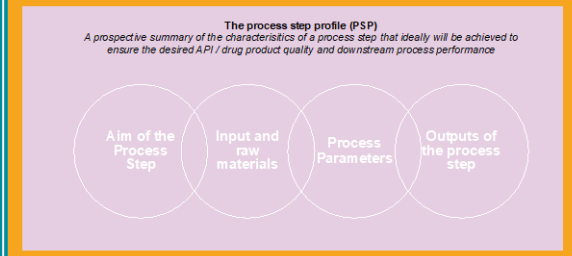


For manufacturing processes, this can be achieved by how we register process controls

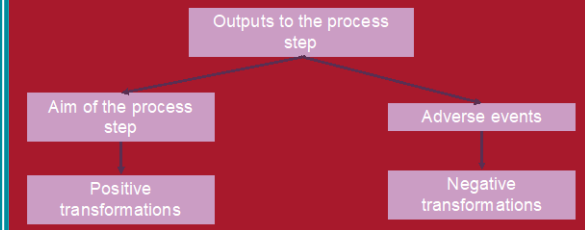
A Systematic And Mature Quality Approach to the Registration and Lifecycle Management of Process Controls

Another 4-Step Process

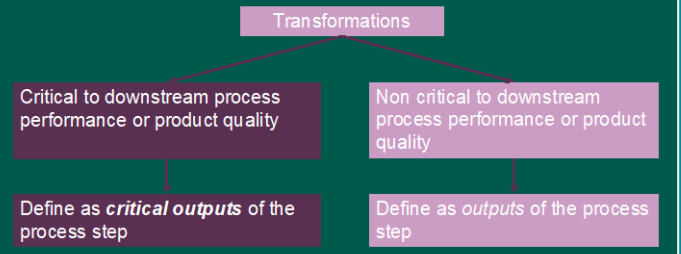
Step 1: Definition of the Process Step Profile



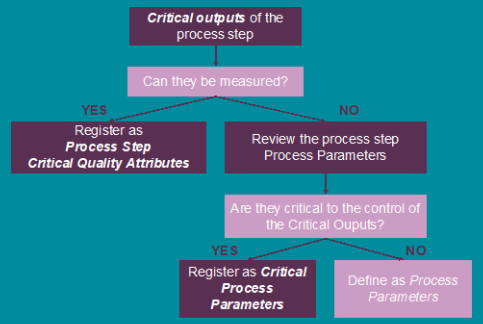
Step 2: Definition of the Process Outputs, Positive Transformations and Adverse Events



Step 3: Definition of Criticality of the Process Step Outputs



Step 4: Analysis of the Critical Process Step Outputs



QBD

Registration of process steps preferentially based on Critical Outputs or process step CQAs, *independent of manufacturing equipment and process scale*

ICH Q12

- Define control of CQAs as established conditions
- Secure health agency concurrence on approach for management of future change and the acceptability criteria, allows the use of PACMP

Benefits

- Increased flexibility of supply and continuity
- Improved process robustness
- Enhanced quality of regulatory submissions
- Regulatory filing relief

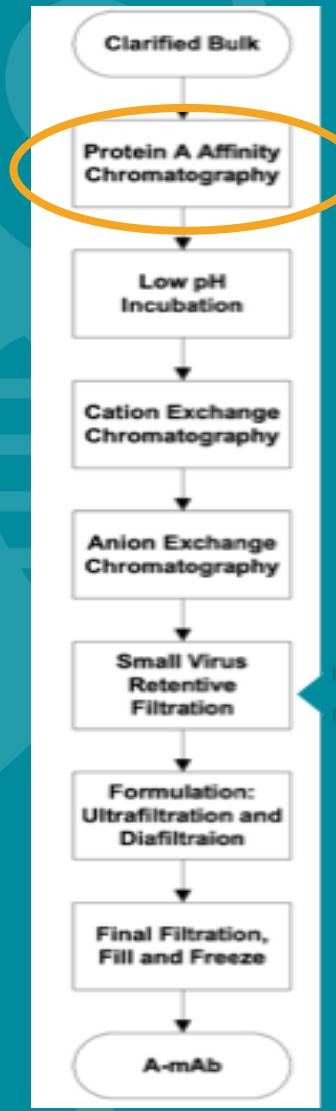
Case Study: Protein A Purification Process Step

