# Knowledge-Aided Assessment and Structured Application (KASA): Part 2 Biological Products

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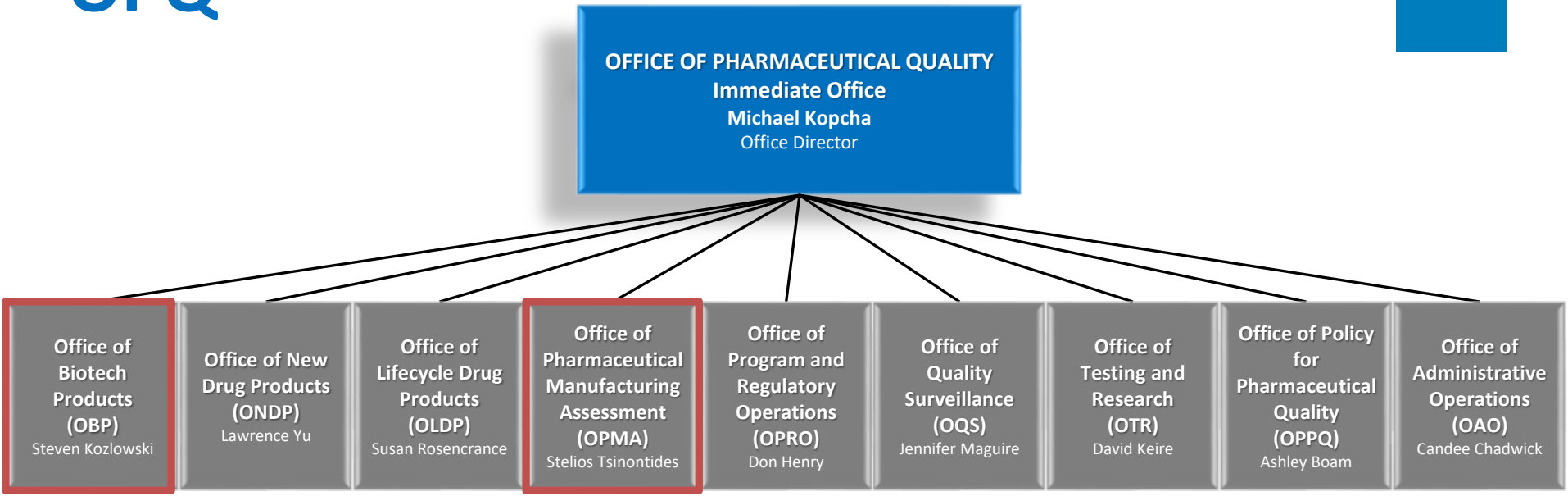
# Learning Objectives

- Understand the Key Benefits of the KASA System
- Identify the Unique Opportunities and Challenges for Biological Products and KASA
- Explain the General Development approach for KASA modules for Biological Products in CDER

# OPQ




OPMA responsible for microbiology and facility assessment

# CDER Application Assessment Challenges

## External Challenges

- Volume of new applications
- User fee program expectations
- Commissioner, Congress, the pharma industry, and the public expectations
- Technology advancements

## Internal Challenges

- Freestyle narrative assessment:
  - Unstructured text
  - Summarization of application information
  - “Copy and paste” data tables
- Cumbersome knowledge sharing and knowledge management
- Subjective assessment based on the assessor’s expertise and knowledge at hand

# Key Objectives of KASA System

1. Capture and **manage knowledge** during the lifecycle of a drug product (Applicable for biological products)
2. Establish **rules and algorithms** to facilitate risk identification, mitigation, and communication for the drug product, manufacturing process, and facilities (Applicable for biological products)
3. Perform **computer-aided analyses of applications** for a comparison of regulatory standards and quality risk across the repository of approved drug products and facilities; (Applicable for biological products)
4. Provide a structured assessment that **radically eliminates text-based narratives** and summarization of information from the applications. (Applicable for biological products)


