MINI CASE STUDIES SESSION 2

CLOUD-BASED PLATFORMS FOR REGULATORY SUBMISSIONS: CMC USE CASES

PRESENTERS: MIKE ABERNATHY (AMGEN), CIBY ABRAHAM (ASTRAZENECA), RODRIGO PALACIOS (ROCHE), RAJU RAYAVARAPU (DNANEXUS)

WCBP 2026

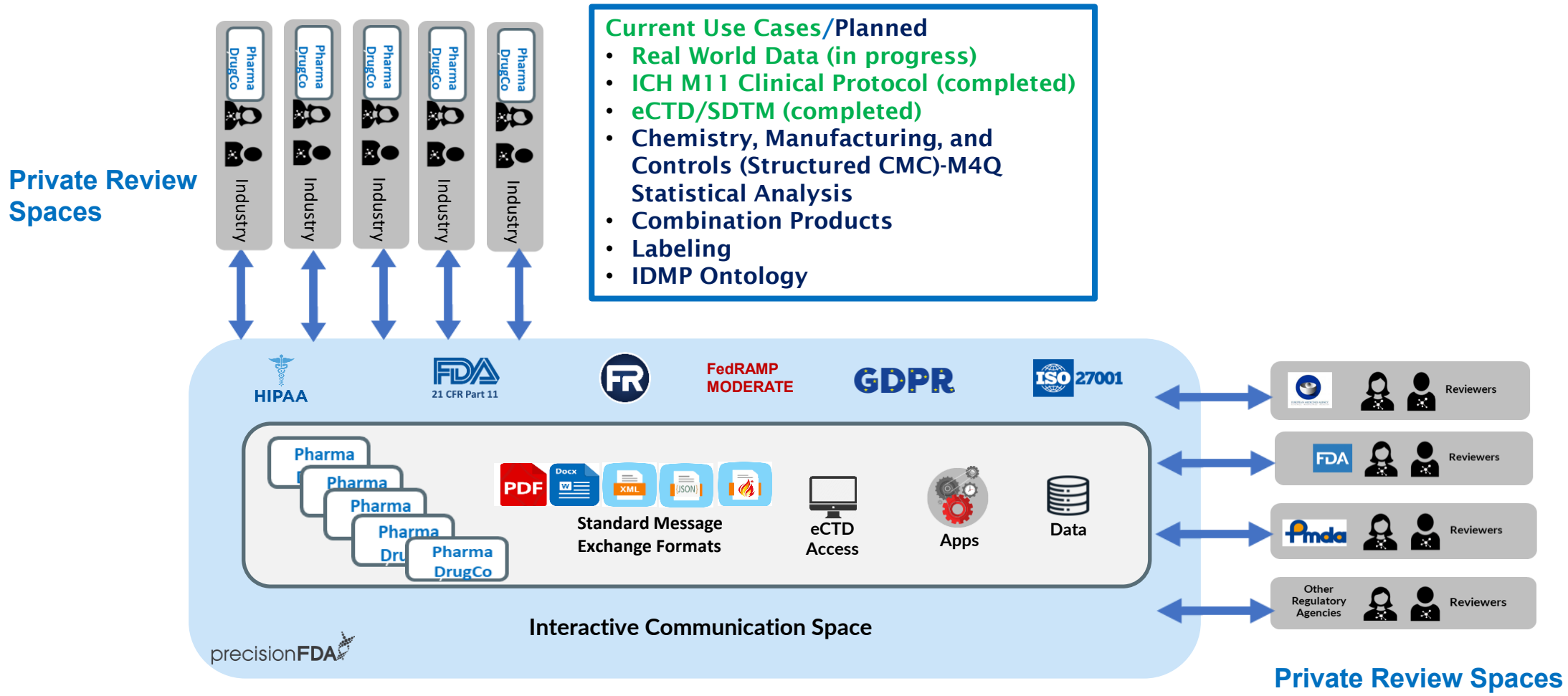
MINI CASE STUDIES SESSION 2

PROJECT PRISM: CMC USE CASE

PRESENTERS: CIBY ABRAHAM (ASTRAZENECA), RAJU RAYAVARAPU (DNANEXUS)

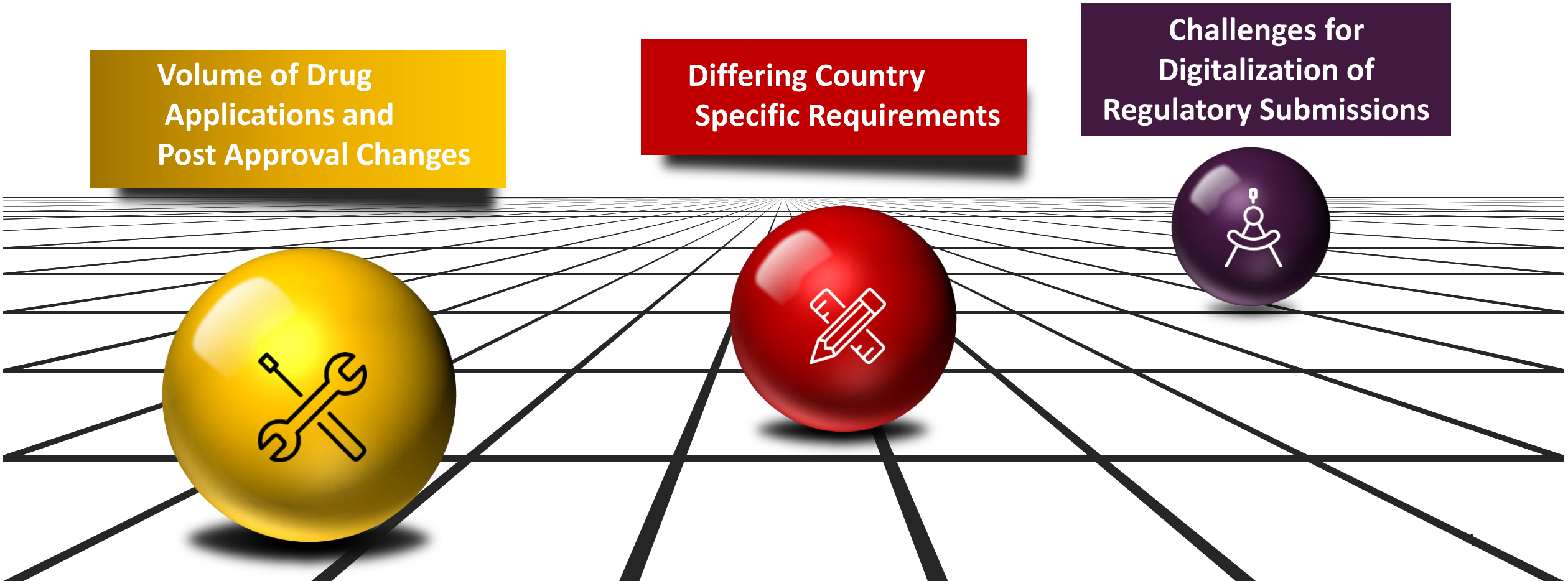
WCBP 2026

PRISM Use for International Regulatory Interaction



Challenges for CMC Regulatory Submissions

- Despite unprecedented advancements in medicines, regulatory filings remain predominantly paper-based, leading to inefficiencies and potential delays in the review, evaluation, and collaboration for drug applications.