- Approach based on Demonstration of Product and Process Knowledge and Understanding

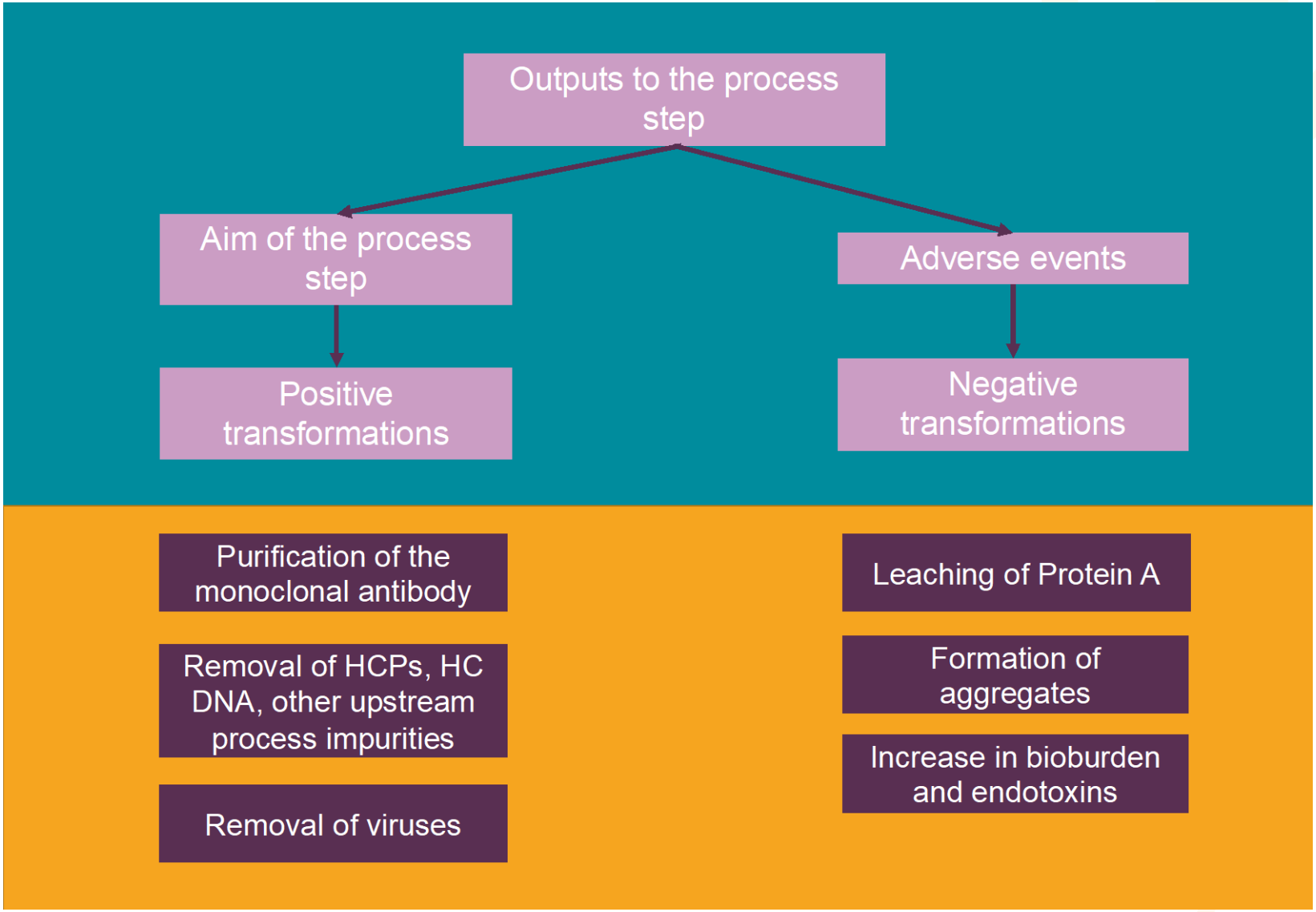
  - Identification of intermediate Critical Quality Attributes
    - Step 1: Definition of the Process Step Profile
    - Step 2: Definition of the Process Outputs: Positive Transformation and Adverse Events
    - Step 3: Definition of Criticality of the Process Outputs
    - Step 4: Analysis of the Process Step Outputs

