Modernizing Manufacturing Assessment through KASA

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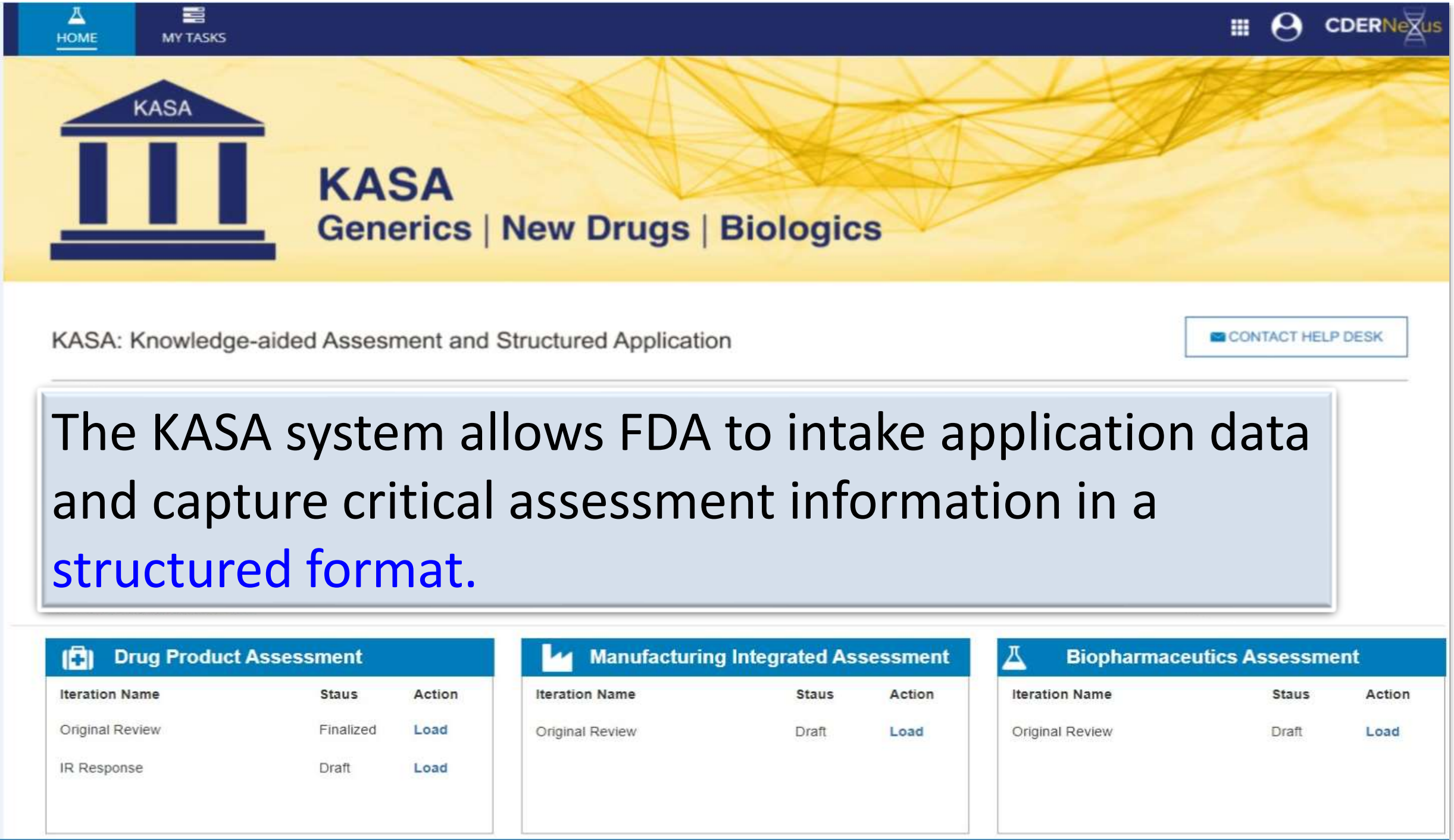
Generic Drug Forum 2022