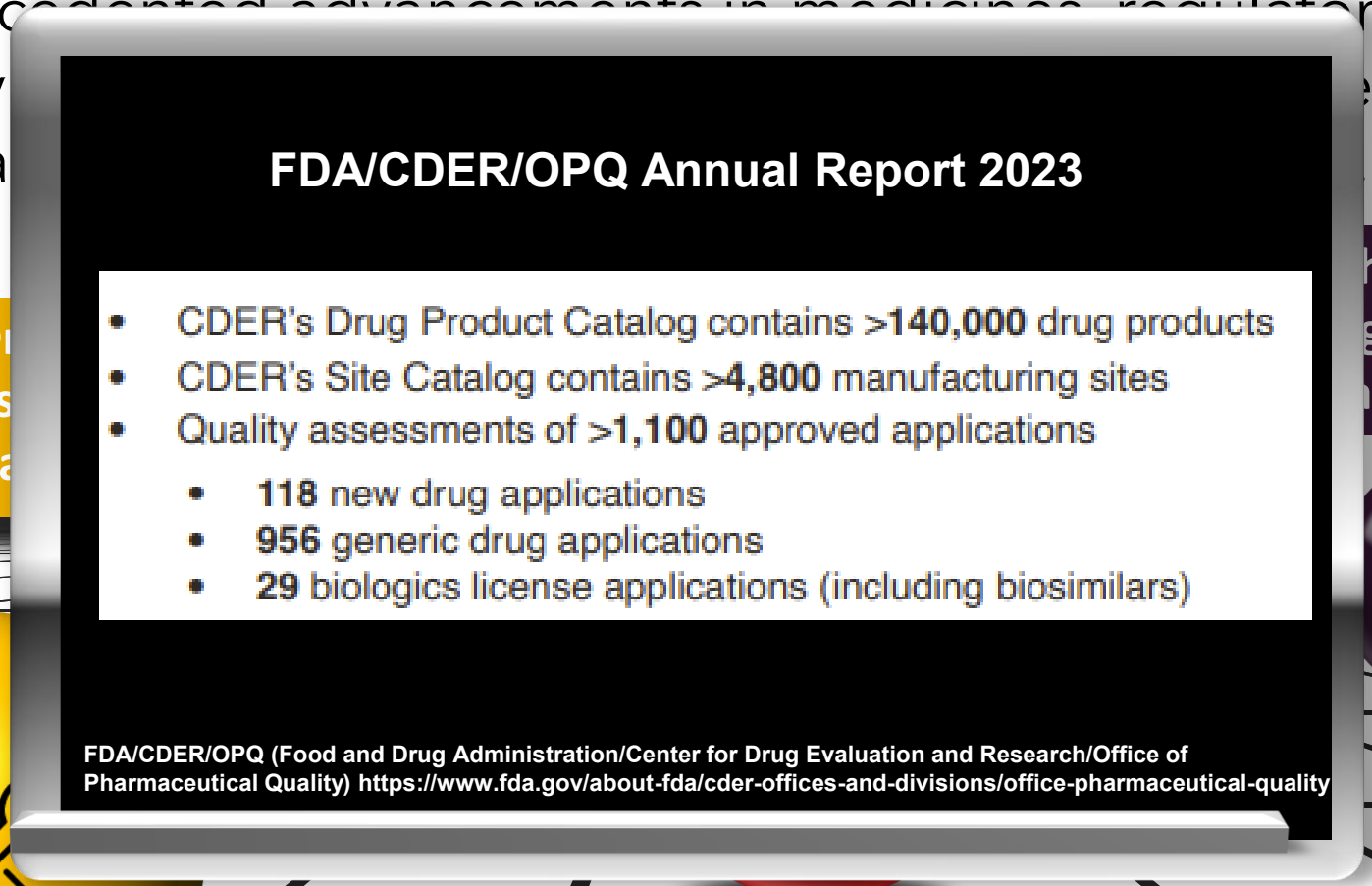


Challenges for CMC Regulatory Submissions

- Despite unprec[illegible]ry filings remain predominantly [illegible]ential delays in the review, eva[illegible]

Volume of Dr[illegible] Applications Post Approva[illegible]

hallenges for gitalization of tory Submissions



Challenges for CMC Regulatory Submissions

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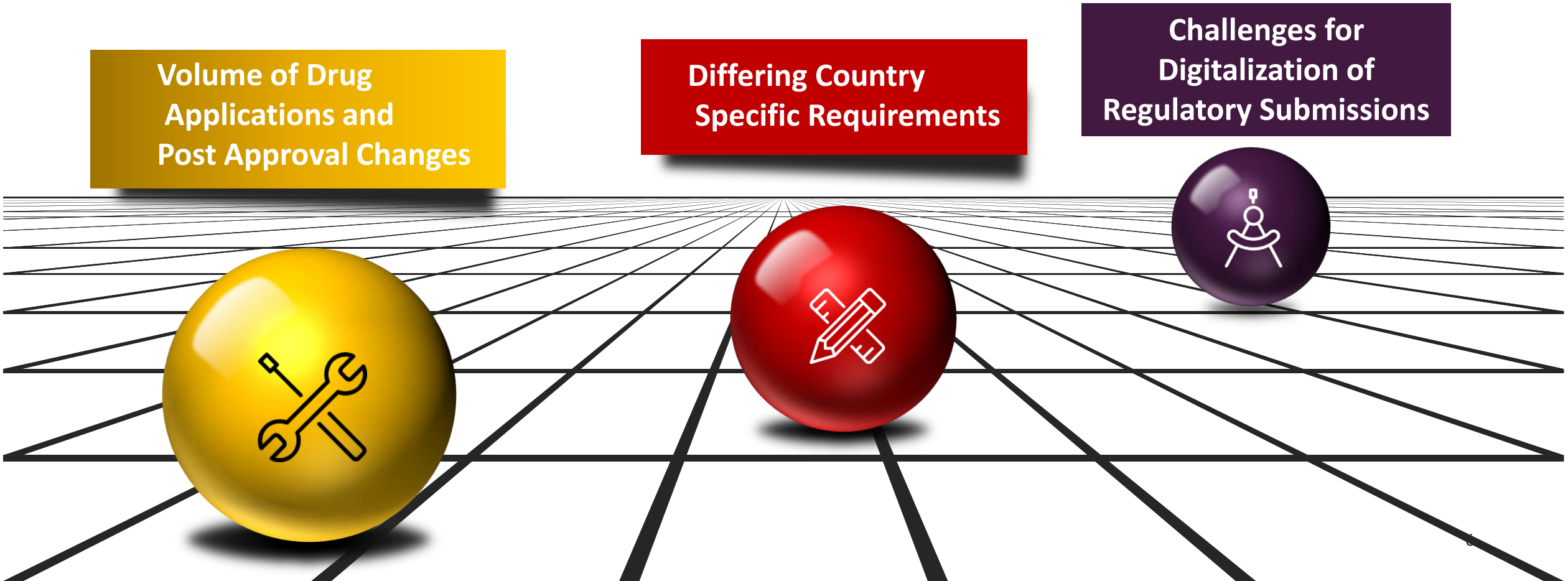