Step 1: Definition of the Process Step Profile

- Aim of the Process Step
  - Isolation of the monoclonal antibody of interest
- Input and raw materials
  - Performed on the clarified bulk, first step of the downstream process
  - Performed using a Protein A resin / membrane
- Process Parameters
  - Column bed height, temperature
  - Load: flow rate, protein load, load concentration
  - Equilibration and wash: buffer pH, buffer molarity, flow rate, volume
  - Elution: buffer pH, flow rate, start and end of collection
- Outputs of the Process Steps
  - Purification of the monoclonal antibody
  - Removal of process impurities : host cell proteins (HCPs), host cell protein DNA, viruses, process upstream impurities (upstream adjuvants, such as antifoam)
  - Potential leaching of protein A: some protein A leaches from the resin during elution of the monoclonal antibody
  - Potential formation of aggregates
  - Potential increase in bioburden and endoxins, especially if the elutes are pooled



Step 2: Definition of the Process Outputs: Positive Transformation and Adverse Events



Step 3: Definition of criticality of the process outputs

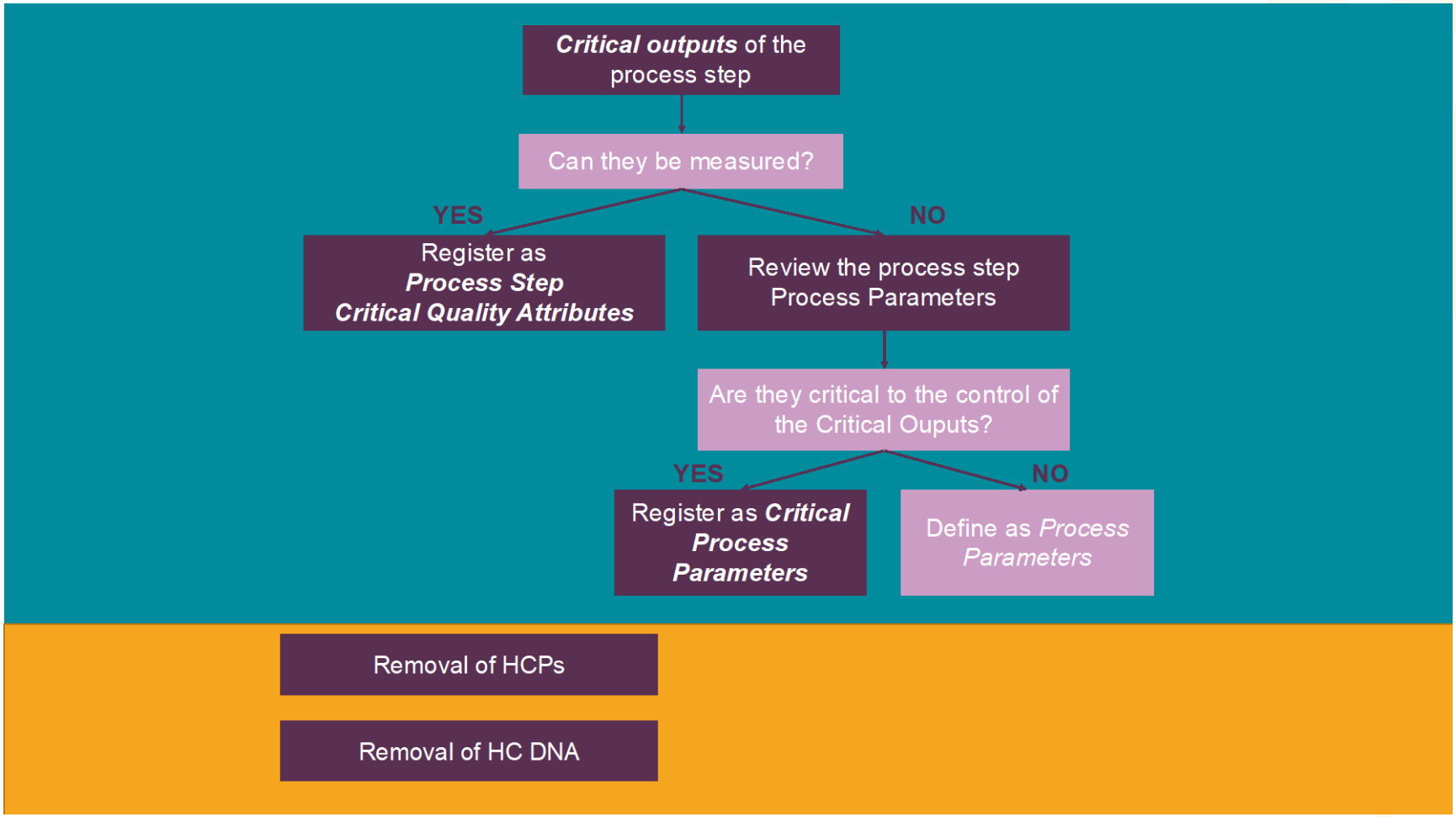
- Based on product and process knowledge and understanding
  - Prior knowledge
  - Development activities

