What's in a KASA?
Knowledge-Aided Assessment and Structured Application (KASA) For Biological Products

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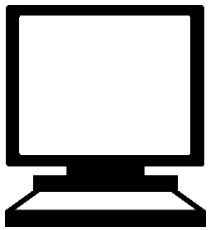
WCBP 2022 "One World, One Submission"
January 27, 2022

Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.



Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.

Drugs are no different.


FDA
Patients expect safe and effective medicine with every dose they take.

Pharmaceutical quality is

assuring *every* dose is safe and effective, free of contamination and defects.


It is what gives patients confidence in their *next* dose of medicine.

Disclaimer

This presentation reflects the views of the author and should not be construed to represent FDA's views or policies

Objectives

- Understand the Key Benefits of the Knowledge-aided Assessment and Structured Application (KASA) System
  - Foundational Knowledge Management
  - Informatics-aided risk assessment
  - Alignment of data-driven assessments and outputs
- Identify the Unique Opportunities and Challenges for Biological Products and KASA
- Explain the General Development approach for KASA modules for Biological Products in CDER

One World, One Submission – One Assessment

KASA is an internal assessment tool intended to streamline practices already in place for assessments, increasing efficiency and consistency

KASA will support:

- Efficiency gains through focused assessment of risk parameters
- Streamlined assessment using concise dropdown menus to replace long written text, generation of direct links to a page/table/figure in submission
- Consistent assessment across product lifecycle
- Standardized knowledge management/analytics

Application Assessment Challenges

External Challenges

- Volume of new applications
- User fee program expectations
- Commissioner, Congress, the pharma industry, and the public expectations
- Technology advancements
- Complexity of Biological Products (OBP)

Internal Challenges

- Freestyle narrative assessment:
  - Unstructured text
  - Summarization of application information
  - "Copy and paste" data tables
- Cumbersome knowledge sharing and knowledge management
- Potential for subjective assessment based on the assessor's expertise and knowledge at hand

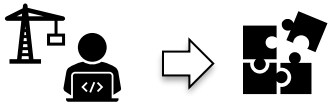
Key Objectives of KASA System for Biological Products

1. Capture and **manage knowledge** during the lifecycle of a drug product

2. Establish **rules and algorithms to facilitate** risk identification, mitigation, and communication for the drug product, manufacturing process, and facilities

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;

4. Provide a structured assessment that **radically eliminates text-based narratives** and summarization of information from the applications.