# Challenge Question #1

**Broadly, KASA has four key objectives: How many apply to KASA for biologics?**

A. Three; computer-based rules and algorithms do not apply

B. None of them- Biologics are too complex

C. One; only the Knowledge Management portion is anticipated for biologics

D. All four objectives still apply

# What's Different with Biological Products?

## Nature of Process

Few "low risk" unit operations

*Viral Safety, Aggregation, etc*

*DNA, HCP Clearance*

*Resin Lifetime*

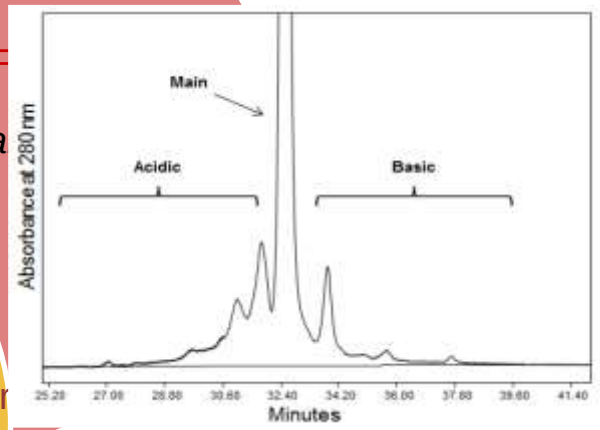
Small Scale Models

Spiking Studies

"Platform" Validation

*Viral Clea*

## Data Submitted




Unique safety concerns

*Adventitious Agents, Viral Clearance*

*Retain Activity?*

Product Related Substances vs. Impurities

COMPLEXITY

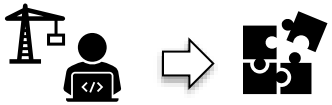
Methods monitor multiple CQAs

*Understanding of target and distribution*

*More than 1?*

MOA

## Molecular Function and Context



# Biotechnology KASA First Prototype Module:

- A risk-based assessment module for drug substance manufacturing
- Applies only to fed batch monoclonal antibodies
  - The majority of BLA submissions
- Prototype applies to new BLAs (though framework can be adapted for supplements)
- Does not include microbiology and facility portion yet
- Designed to capture description for manufacturing steps, including:
  - Process parameter Criticality assessment
  - Process parameter Range evaluation
  - Key elements that aren't characterized, but need to be described

# OBP KASA 1.x prototype: Key Features

- Data submitted by the sponsor can drive risk ranking up or down
- Initial risk ranking based on assessor expertise and scientific consensus
- Flags for assessment issues and IRs (to facilitate discussion between primary and secondary assessors)
- Able to capture revisions during assessment cycle
- Generates a summary output to be integrated in assessment document
- Designed to be consistent with ICH Q12 concepts