Overview

- KASA for generic drug application
- Integrated manufacturing assessment
- Facilities and manufacturing risk assessment
- Facilities and unit operations assessment in KASA
- KASA analytics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MY TASKS
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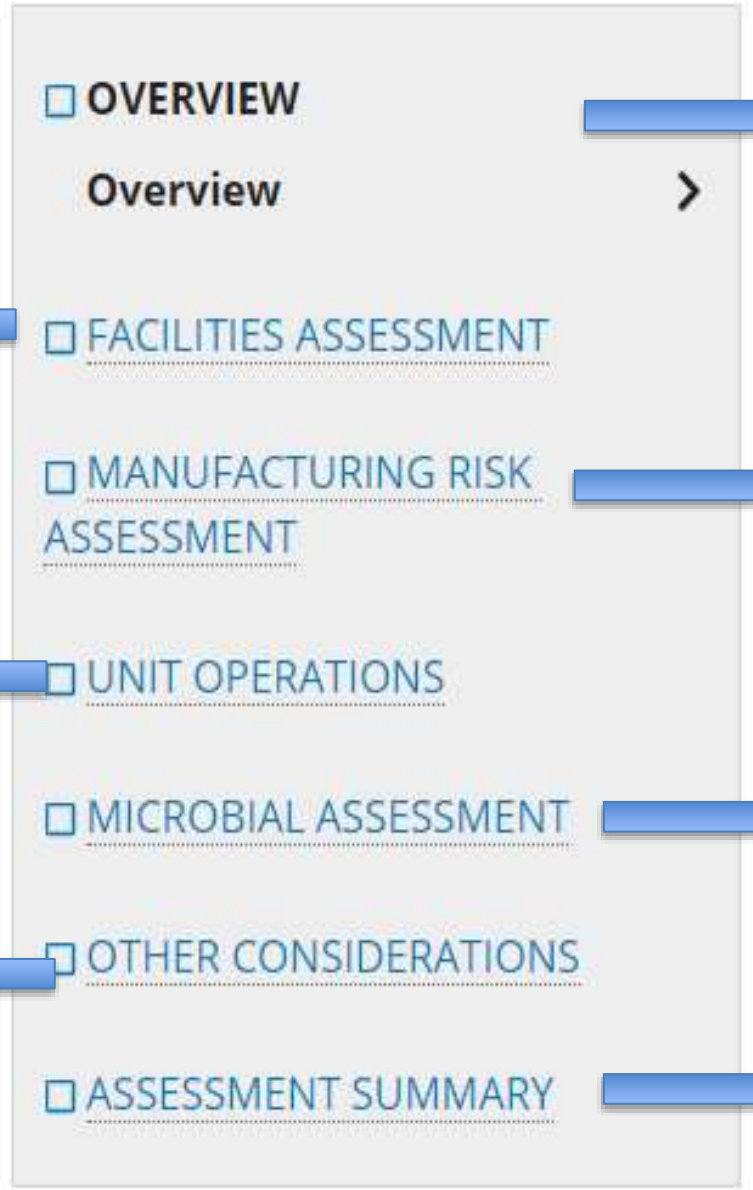
KASA
KASA
Generics | New Drugs | Biologics
KASA: Knowledge-aided Assesment and Structured Application
CONTACT HELP DESK
The KASA system allows FDA to intake application data and capture critical assessment information in a structured format.
Drug Product Assessment
Iteration Name Staus Action
Original Review Finalized Load
IR Response Draft Load
Manufacturing Integrated Assessment
Iteration Name Staus Action
Original Review Draft Load
Biopharmaceutics Assessment
Iteration Name Staus Action
Original Review Draft Load

Integrated Manufacturing Assessment



Basic ANDA Information, drug substance, drug product, facilities list

Facilities risk assessment for all commercial drug substance and drug product manufacturing, testing, and primary packaging facilities

Initial risk for drug product manufacturing assessment include factors for drug product, drug substance, facilities, unit operations