First Prototype KASA Module for Biologics

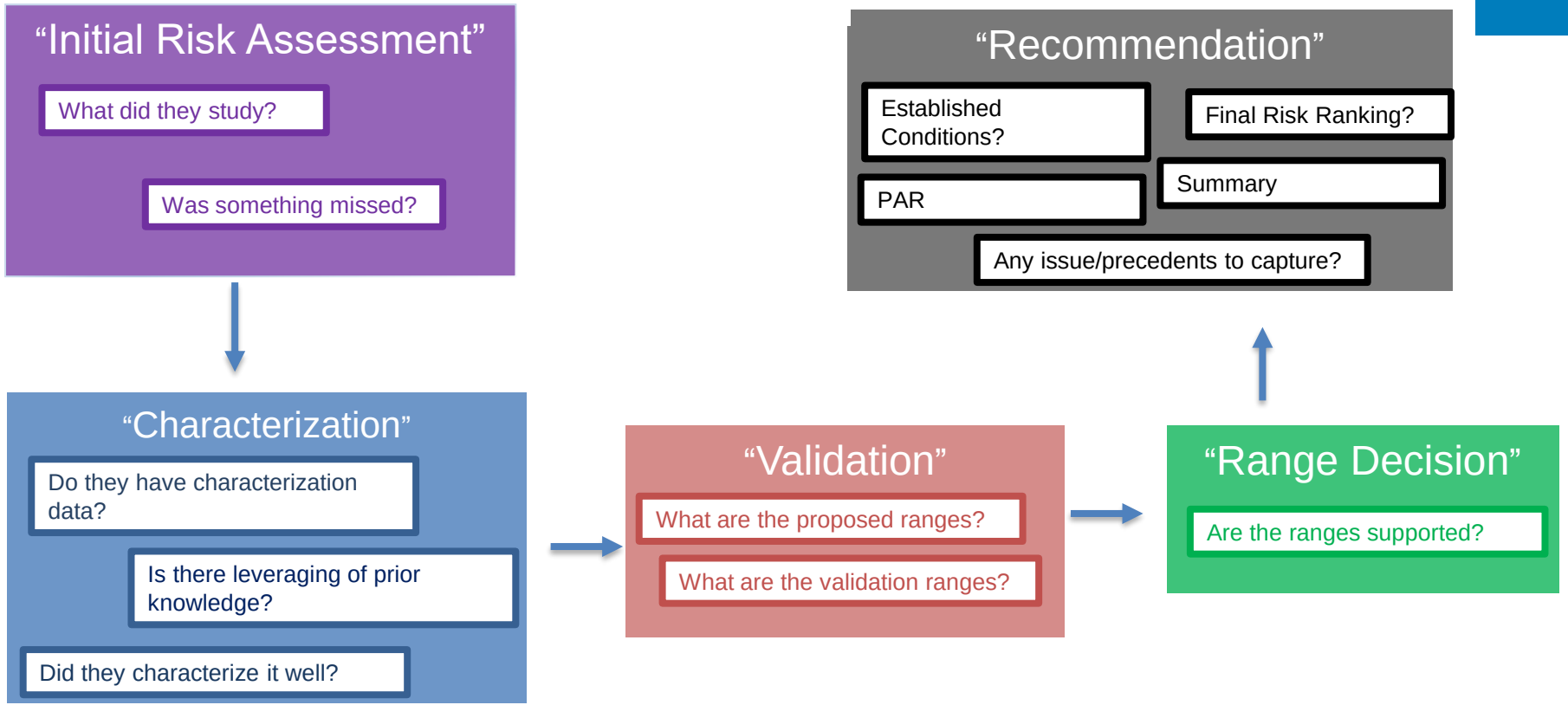
A risk-based assessment module for **Drug Substance manufacturing**

- Applies only to fed batch monoclonal antibodies
- 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:
    - Key manufacturing elements that are not characterized, but need to be described
    - Process Parameter Criticality assessment
    - Process Parameter Range evaluation

OBP KASA 1.x prototype: Key Features

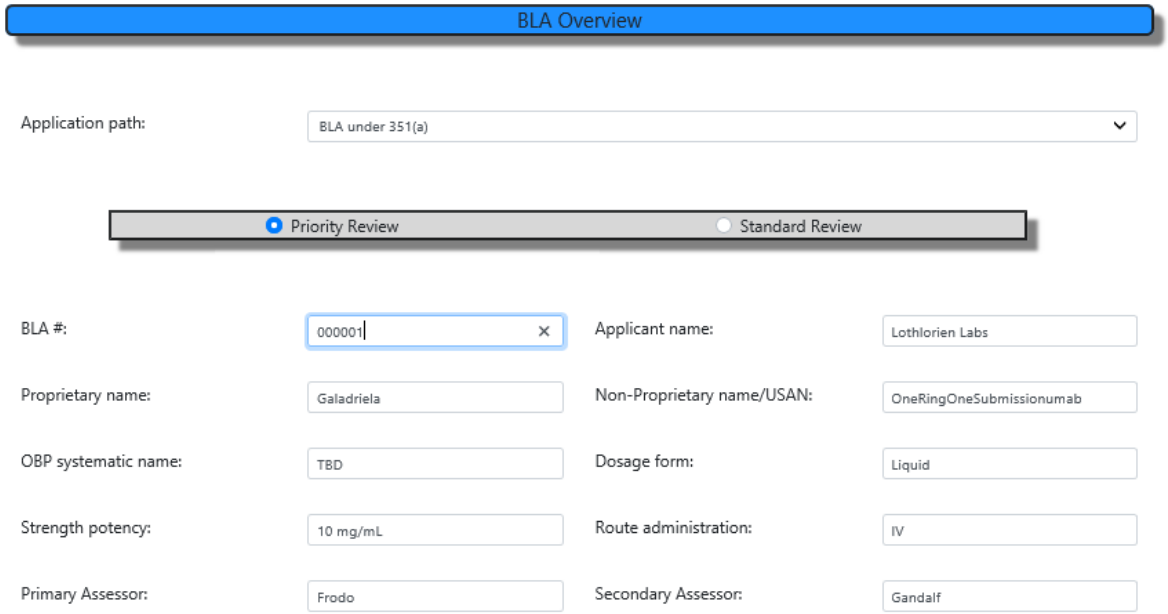
- The process parameter risk assessment is based on a combination of the sponsor's data and accumulated knowledge in the field
- Flags for assessment issues and IRs (to facilitate discussion between primary and secondary assessors)
- Able to capture revisions during assessment cycle
- Provides a clear connection between available development data, validation results, and the proposed PAR for critical process parameters
- Generates a summary output to be integrated in assessment document
- Designed to be consistent with ICH Q12 concepts