# Challenge Question #2

**What assessment activity is KASA for Biological Products beginning with?**

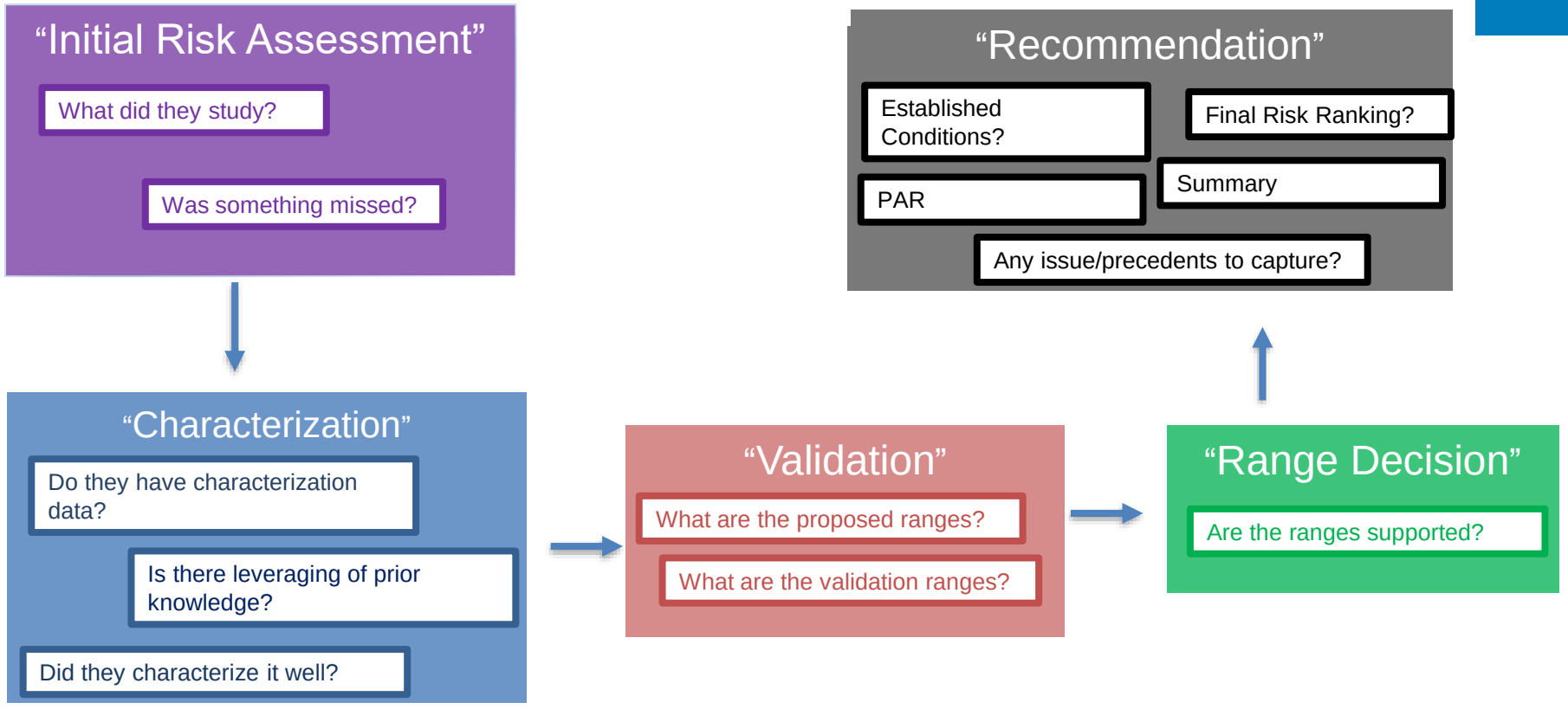
A. KASA piloting will include all portions of BLA in its pilot

B. Fed-batch drug substance manufacturing for monoclonal antibodies

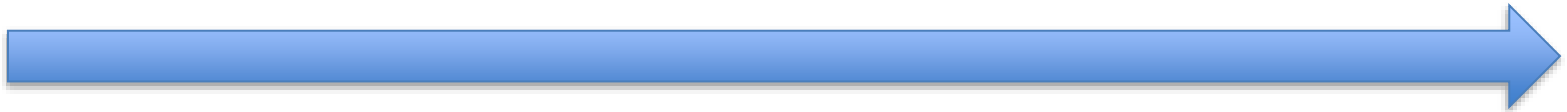
C. Both stability and specifications for drug substance and drug product

D. Drug product manufacturing

# Basic Algorithm Module



# Where to Next for KASA for Biologics?



Module Development

Drug Substance Unit Operations 1.0

DS 2.0 (More Molecules and More Processes)