Outputs	Impact on Product Quality
Purification of the monoclonal antibody	Medium
Removal of HCPs, HC DNA, other process impurities	Critical
Removal of viruses	Medium / Low
Leaching of Protein A	Medium
Formation of aggregates	Medium
Increase in bioburden and endotoxins	Low

- Systematic review of process step outputs and scoring on impact on product quality
  - High impact is a Process Step CQA
  - Medium impact requires control and verification
- For control strategy associated with Protein A affinity chromatography, 2 CQAs were identified
  - Removal of HCPs
  - Removal of HC DNA
  - Removal of HCPs and HC DNA are considered to be an appropriate surrogate measure to the removal of other process impurities (no CQA defined)
- **An equivalent Protein A may be used or changes to the process parameters or conditions implemented, that meet the acceptance criteria for the process step CQAs**
  - Verification informed by scoring must be performed via manufacturability study, verification of the viral control strategy, assessment of the downstream process to clear leached protein A and aggregates

Step 4: Analysis of the Process Outputs

- Based on product and process knowledge and understanding
  - Prior knowledge
  - Development activities



Registration: Traditional Versus Mature Quality Approach

Elements of the Control Strategy	Traditional Approach	Mature Quality Approach
Protein A affinity chromatography	Name and Part ID of the Protein A	Protein A *Intende commercial process: Protein A (Name and Part ID) or equivalent** *PPs*
Affinity performance	**CPPs: Elution buffer pH, linear velocoty, load ratio, start/end collection…**	**CQA: Maximum residual HCPs A in the intermediate purified bulk of Y**
		CQA: Maximum residual HC DNA in the intermediate purified bulk of Z

Note:
* Equivalent is defined as being able to achieve the same process step CQAs, process parameters may be different

BioPhorum Next Steps: Convey messages and knowledge sharing for support in member companies. Share “wins” and lessons learned.

BioPhorum Approach Is The Start of A Transformational Journey In Registration and Lifecycle Management of Biologics

Questions

- As industry, do we see any barrier to implementation?
- Raw materials
  - Kavita – to populate
  - M4Q is being updated, are any of the industry teams looking at incorporating control strategies in the new CTD structure?
  - What are the next steps? How do we implement the approach?
  - Are we already using this approach? What is the feedback, how is the experience?


BioPhorum - Collaborating Responsibly

Anti-trust compliance statement v4.0

It is the clear policy of BioPhorum that BioPhorum and its members will comply with all relevant anti-trust laws in all relevant jurisdictions.

All BioPhorum meetings and activities shall be conducted to strictly abide by all applicable antitrust laws. Meetings attended by BioPhorum members are not to be used to discuss prices, promotions, refusals to deal, boycotts, terms and conditions of sale, market assignments, confidential business plans or other subjects that could restrain competition.