Interpretation of Quality

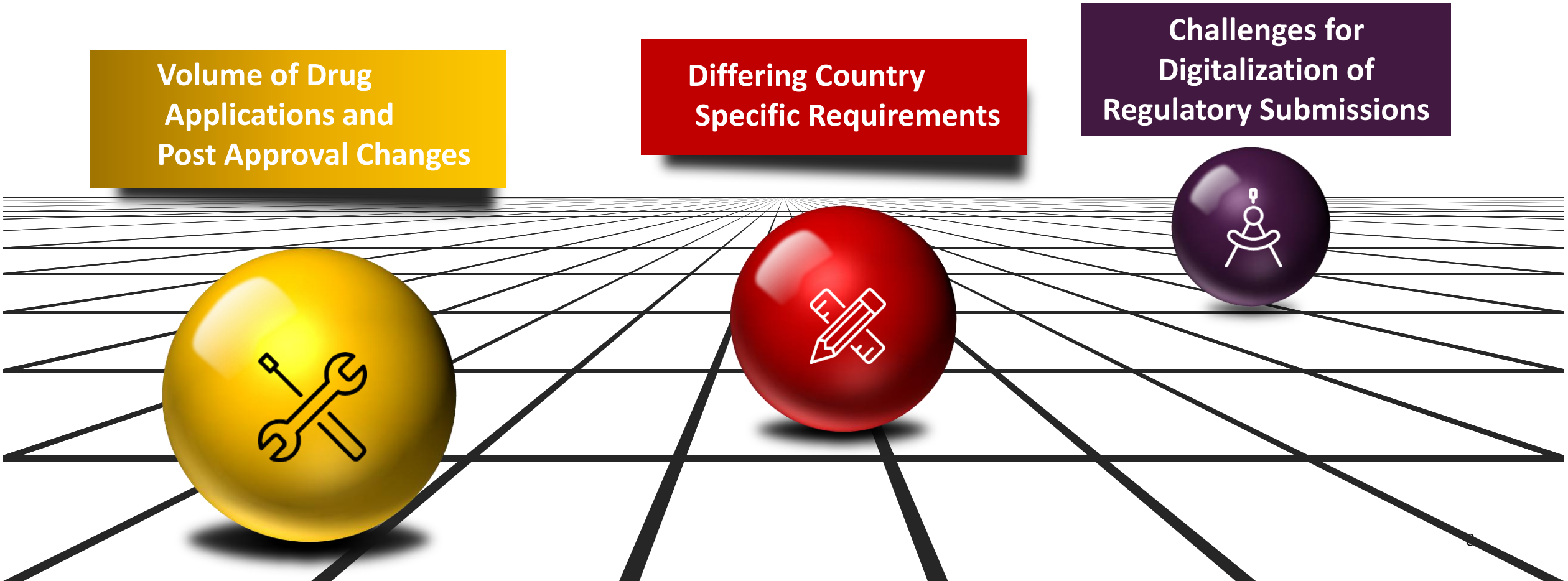
	Submissions	Core Document Acceptance Rate [a]										Average Acceptance
		S.2.2	S.2.3	S.2.4	S.4.1	S.7	P.3.2	P.3.3	P.3.4	P.5.1	P.8	
USA	30	63%	67%	63%	50%	57%	87%	47%	53%	23%	57%	57%
Japan	17	35%	41%	53%	47%	76%	76%	47%	71%	18%	65%	53%
EU	35	34%	34%	31%	29%	71%	71%	49%	54%	17%	57%	45%
Canada	30	67%	63%	80%	50%	80%	80%	43%	63%	40%	70%	64%
Overall Acceptance	112	51%	52%	56%	43%	71%	79%	46%	59%	25%	62%	54%
Probability of Acceptance by All 4 Countries [b]		5.0%	5.9%	8.3%	3.4%	24.6%	37.6%	4.7%	12.8%	0.3%	14.8%	8.7%

Total of **112** submissions from **11** companies.

Toward a Single Global Control Strategy: Industry Study | Pharmaceutical Engineering (ispe.org) International Society for Pharmaceutical Engineering; January / February 2022

Challenges for CMC Regulatory Submissions

- Despite unprecedented advancements in medicines, regulatory filings remain predominantly paper-based, leading to inefficiencies and potential delays in the review, evaluation, and collaboration for drug applications.



Challenges for CMC Regulatory Submissions

- Despite unprecedented advancements in medicines regulatory filings remain predominantly pa al delays in the review, evalua

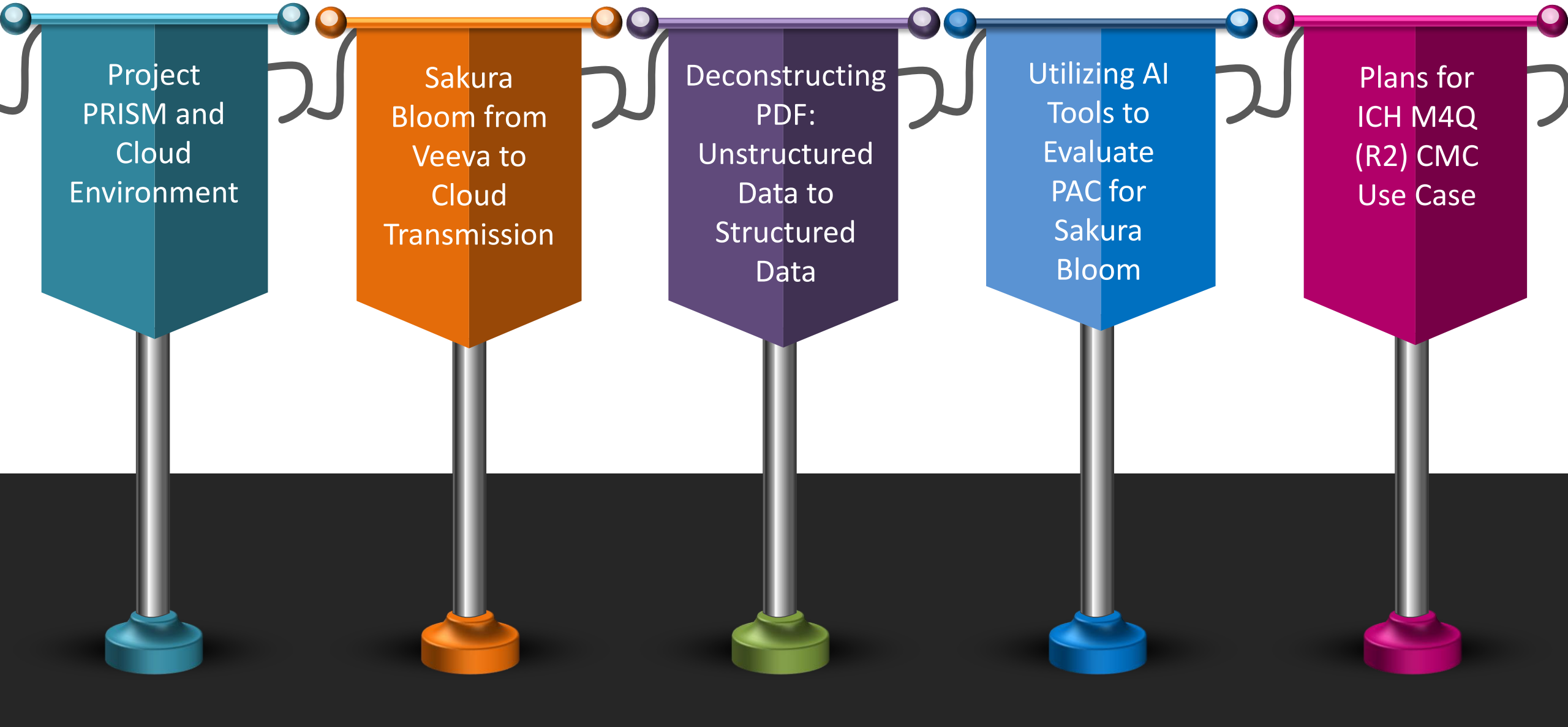
Volume of Drug Applications an Post Approval Cl