Viral Clearance/AA

Drug Product

Stability

Methods

Specifications

Fully Implement KASA for BLAs

Identify Key Outputs

Characterization

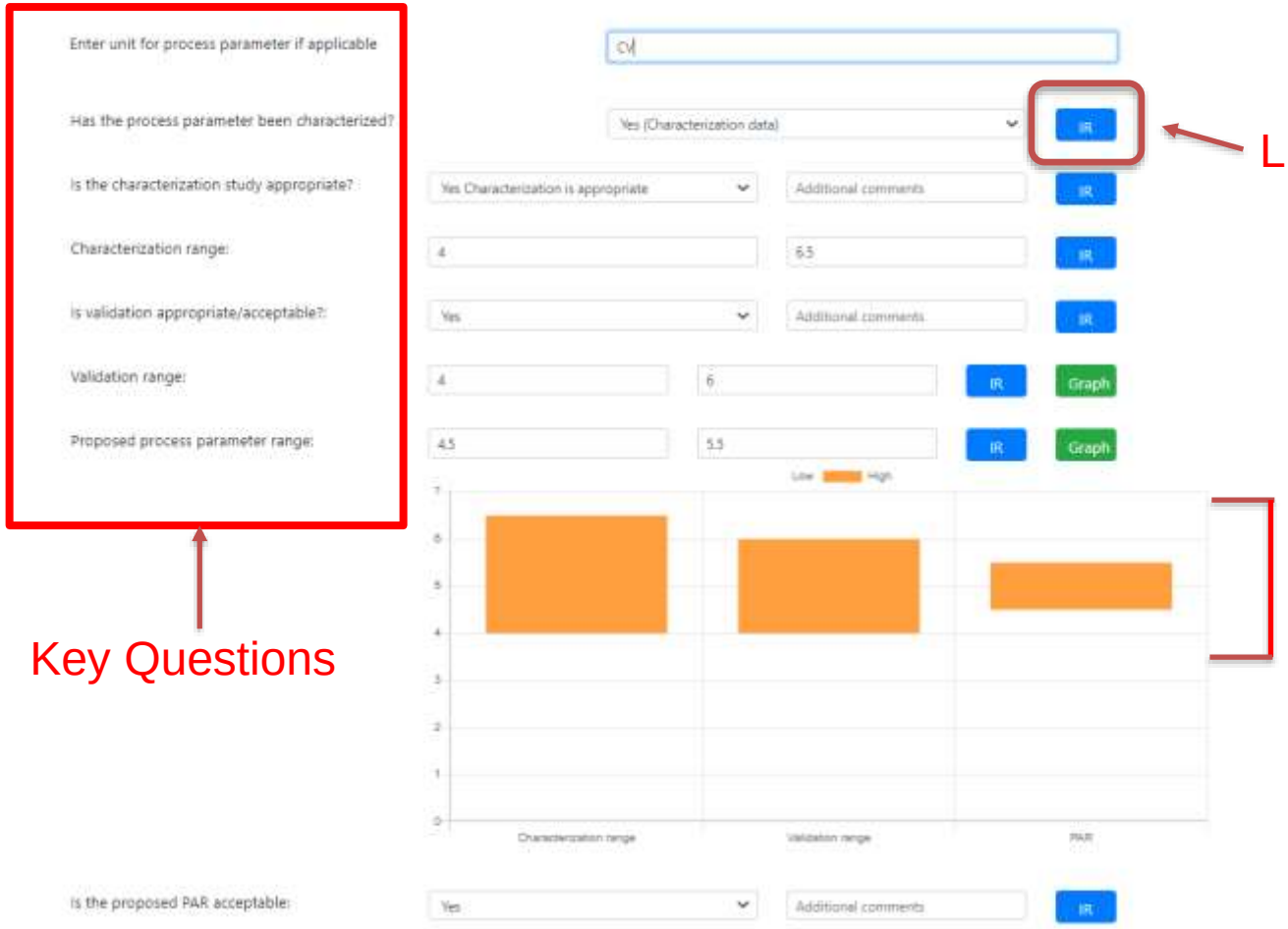
CQA and Attribute Tables

Comparability

ECs

Comparative Analytical Data for Biosimilars

# KASA at a Glimpse - DS



# KASA at a Glimpse

## Viral Clearance Module:

Select a Unit Operation for viral clearance study: Virus Inactivation - Low pH

Does VC study used a modular or platform approach? No

| Process Parameters | Check Box (Link to Commercial Manufacturing Process) | Parameter Values |
|---|---|---|
| **Hold Constant** | | |
| Liquid pH | ☐ | 3.90-3.95 |
| Liquid composition (i.e. buffer composition and molarity) | ☑ | |
| Protein concentration | ☑ | |
| Time | ☐ | 5, 10, 20, 30, 55 |
| Temperature | ☐ | 14.5-15.4 |
| **Scaled Down** | | |
| Liquid Volume | ☑ | |

Are Unitoperations for Viral Clearance study done? Yes

# Conclusions

- KASA presents incredible opportunity for knowledge management, consistency in decision making, and improving efficiency
- KASA for biologics is beginning a pilot to assess its prototype modules
- The biologic KASA module builds on the same approach as others but includes unique elements based on nature of biotechnology products

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