Anti-trust violations may be alleged on the basis of the mere appearance of unlawful activity. For example, discussion of a sensitive topic, such as price, followed by parallel action by those involved or present at the discussion, may be sufficient to infer price-fixing activity and thus lead to investigations by the relevant authorities.

Criminal prosecution by federal or state authorities is a very real possibility for violations of the antitrust laws. Imprisonment, fines or treble damages may ensue.

BioPhorum, its members and guests must conduct themselves in a manner that avoids even the perception or slightest suspicion that antitrust laws are being violated. Whenever uncertainty exists as to the legality of conduct, obtain legal advice. If, during any meeting, you are uncomfortable with or questions arise regarding the direction of a discussion, stop the discussion, excuse yourself and then promptly consult with counsel.

The antitrust laws do not prohibit all meetings and discussions between competitors, especially when the purpose is to strengthen competition and improve the working and efficiency of the marketplace. It is in this spirit that the BioPhorum conducts its meetings and conferences.

Minutes and communication of F2F meetings v1.2

Minutes

The BioPhorum facilitator(s) will capture the key discussions, proposals and decisions in an **Event Report**. This report will act as the **Minutes** of the meeting and will

- detail the objectives, attendees and agenda
- include **hyperlinks** to all the materials shared in the event and an **executive summary**. All materials shared via hyperlinks will be in pdfs to lock down the contents in their presented form.
- Contain **photos** of the presenters and the team to help participants put names to faces after the event. If you do not want to be photographed please let the facilitator know.

Our aim is to **circulate** the Event Report in draft form within six working days of the meeting, to all the participants. A final draft will then be made available to all other workstream reps and Phorum Leaders (L2s).

Circulation to guests will be at the discretion of the facilitator(s) and team.

Photos of presentations must only be taken with the express agreement of their author.

Communication

Often discussions in meetings are exploratory and involve testing ideas, solutions and approaches.

We ask that all representatives in the meeting and dialling in respect the unformed state of discussions and agree not to comment on the discussions publicly on social media or report on the discussions on open public channels, during the meeting and until the final draft of the Event Report has been circulated and any messaging and communications strategy of the team has been agreed.

This is not a bar to representatives communicating about the meeting with peers, colleagues and stakeholders in their own organisation, this is very much encouraged.

Supplier interactions policy v3.0

The BioPhorum Operations Group (BioPhorum) facilitates a cross industry collaboration process for Biopharmaceutical developers and manufacturers with the aim of accelerating the rate at which the biopharma industry attains a mature and lean state benefitting patients and stakeholders alike. Collaboration modes include best practice sharing, benchmarking, joint-solution development to common challenges, definition of standards requirements and formation of collective perspectives to mutual opportunities and regulatory guidelines.

Biopharmaceutical developers and manufacturers recognize the legally enforceable duties they have including the responsibility to control the quality of materials from their suppliers. From time to time BioPhorum-facilitated collaboration requires, and benefits from, supplier interaction.

Suppliers are providers of supply chain materials such as chemicals, glass, components, excipients, and media. They are also providers of process equipment such as single use systems, engineering parts and consumables. BioPhorum-facilitated supplier interactions may involve: harmonizing manufacturer requirements and communicating these to suppliers; seeking feedback on proposed standards; gaining opinions and ideas related to business process improvement; use of problem solving tools; and gaining support for new ways of working.

The ultimate goal of the BioPhorum collaboration is to strengthen competition, assure product quality and protect patient supply.

The purpose of this document is to set out the principles and policies that BioPhorum follows to ensure that BioPhorum-facilitated supplier interactions are conducted in the correct and appropriate way to meet all legal and business compliance requirements.

Underlying Principles and Policies

Competition Laws: All supplier interactions will comply with anti trust and competition laws and have regard to BioPhorum's anti-trust compliance statement

Member responsibilities: Individual biopharma companies are responsible for defining their requirements of suppliers.

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Intellectual Property: All supplier interactions will respect suppliers' intellectual property rights.

Confidentiality / Non Disclosure: All supplier interactions will take into account, respect and encourage compliance with confidentiality and non-disclosure agreements.