KASA Decision Making Overview



KASA at a Glimpse *(Under Construction)* – DS Manufacture

Knowledge-Aided Assessment and Structured Application



KASA at a Glimpse *(Under Construction)* – DS Manufacture

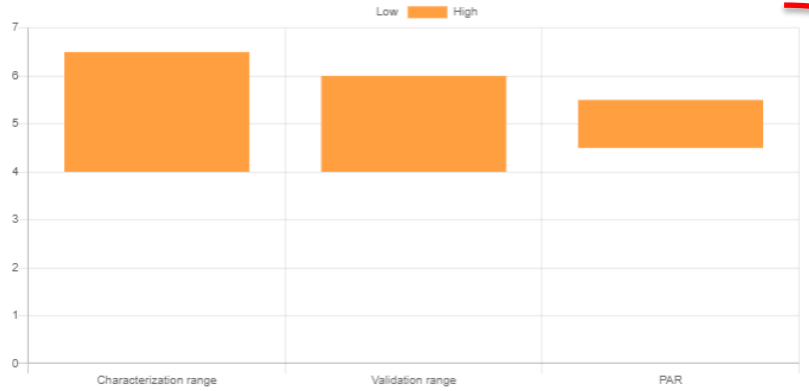
Select the Unit Operations included in the application

Cell culture - Harvest	Cell culture – Production bioreactor	Cell culture – Seed bioreactor
Cell culture – Vial thaw & inoculation expansion	Chromatography – Anion exchange	Chromatography – Cation exchange
Chromatography – Hydrophobic interaction	Chromatography – Mixed mode	Chromatography – Protein A
Ultrafiltration/Diafiltration	Viral filtration	Virus inactivation – Low pH

Common Unit Ops

KASA at a Glimpse *(Under Construction)* – DS Manufacture

Enter unit for process parameter if applicable	CV		
Has the process parameter been characterized?	Yes (Characterization data)		IR
Is the characterization study appropriate?	Yes Characterization is appropriate	Additional comments	IR
Characterization range:	4	6.5	IR
Is validation appropriate/acceptable?:	Yes	Additional comments	IR
Validation range:	4	6	IR Graph
Proposed process parameter range:	4.5	5.5	IR Graph



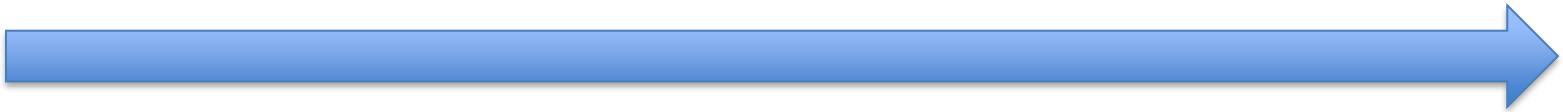
Is the proposed PAR acceptable:	Yes	Additional comments	IR

Link to IR

Key Questions

Comparisons of Ranges

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 *(Under Construction)* – Viral Clearance

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 opportunities for knowledge management, consistency in decision making, and improving efficiency
- The biological product KASA includes unique elements based on the nature of biotechnology products
- Prototype KASA modules for biological products are in step-wise development and the Drug Substance Manufacture component is undergoing an internal pilot for assessment

Acknowledgments

- Joel Welch
- Bazarragchaa Damdinsuren
- Kristen Nickens
- Fabiola Gomez
- Emine Guven-Maiorov
- Steve Kozlowski
- Sireesha Vardhineedi
- Christelle Yemeck
- Larisa Wu
- Andre Raw

<u>Former Members:</u>

- Pick-Wei Lau
- Ramesh Potla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