enges for lization of y Submissions

Challenges for Digitalization

- **Shifting from static document-based submissions to dynamic, structured data submissions could necessitate a major overhaul of IT infrastructure.**
- **How to utilize decades of institutional knowledge from documents?**
- **Need harmonized data standards across regions and organizations.**

Project PRISM: Sakura Bloom CMC (ICH M4Q R1) Demo



Sakura Bloom ICH M4Q (R1) PAC Use Case

Original NDA

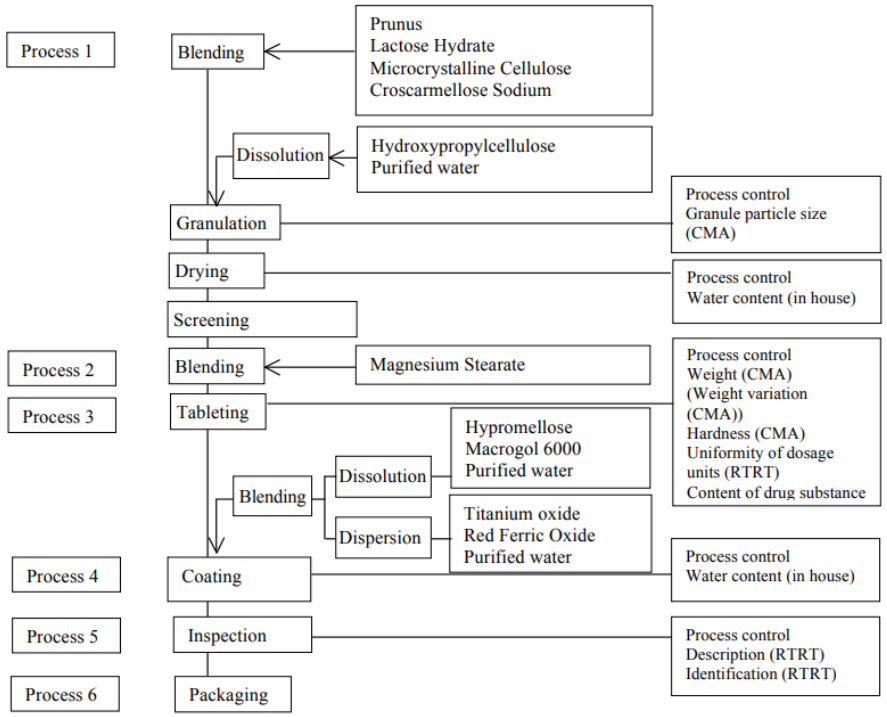


Table 3. Process parameters for Process 3

Process	Items	Application Form (Notification matter)	Product Master formula etc. (Control range)	PAR and its study scale	Justification
Process 3: Tableting Process	Compression force	6-14 kN	6-14 kN	5-15 kN (Commercial scale)	Compression force is a CPP and has an impact to the CMA. The new compression force of 6-17kN compared to 6-15 kN is neglible and does impact the quality of the product. This is confirmed with hardness testing and ongoing stability studies that meet release specifications.

https://www.nihs.go.jp/drug/section3/QbD_P2_mock_SakuraBloomTab_E_Feb2015.pdf

PAC: Addition of 2nd Manufacturing Site

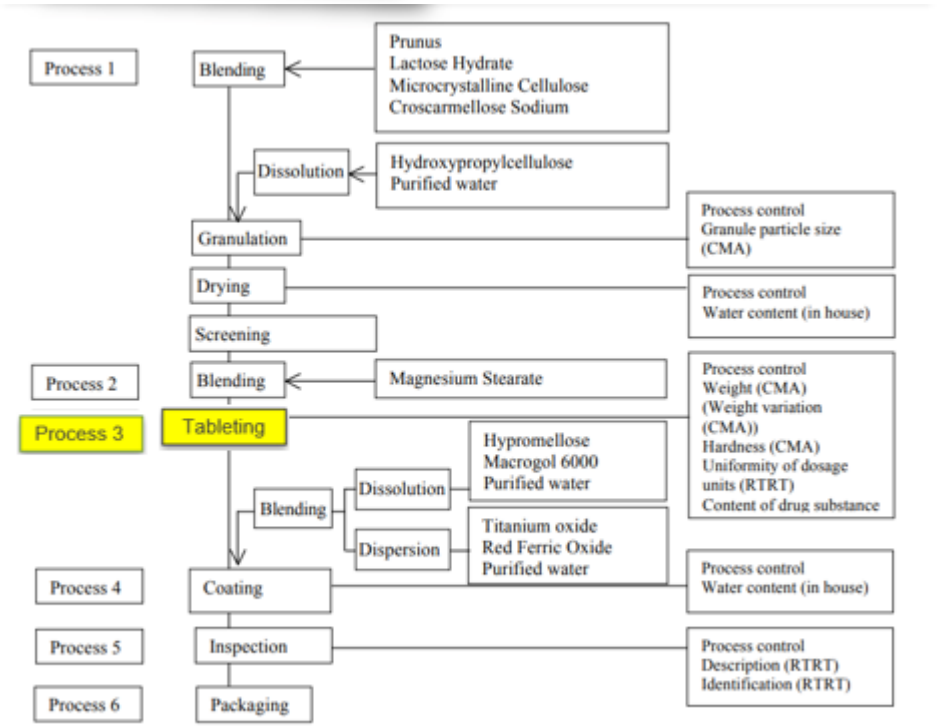


Table 3. Process parameters for Process 3

Process	Items	Application Form (Notification matter)	Product Master formula etc. (Control range)	PAR and its study scale	Justification
Process 3: Tableting Process	Compression force	6-17 kN	6-15 kN	5-16 kN (Commercial scale)	Compression force is a CPP and has an impact to the CMA. The new compression force of 6-17kN compared to 6-15 kN is neglible and does impact the quality of the product. This is confirmed with hardness testing and ongoing stability studies that meet release specifications.