Equal Treatment: All suppliers will be treated equally

Communication: These principles, policies and procedures will be communicated to BioPhorum members and suppliers whenever supplier interactions are planned or are taking place.

BioPhorum responsibilities

- It is the responsibility of BioPhorum Directors to ensure that these principles and policies are upheld and procedures are in place to support them.
- BioPhorum will educate and train its staff so they understand and follow these principles and policies and are able to communicate them when needed.
- BioPhorum documentation will reference or directly include relevant parts of the Supplier Interaction Policy.
- BioPhorum will establish and maintain records to demonstrate compliance with these principles and policies.

Code of Conduct – BioPhorum information sharing v5.0

Introduction

BioPhorum Operations Group (BioPhorum) is a cross industry collaboration with the aim of sharing best practice in the area of Operational Excellence. Participation in BioPhorum is restricted to authorized member company representatives as described in the Principles of Membership Agreement.

While sharing information is central to the process of this collaboration, it is important to understand what information is appropriate to share. Our companies have a great deal of confidential information and intellectual property that should not be shared within BioPhorum.

This document seeks to guide the reader so that the individuals and companies involved follow the correct code of conduct and problems are avoided. It is the clear and stated intention of BioPhorum that the Group and its activities are conducted at all times in full compliance with relevant competition/anti-trust rules.

Responsibilities

It is the responsibility of every person who participates in a BioPhorum event or sharing activity to make sure they are aware of what information is appropriate to share.

When sharing third party documents on The BioPhorum Hub (or other IT systems), participants should use links to documents to avoid breaching copyright requirements.

The BioPhorum facilitators are responsible for reminding all participants of their obligations with respect to information sharing and will ensure that the relevant watermark will be included on documents.

Participants should not share outside workstream/Phorum teams unpublished material including but not limited to:

- Ask BioPhorum or survey responses including summary data
- Meeting preparation material or minutes of BioPhorum meetings
- Draft papers
- Individual opinions of representatives or their companies spoken at BioPhorum meetings
- Industry feedback captured using tools such as virtual whiteboards, polls or surveys.

Members can share BioPhorum confidential information within their own organization, but the key contact (L2) for each member should ensure confidentiality and that IP issues are highlighted to their colleagues and all applicable company policies regarding external collaboration and public disclosure are adhered to. All participants are responsible for vetting information to be shared via their company's public disclosure review processes and that all information shared is free of any 'Confidential' label .

Participants' contact details

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- Use of these contact details by participants in the following circumstances is prohibited:
- Compilation of mailing lists and advertising or marketing of any kind
- Creating a database of contact details in any circumstances
- Recruitment and job advertising
- Participants who are unsure as to whether their use of contact information is acceptable or not should refer to their BioPhorum representative.

Sharing information

The following list is representative of the types of disclosures commonly allowed by corporate policies. BioPhorum participants should review their company policies to ensure they are in compliance prior to any disclosures. Information in the following areas is typically allowed:

- Operational excellence best practice models
- Management approaches and philosophies
- Organizing and planning ways of working
- Non-product or process specific generic operating procedures
- Information in the public domain
- Information provided by suppliers which would ordinarily be shared with customers
- Non-product or process specific generic engineering or technical information relating to process equipment
- General learning and 'context' conclusions from QA and Regulatory activity

Sharing information from the following areas is typically prohibited by corporate policies

- Product related information
- Product related process data which constitutes intellectual property
- Specific audit or regulatory inspection findings or observations
- Product specific analytical methods
- Specific cost numbers where a market advantage may result or a supplier might be disadvantaged
- Information that is marked as confidential by the member company or a supplier
- Price information of any type
- Proprietary information including intellectual property and patented processes and equipment.

BioPhorum event participants should direct all questions regarding information disclosure to their L2 BioPhorum representatives or corporate legal departments.