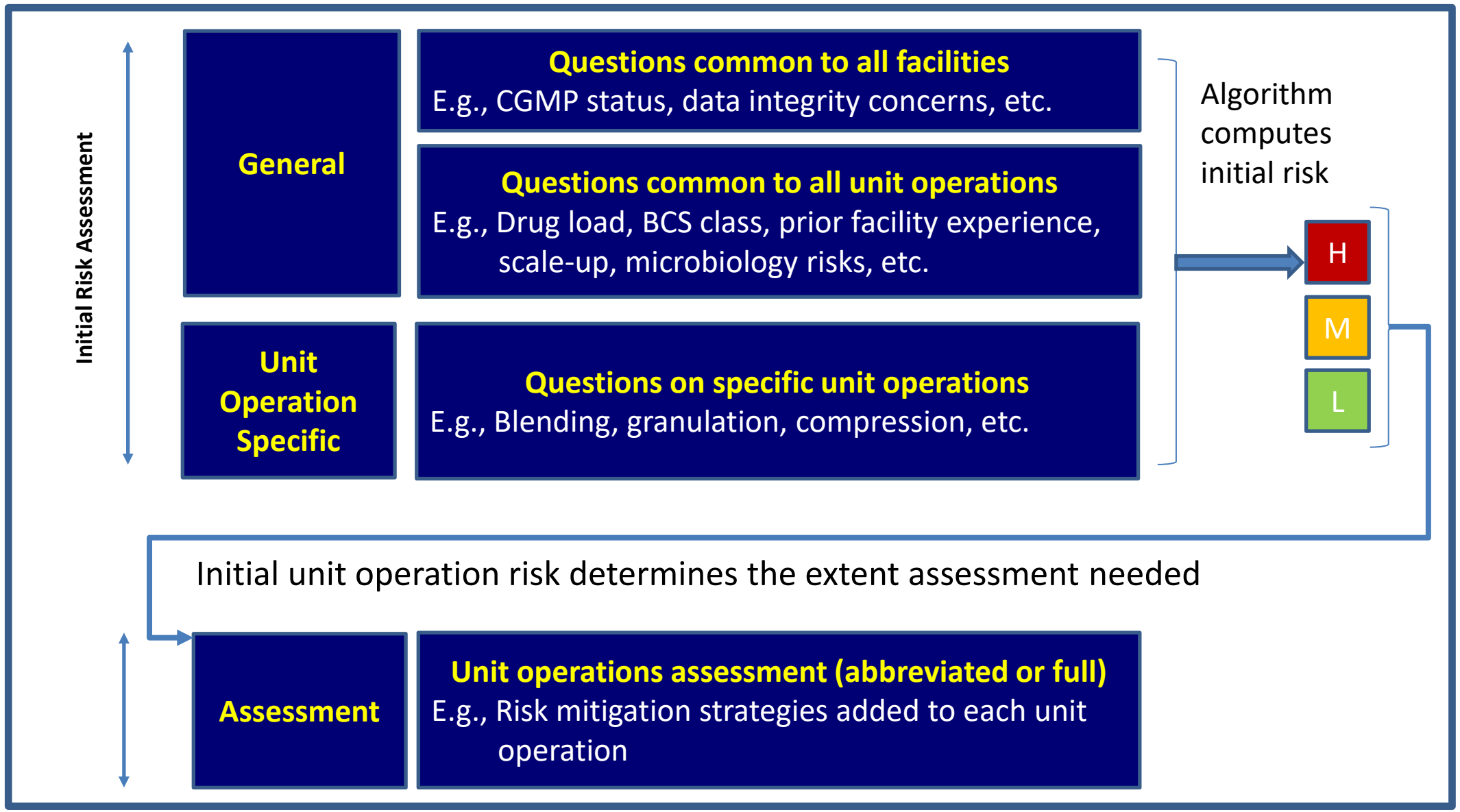
Each drug product unit operation assessment includes type, equipment, in-process controls, process parameters design & development consideration, process development, scale up

Microbial assessment for drug product control

Executed and master batch records, yield, reconciliation, hold time, comparability protocol, process validation (if applicable)