Sakura Bloom ICH M4Q (R1) Stability Data

Original NDA

Stability data for Sakura Bloom 20 mg tablet in HDPE Bottle stored at 25°C/60% RH

Test	Acceptance Criteria	Initial	1	3	6	9	12	18	24
Description	Pale red tablet	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass
Assay (% label claim)	90-100%	97	97	96	96	96	95	95	94
Impurity A	<2.0%	0.8	0.85	0.9	0.9	1.1	1.3	1.3	1.4
Impurity B	<3.0	1.7	1.7	1.9	2	2.1	2.1	2.2	2.2
Impurity C	<.20	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15
Total Impurities	<6.0	2.65	2.7	2.95	3.05	3.35	3.55	3.65	3.8
Dissolution	>85% at 30 min	88	90	91	92	92	90	90	90
Microbiological quality	Meets Pharmacopeia	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass

Stability data for Sakura Bloom 20 mg tablet in HDPE Bottle stored at 30°C/75% RH

Test	Acceptance Criteria	Initial	1	3	6	9	12
Description	Pale red tablet	Pass	Pass	Pass	Pass	Pass	Pass
Assay (% label claim)	90-100%	97	96	95	95	95	94
Impurity A	<2.0%	0.8	0.9	0.97	1.05	1.15	1.4
Impurity B	<3.0	1.7	1.7	1.8	2.1	2.2	2.2
Impurity C	<.20	0.15	0.15	0.15	0.15	0.15	0.15
Total Impurities	<6.0	2.65	2.75	2.92	3.3	3.5	3.75
Dissolution	>85% at 30 min	88	90	91	92	92	90
Microbiological quality	Meets Pharmacopeia	Pass	Pass	Pass	Pass	Pass	Pass

Stability data for Sakura Bloom 20 mg tablet in HDPE Bottle stored at 40°C/75% RH

Test	Acceptance Criteria	Initial	1	3	6
Description	Pale red tablet	Pass	Pass	Pass	Pass
Assay (% label claim)	90-100%	97	96	94	93
Impurity A	<2.0%	0.8	1.2	1.6	1.8
Impurity B	<3.0	1.7	1.9	2.2	2.4
Impurity C	<.20	0.15	0.15	0.15	0.15
Total Impurities	<6.0	2.65	3.25	3.95	4.35
Dissolution	>85% at 30 min	88	94	94	95
Microbiological quality	Meets Pharmacopeia	Pass	Pass	Pass	Pass

PAC: Addition of 2nd Manufacturing Site

Stability data for Sakura Bloom 20 mg tablet in HDPE Bottle stored at 25°C/60% RH

Test	Acceptance Criteria	Initial	1	3	6	9	12	18	24
Description	Pale red tablet	Pass	Pass	Pass	Pass				
Assay (% label claim)	90-100%	97	94	93	94				
Impurity A	<2.0%	0.8	0.9	0.98	1.1				
Impurity B	<3.0	1.7	1.7	1.8	1.95				
Impurity C	<.20	0.15	0.15	0.15	0.15				
Total Impurities	<6.0	2.65	2.7	3.1	3.25				
Dissolution	>85% at 30 min	93	93	92	92				
Microbiological quality	Meets Pharmacopeia	Pass	Pass	Pass	Pass				

Stability data for Sakura Bloom 20 mg tablet in HDPE Bottle stored at 30°C/75% RH

Test	Acceptance Criteria	Initial	1	3	6	9	12
Description	Pale red tablet	Pass	Pass	Pass	Pass		
Assay (% label claim)	90-100%	97	94	93	92		
Impurity A	<2.0%	0.8	0.84	1.05	1.1		
Impurity B	<3.0	1.7	1.68	1.75	2.2		
Impurity C	<.20	0.15	0.15	0.15	0.15		
Total Impurities	<6.0	2.65	2.73	3.05	3.31		
Dissolution	>85% at 30 min	92	94	94	94		
Microbiological quality	Meets Pharmacopeia	Pass	Pass	Pass	Pass		

Stability data for Sakura Bloom 20 mg tablet in HDPE Bottle stored at 40°C/75% RH

Test	Acceptance Criteria	Initial	1	3	6
Description	Pale red tablet	Pass	Pass	Pass	Pass
Assay (% label claim)	90-100%	97	93	92	92
Impurity A	<2.0%	0.8	1.3	1.7	1.8
Impurity B	<3.0	1.7	1.9	2.22	2.45
Impurity C	<.20	0.15	0.15	0.15	0.15
Total Impurities	<6.0	2.65	3.35	4.05	4.55
Dissolution	>85% at 30 min	94	93	92	94
Microbiological quality	Meets Pharmacopeia	Pass	Pass	Pass	Pass

Sakura Bloom ICH M4Q (R1) Stability Data

Original NDA

Stability data for Sakura Bloom 20 mg tablet in HDPE Bottle stored at 25°C/60% RH

Test	Acceptance Criteria	Initial	1	3	6	9	12	18	24
Description	P								
Assay (% label claim)									
Impurity A									
Impurity B									
Impurity C									
Total Impurities									
Dissolution	>								
Microbiological quality	Mee								

Stability data for Sakura Blo

Test	Acc
Description	P
Assay (% label claim)	
Impurity A	
Impurity B	
Impurity C	
Total Impurities	
Dissolution	>
Microbiological quality	Mee

Stability data for Sakura Blo

Test	Acc				
Description	P				
Assay (% label claim)					
Impurity A					
Impurity B					
Impurity C					
Total Impurities	<6.0	2.65	3.25	3.95	4.35
Dissolution	>85% at 30 min	88	94	94	95
Microbiological quality	Meets Pharmacopeia	Pass	Pass	Pass	Pass

PAC: Addition of 2nd Manufacturing Site

Stability data for Sakura Bloom 20 mg tablet in HDPE Bottle stored at 25°C/60% RH

Test	Acceptance Criteria	Initial	1	3	6	9	12	18	24
			Pass	Pass	Pass				
			94	93	94				
			0.9	0.98	1.1				
			1.7	1.8	1.95				
			0.15	0.15	0.15				
			2.7	3.1	3.25				
			93	92	92				
			Pass	Pass	Pass				

le stored at 30°C/75% RH

		1	3	6	9	12
		Pass	Pass	Pass		
		94	93	92		
		0.84	1.05	1.1		
		1.68	1.75	2.2		
		0.15	0.15	0.15		
		2.73	3.05	3.31		
		94	94	94		
		Pass	Pass	Pass		

le stored at 40°C/75% RH

			1	3	6
			Pass	Pass	Pass
			93	92	92
			1.3	1.7	1.8
			1.9	2.22	2.45
			0.15	0.15	0.15
Total Impurities	<6.0	2.65	3.35	4.05	4.55
Dissolution	>85% at 30 min	94	93	92	94
Microbiological quality	Meets Pharmacopeia	Pass	Pass	Pass	Pass