Privacy policy

To learn more about how we collect, keep, and process your private information, please view **our privacy policy.**

Collaboration tools and legals

Legal and policy framework

Our mission is:
To create an environment where the global biopharmaceutical industry can collaborate and accelerate their rate of progress, for the benefit of all

Legal framework

- principles of membership
- anti-trust
- supplier interactions
- code of conduct
- information sharing

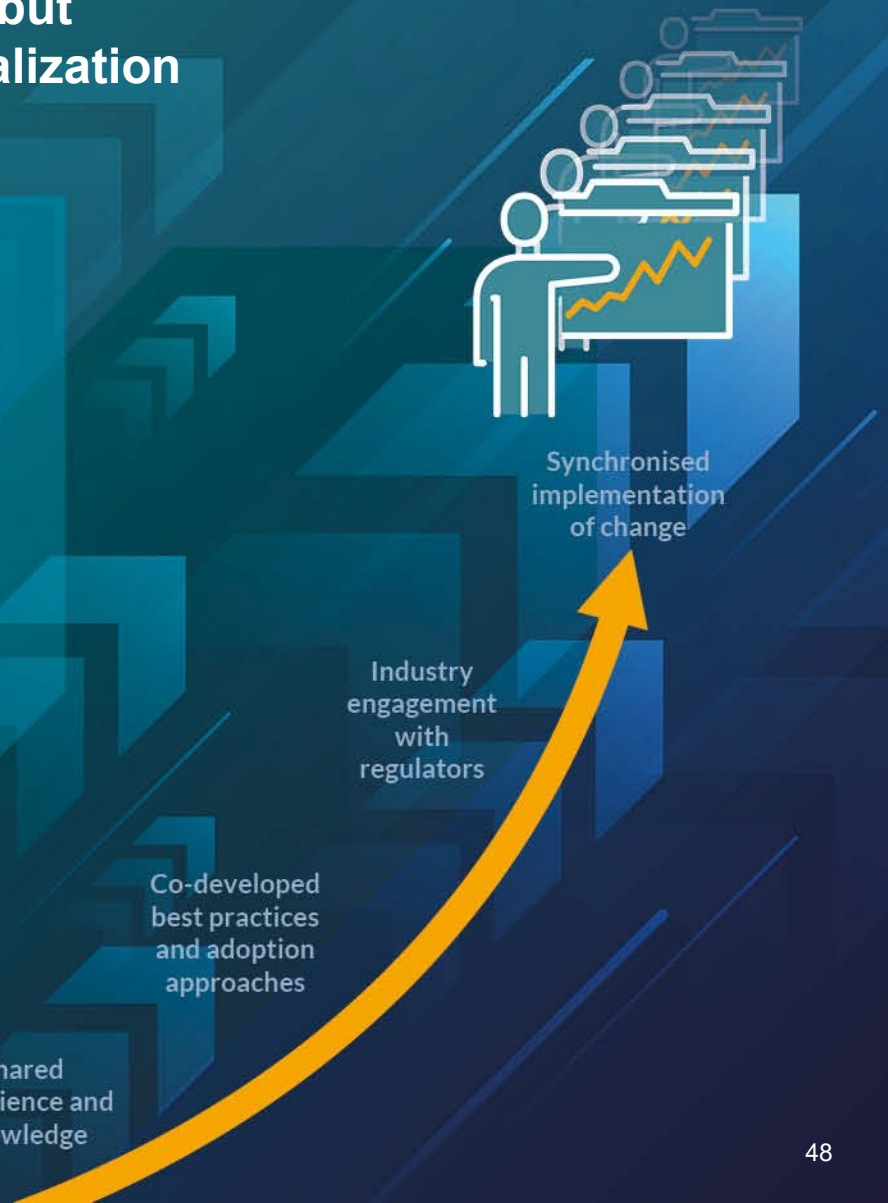
Policy framework

- equitable contributions
- consensus driven
- end user led
- sales free
- safe and confidential

Implementation and benefit realization

In BioPhorum the publication is not the END but the START of industry change and benefit realization

- engage and align the power of all stakeholders across the biologics industry
- drive appropriate synchronized change to create value across the biologics industry
- provide long term support to sustain and grow industry value realization



BioPhorum Hub – our online collaboration platform

Members only area password controlled

Searchable database > 11,000 documents

- member only whitepapers
- detailed benchmarks
- events reports from every F2F meeting
- all meeting minutes