Assessment discipline summary and risk update table

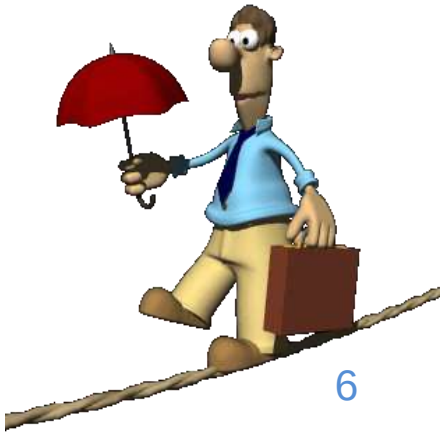
Manufacturing Risk Assessment & Control



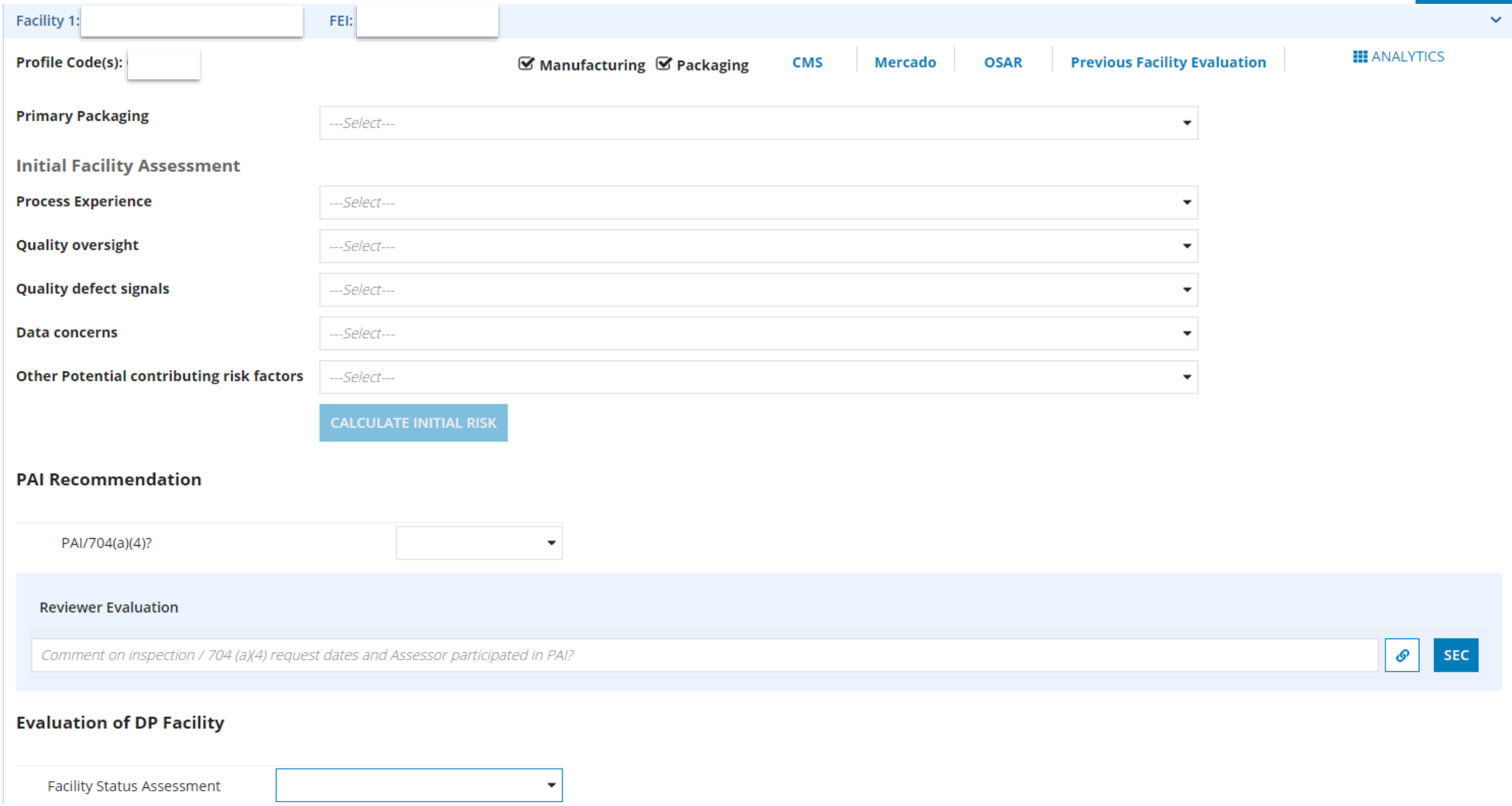
Facility: Risk based Assessment

- Establishment is named for the first time
- First application filed by applicant
- New dosage form not previously approved at the site
- Substantially different or novel manufacturing process/design than previously approved
- Concerns about firm's quality systems
- Questions about the firm's capability of manufacturing quality products
- Scale-up concerns
- Product specific concerns

Pre-Approval Inspection: Supports review & approval of marketing applications for drug products
Post approval Inspection: Initiated after approval to verify that commercial-scale manufacturing and drug quality are per approved application
Alternate tools: could be used in advance or in lieu of inspection. 704(a)(4), remote interactive evaluations, mutual recognition agreements are some examples



Facility Assessment in KASA



Unit Operation Risk based Assessment

- **Product & process development**
  - **Drug load**: Low, medium, high
  - **Solubility of API**: High or low
  - **Physical properties of API/Excipients**: Flow, static charges, particle size, polymorphism as they relate to manufacturability or product performance
  - Stability
    - Aqueous stability: wet granulation versus direct compression
    - Thermal stability: possibility of form conversion, degradation
  - **Formulation**: Impact on CQAs, stability
    - API & Excipient Compatibility: possibility of degradation with the process selected

- **Process reliability** **(e.g., performance under different operating conditions, at different scales or with different equipment)**
  - **Process control**: On-line/in-line/at-line or off-line

Keep an end in mind: Are the process & control strategies fit for purpose & scalable?

Unit Operation Assessment in KASA

1 Lubrication

FEI: Drug Substance: Manufacturing Risk Score:

Commercial Manufacturing Conditions

Type of Blending		Equipment	
---Select---	SEC	---Select---	SEC

Additional Comment

SEC

Proposed In-Process Control Not applicable ☐ ANALYTICS

In-Process Controls	Proposed Specification and Sampling Plan				
---Select---			SEC	+	×

Proposed Process Parameter Not applicable ☐

Process Parameters	Comment				
---Select---			SEC	+	×

Unit Operation Assessment in KASA contd

Design & Development

Special Considerations Not applicable ☐

Special Considerations		Supporting Information & Comment					
---Select---	ℹ		🔗	SEC	+	×	