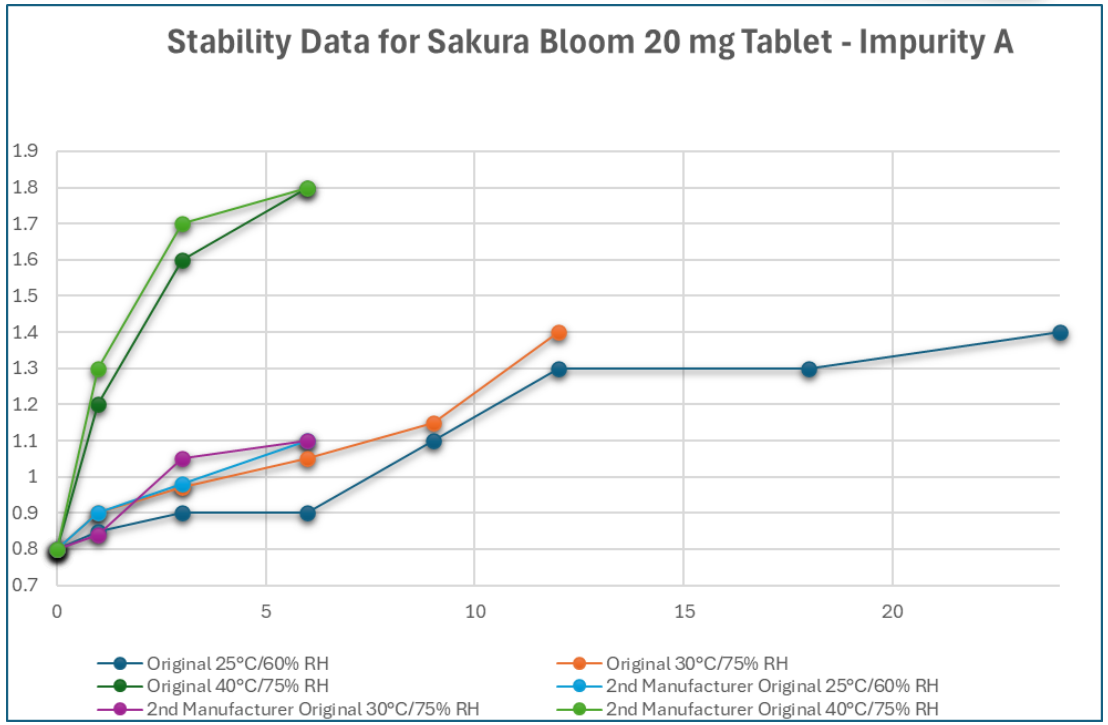
AI Prompt

< Provide a graphical analysis of the impurity profile from the original Sakura Bloom manufacturing site and the second manufacturing site.

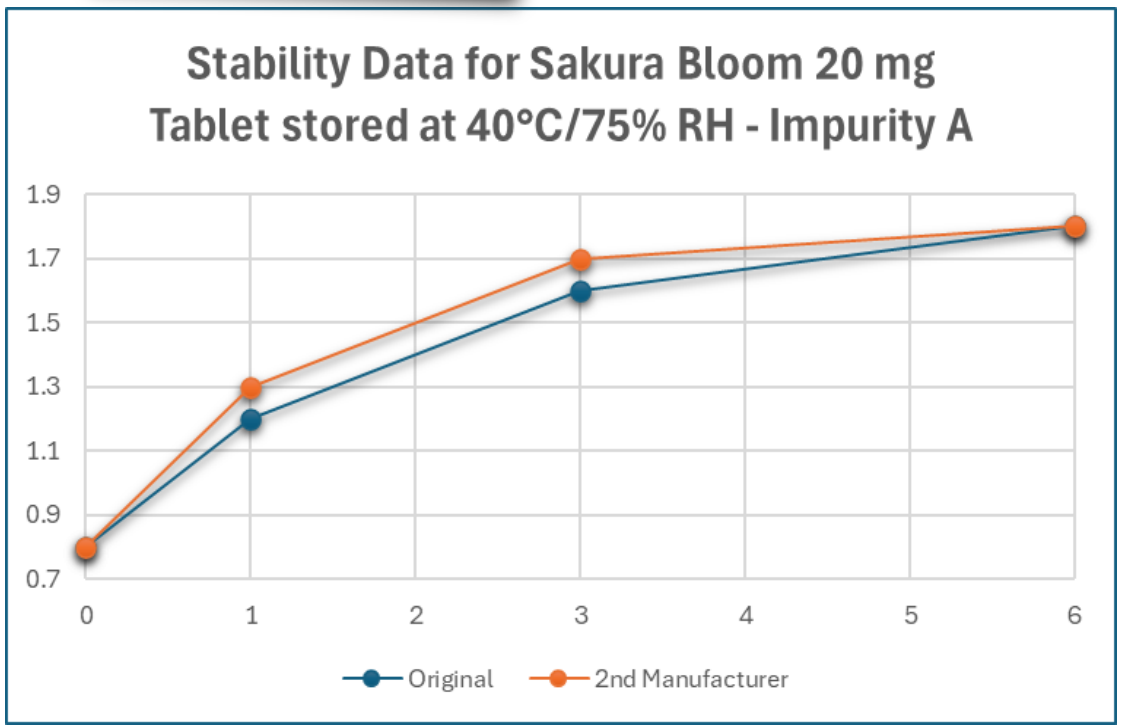
< Provide a graphical analysis of the impurity profile for Impurity A from the original Sakura Bloom manufacturing site and the second manufacturing site at 40°C/75% RH.

Sakura Bloom ICH M4Q (R1) Stability Comparison

Impurity A Comparison for Original and 2nd Manufacturing Site



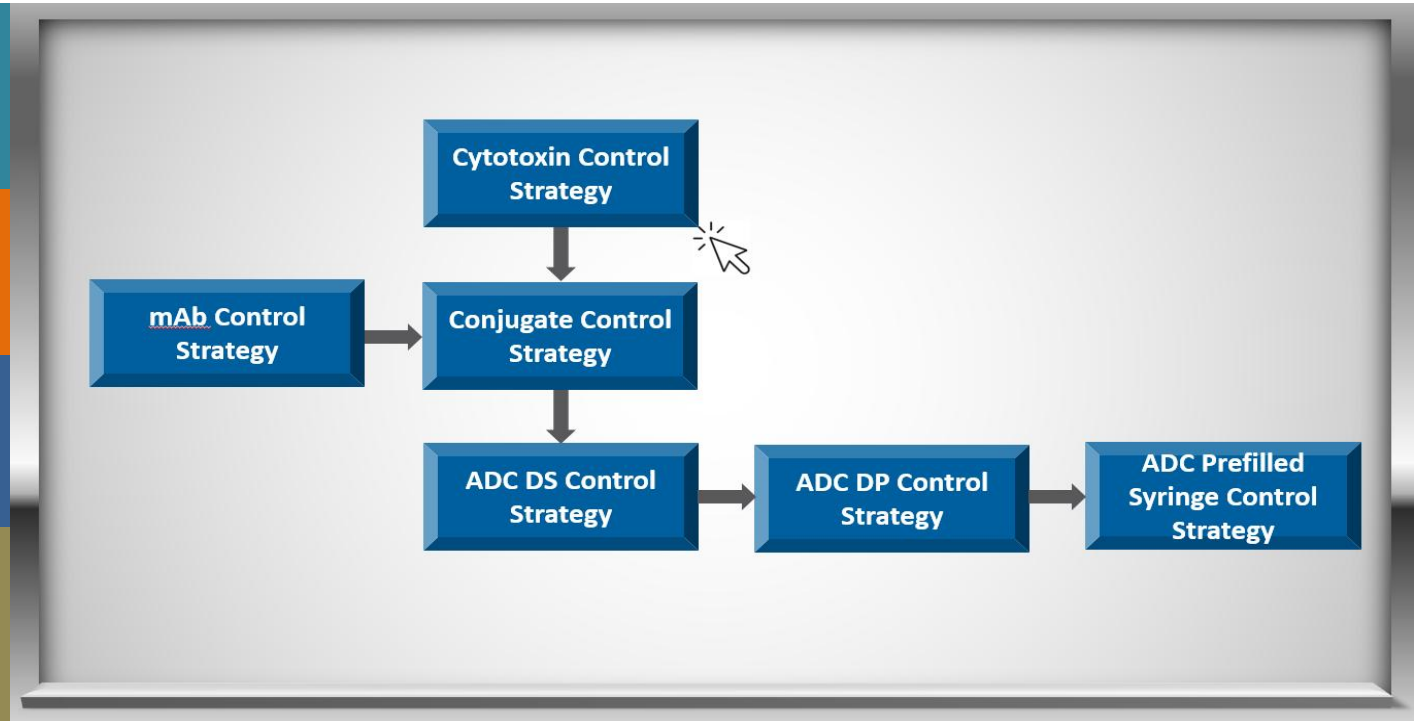
Impurity A Comparison for Original and 2nd Manufacturing Site at 40°C/75% RH