Contact details of all BioPhorum reps

Workstream charters

Ask BioPhorum facility and 2000 mini benchmarks

Ask BioPhorum

The industry leading online Q&A tool

Connect directly to 100s of industry experts FAST

- benchmark and compare practices
- check you are making good decisions
- answer unexpected audit challenges

Ask BioPhorum

Our facilitators will help you

- phrase the question to get the best response
- search the database of over 2000 benchmarks
- go beyond the database and connect you directly to the industry's top practitioners on one-to-one calls

Competition compliance guidance v1.0

Introduction

BioPhorum takes compliance with anti-trust / competition law seriously and this guidance applies to all members and attendees of the Phorums. Members represent competing firms and certain activities / discussions might lead to a breach of competition law, which can have serious consequences both for the members and BioPhorum itself. These include substantial financial penalties of up to 10% of the annual worldwide group turnover, private actions for damages, reputational damage, and criminal liability in some countries for price fixing /market sharing. It is therefore paramount to make sure that activities of members of the Phorums are fully compliant with the requirements of competition law.

Possible breaches

1. Cartels / Price fixing / market sharing

A fundamental requirement of competition law is that companies act autonomously in the market and take commercial decisions independently of their competitors. Any actions which might lead to fixing prices or sharing markets and which therefore reduce strategic uncertainty as to the future market behavior of competitors will be in breach of competition law.

2. Exchange of competitively sensitive information

While discussions between members on best practice and how to improve safety and efficiency as well as discussions on how to respond to legislative proposals are all welcomed, the exchange of competitively sensitive information might be a breach of competition law. Importantly, even a single and one-way exchange of competitively sensitive information suffices for there to be a breach, and even if the parties have not implemented what was discussed.

The exchange of information that is in the public domain, which is old and aggregated (see section on benchmarking) is unlikely to raise competition concerns. On the other hand, information not in the public domain, which is current (or relates to future) as well as individualized could be a breach of the law.

In particular, this is likely to cover any information regarding:

- prices and pricing, including price components, discounts, price changes, price calculations, price strategies, costs
- market shares, profit margins, product portfolio development and optimization
- details of contracts with third parties, terms of delivery or payment, delivery quantities, capacities
- current and future market strategy (e.g., size, numbers, areas of activity, planned investments).

3. Benchmarking

Benchmarking exercises (and market surveys) are generally intended to improve the efficiency and competitiveness of the participants and can therefore have pro-competitive effects. However, they may also raise competition law concerns when the companies involved are actual or potential competitors, particularly where the benchmarking exercise entails the exchange of confidential information.

In order to avoid competition issues, benchmarking exercises should be carried out by an independent third party (which could be BioPhorum) and should be limited to topics necessary to understand the area being benchmarked. Data should be anonymised and aggregated and should include a sufficient large number of participants so that it is not possible to reverse engineer the data.

Benchmarking should never be carried out on competitive sensitive information such as future plans (especially on pricing, new product development, marketing strategies), profitability models, etc. If in doubt, please seek competition law advice.

Best practice for the meetings of the Phorums

Members participating in the Phorums are strictly prohibited from exchanging *competitively sensitive information* with competitors not only during meetings of the Phorums but also outside of meetings of the Phorums. This includes off-the-record occasions such as coffee breaks and social events as well as online collaboration platforms.

Representatives of members of the Phorums should be required to complete a competition law training annually provided by their employer (the Member company) and at the beginning of each meeting of the Phorums, the chairperson of the meeting should remind the participating members of their obligations under competition law and arrange for this reminder to be mentioned in the minutes.

A draft agenda should be agreed by the participants and circulated prior to each meeting. The agenda should have a clear wording and be as detailed as possible. Generic points such "Any other business" should be avoided. The participants should always follow the agenda.

If members participating in the Phorums believe that a point on the agenda is likely to give rise to competition law issues, they should contact the chairperson of the meeting in order to object to the point being included in the agenda and ask for a legal review.

The chairperson should stop the discussion if it digresses into subject matter which involves *competitively sensitive information.*

After each meeting of the Phorums, the minutes should be prepared and promptly made available to all participants. The participants should have an opportunity to comment on the contents of the minutes and object to any misleading wording.

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