Process Development Not applicable ☐

Consideration	Supporting Information & Comment					
---Select---		🔗	SEC	+	×	

Scale Up Proposal

Consideration	Supporting Information & Comment					
---Select---		🔗	SEC	+	×	

Overall Evaluation of Lubrication

Assessment	Reviewer Evaluation			
---Select---		🔗	SEC	DEF

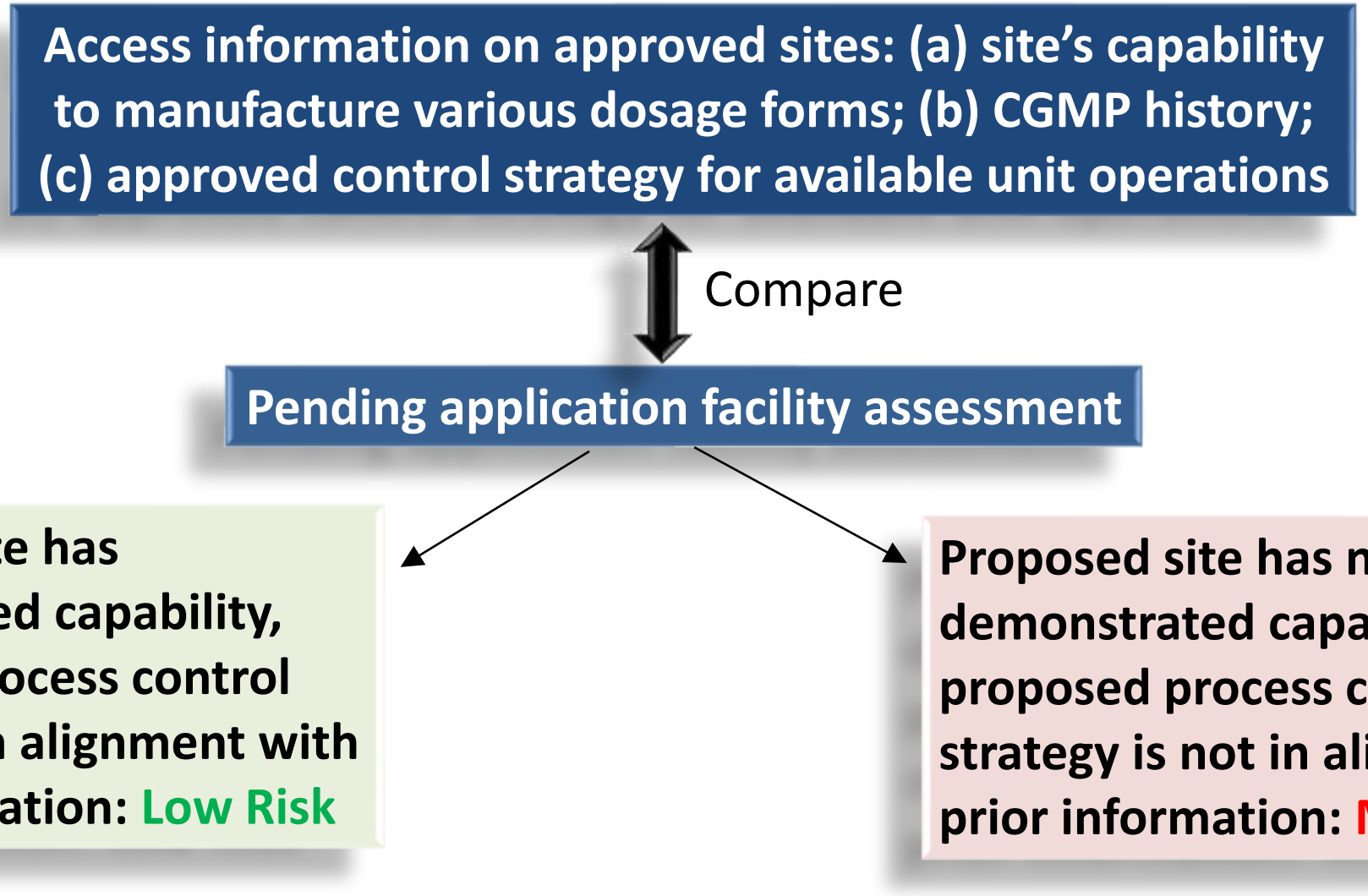
Manufacturing Risk Control

	Initial Risk	Unit Operation	Manufacturing Risk Control Dropdown Menu		Assessment Comment	Supporting Information Link
CQA 1 / Dissolution	High/ Medium/ Low	Wet Granulation	Process Factor	Approach A Approach B Approach C		
			Facility Factor	Approach H Approach I Approach J		
		Compression	Process Factor	Approach M Approach N Approach O		
			Facility Factor	Approach S Approach T Approach V		

Descriptors:
Process Design & Development, In-Process Controls, Scale up approaches

Descriptors:
Prior experience, Site History

KASA Analytics-Facilities



KASA improves overall efficiency and helps making regulatory decision by improving the manufacturing and facilities knowledge management

The End Game

IT advancements to modernize how regulatory assessments are conducted

Structured data and knowledge management will ensure consistency and objectivity in regulatory decision making

Leads to quality drugs that are reliable throughout their lifecycle

Thank You

U.S. FOOD & DRUG ADMINISTRATION

Effective leadership Collaborative relationships

Encourage innovation **Risk-based approaches**

One Quality Voice

Patients first Team-based processes

Developing and utilizing staff expertise

Scientifically-sound quality standards

Challenge Question: KASA for Manufacturing Assessment

KASA improves overall efficiency and helps making regulatory decision by improving the manufacturing and facilities knowledge management

A. True

B. False