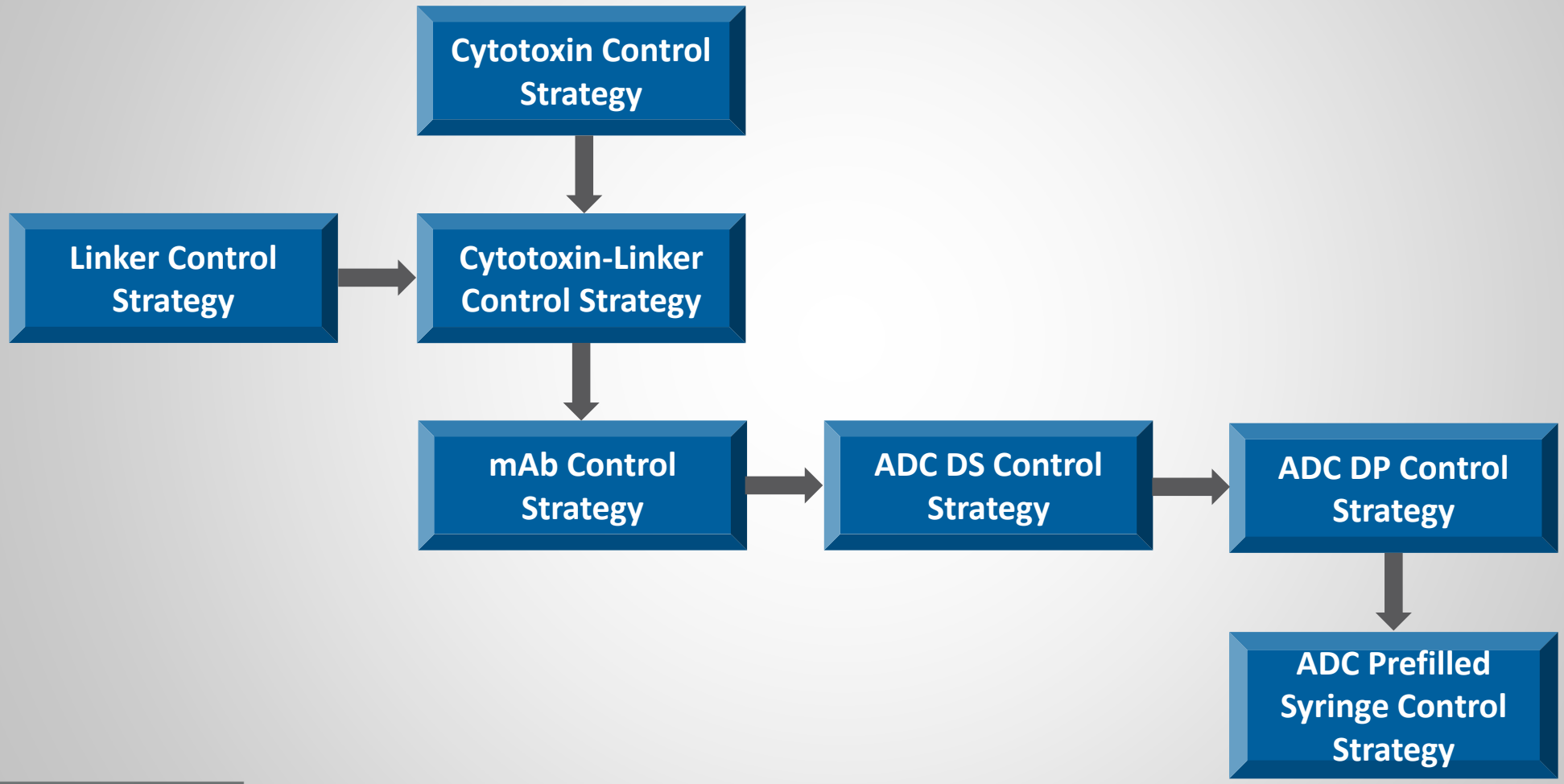
Project Prism Demonstration

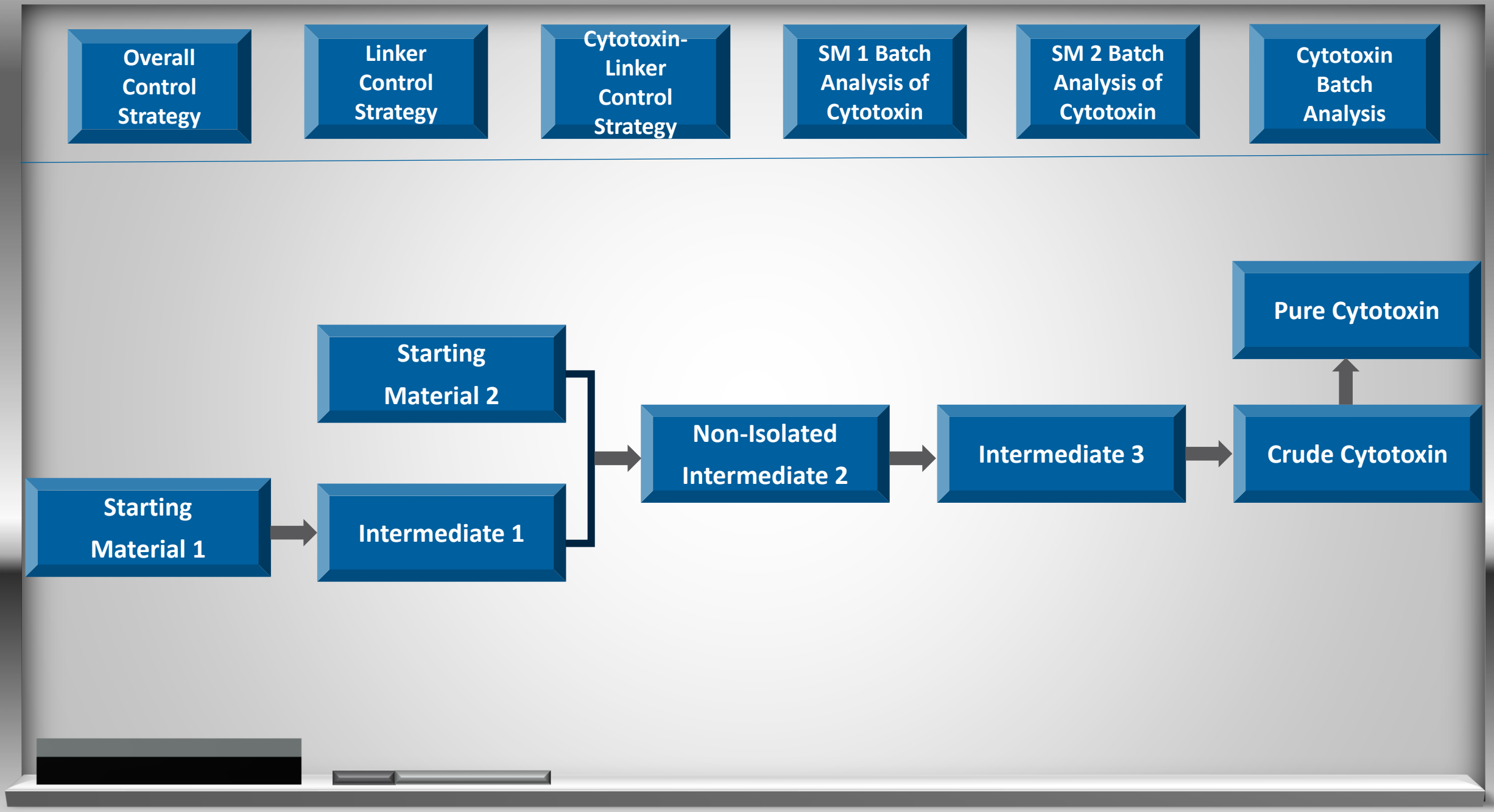
Project PRISM: ICH M4Q (R2) Use Case

- Illustrate the Overall Control Strategy to Summarize Product Quality
- Test the Conversion of CMC Data to Convert to IDMP Standards
- Test Gen AI Tools
- Receive Feedback from Industry and Regulators



ADC Overall Control Strategy Concept




Overall Control Strategy
Linker Control Strategy
Cytotoxin-Linker Control Strategy
SM 1 Batch Analysis of Cytotoxin
SM 2 Batch Analysis of Cytotoxin
Cytotoxin Batch Analysis
Starting Material 2
Starting Material 1
Intermediate 1
Non-Isolated Intermediate 2
Intermediate 3
Crude Cytotoxin
Pure Cytotoxin

Cytotoxin

- Chemical Structure
- IUPAC Name
- Chemical Formula
- Molecular Weight
- CAS Number
- General Properties
- Elucidation of Structure & Other Characteristics
- Impurities
- Manufacturer (S)
- Reference Standard
- Container Closure
- Stability

Cytotoxin Batch Analysis

Critical Quality Attributes

Cytotoxin Risk Analysis

Justification of Starting Material 1

Justification of Starting Material 2

Cytotoxin Batch Analysis

Test	Acceptance criteria	Results
Description	A white to brown solid	White
Identification by IR	Conforms with reference spec	Confirmed
