New PDA Technical Report: *Contamination Control in Pharmaceutical Manufacturing*

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Providing the Building Blocks to Contamination Control

Status: Currently Being Drafted

- We've had a few meeting thus far, so it's early in the development stage
- The team is consisted of professionals from industry, as well as regulatory authorities
- Goal is to ensure that we are providing the industry with a useful tool to ensure Contamination Control Programs and strategies are robust and compliant
- There are many references available that tell us **WHAT** we need to do, but not **HOW**; our goal is to provide the **HOW** in this report

Team

First Name	Last Name	Company
Renee	Blosser	FDA
Reyes	Candau-Chacon	FDA
Adam	Carusa	Merck
Biswarup	DasGupta	Bioverativ (a Sanofi company) (LEAD)
Josh	Eaton	Chair
Cheryl	Essex	Sanofi (CO-LEAD)
David	Keen	Ecolab Life Sciences
Maureen	Mueller	Quality Systems Consulting. Inc. (CO-LEAD)
Christopher	Murdock	Bristol-Meyers Squibb
Patrick	Nieuwenhuizen	Sanofi
Paula	Peacos	Valsource, LLC
Christine	Sherman	Takeda
Joseph	Sondej	Celgene
Edward	Tidswell	Merck
Andrew	Hopkins	Abbvie
Staci	Williams	Adaptimmune

Definitions

- **Contamination:**

  The undesired introduction of impurities of a chemical or microbiological (quantity and type of microorganisms, pyrogens) nature, or of foreign matter, into or onto a raw material, intermediate, API or drug product during production, sampling, packaging or repackaging, storage or transport with the potential to directly adversely impact product quality.

  This Technical Report is going to focus on microbiological contamination, including microbial by-products

Definitions

- **Control Strategy:**

  (ICH Q10): A planned set of controls for microorganisms, pyrogens and particles, derived from current product and process understanding, that ensures process performance and product quality.

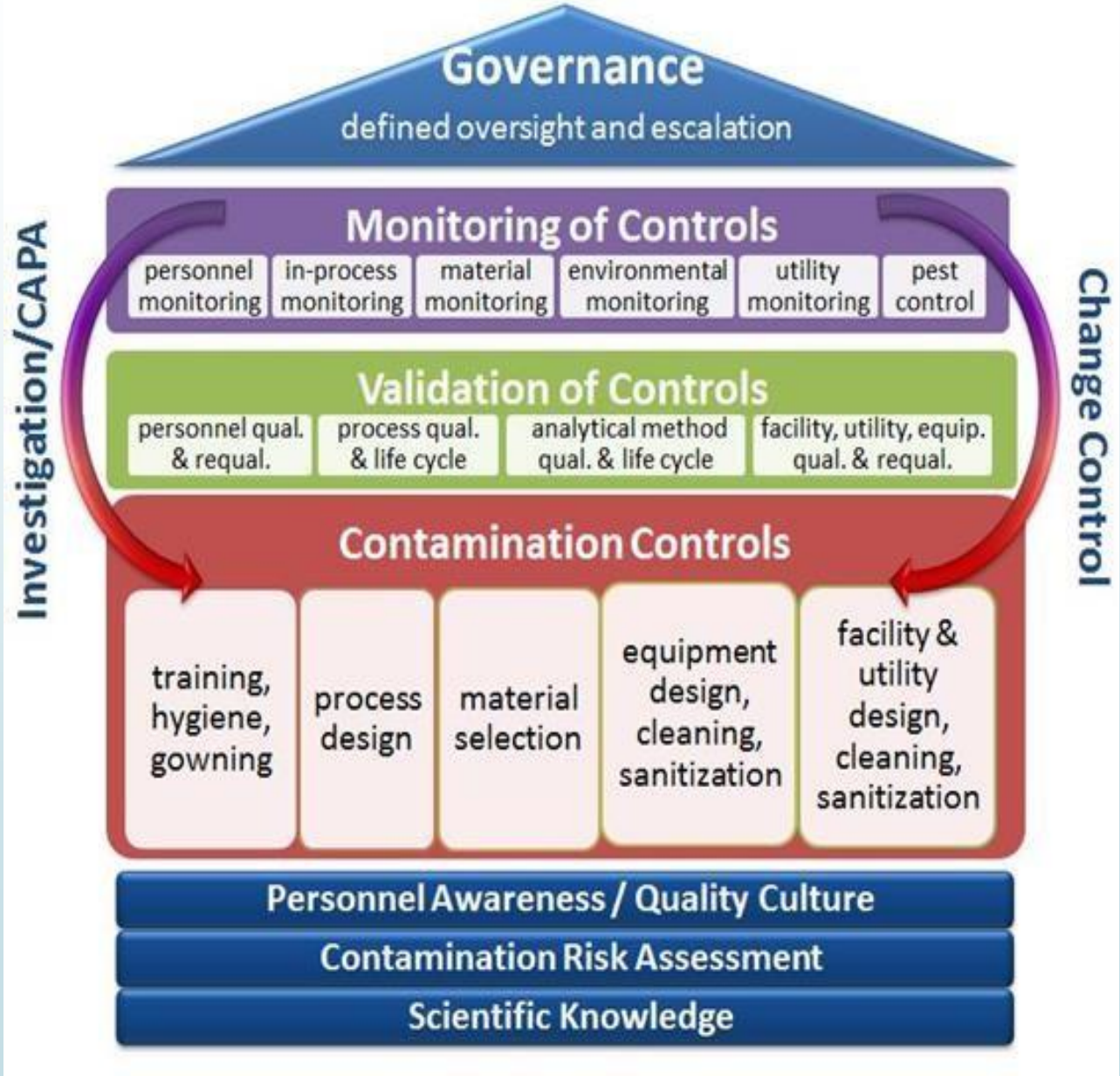
  The controls can include parameters and attributes related to:

  - **Drug substance and drug product materials and components**
  - **Facility and equipment operating conditions**
  - **In-process controls**
  - **Finished product specifications**
  - **Associated methods and frequency of monitoring and control**

  A risk based approach based on facility and process design to reduce and/or eliminate the risk of contamination.

  - **Both proactive and reactive**
  - **The proactive part is based on risk assessments; i.e., knowledge based**
  - **The reactive part is based on monitoring, test results, investigations, trends, etc.**
  - **A lifecycle approach**

Contamination Control Strategy Life Cycle



Created By:
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Purpose

- Describe how to implement effective contamination control strategies that comply with regulatory requirements, industry standards and guidelines
- Guide companies on creating or optimizing existing control strategies
- The purpose of this TR is different in that it will focus on the **HOW**

Scope

In Scope

- Focus is on microbial, endotoxin and particulate control
- Includes:
  - Sterile products manufactured by aseptic processing
  - Terminally sterilized products
  - Clinical manufacturing
  - Non-sterile low-bioburden manufacturing intermediates
  - And others…..

Scope

Out of Scope

- Chemical Contamination
- Detailed Facility Design
- And others….

Elements of a Contamination Control Strategy

- Manufacturing process design and validation
- Facility design, including material / personnel / waste flow patterns
- Environmental control programs and validation
- Equipment handling and cleaning / validation
- Personnel training
- Utility design, controls, and validation
- Raw materials
- Product containers and closures

Elements of a Contamination Control Strategy

- Maintenance
- Process and facility monitoring
- Contamination and utility interruption response
- Quality Systems
  - Trending and metrics
  - Investigations
  - CAPA
  - Change control for modifications
  - Etc.
- Governance and oversight

Road Map

- Intention is not to repeat the information presented in other PDA Technical Reports, regulatory documents, guidances, etc.
- Includes references to published guidances, industry standards, as appropriate rather than recreate or present similar content
- Aids in the identification of gaps and areas to be addressed in the TR

Inputs and Outputs

INPUTS:

- Identifies what systems provide information and support to the Contamination Control Programs and Strategy
  - Engineering drawings: facility layout, utilities layout, area classifications, etc.
  - Pressure cascade diagrams
  - Personnel / Material / Waste Flow diagrams
  - Process flow maps
  - Procedures
  - Batch records

Inputs and Outputs

OUTPUTS:

- Identifies what data is generated that provide objective evidence that the contamination control programs are robust
  - Sterility test results
  - Bioburden test results
  - Environmental monitoring data and trends
  - Critical utilities monitoring data and trends
  - Media Fill Studies results
  - Other proactive indicators

Pre-Requisites to Contamination Control Strategy

- Scientific Understanding
  - Principles of how contamination occurs
  - Process growth potential, removal steps, formulation
- Contamination Risk Assessment
  - Applicability to control strategy and how to be expedient and cost-efficient while still being compliant and effective; tailor strategy as much as possible to the process/plant
  - Identifies all contamination ingress points and proliferation hazards
  - What are the QRM aspects for these and how do we approach them?
- Personnel Awareness / Quality Culture
  - Education, not just training
  - Effects all aspects of contamination control strategy

Your input and questions today are welcomed