Assay by LC	97% to 102% w/w	98.20%
Organic impurities by LC		
Impurity 1	NMT 1.0% w/w	0.30%
Impurity 2	NMT 0.3% w/w	0.05%
Any individual unspecified impurity	NMT 0.2% w/w	0.05%
Total organic impurities	NMT 1.5% w/w	0.40%
Mutagenic Impurities		
Mutagenic Impurity 1	NMT 5 ppm	2 ppm
Residual Solvents		
Ethanol	<5000 ppm	300 ppm
Particle Size		
Particle Size range	<25 um	12 um

DP Analysis Cytotoxin

Linker Batch Analysis

Linker-Cytotoxin Risk Analysis

mAb Control Strategy

Overall Control Strategy

DS & DP Comparison of Cytotoxin

		Drug Substance	Drug Product
Test	**Acceptance criteria**	**Results**	**Results**
Assay by LC	97% to 102% w/w	98.20%	97.90%
Organic impurities by LC			
Impurity 1	NMT 1.0% w/w	0.30%	0.30%
Impurity 2	NMT 0.3% w/w	0.05%	0.05%
Any individual unspecified impurity	NMT 0.2% w/w	0.05%	0.05%
Total organic impurities	NMT 1.5% w/w	0.40%	0.75%
Mutagenic Impurities			
Mutagenic Impurity 1	NMT 5 ppm	2 ppm	2 ppm

DP Stability Cytotoxin Impurity 1

Linker-Cytotoxin Batch Analysis

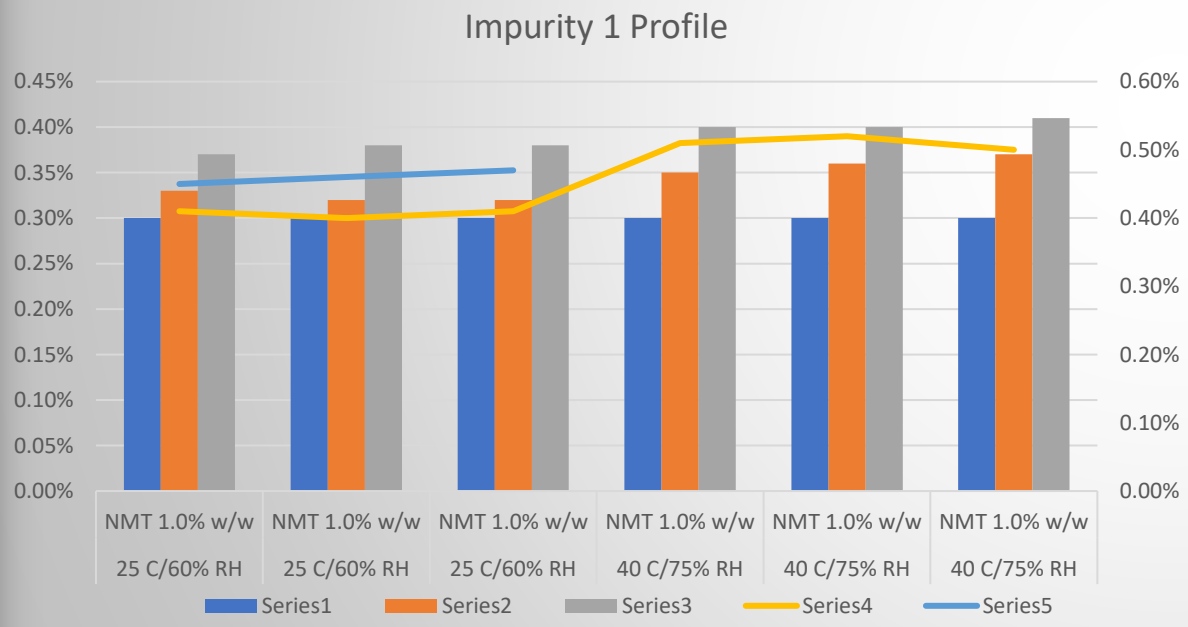
Linker-Cytotoxin Risk Analysis

mAb Control Strategy

Overall Control Strategy

DP Stability Data for Cytotoxin Impurity 1

Stability Data for Drug Product - Impurity 1		Time Points (months)				
Test	Acceptance Criteria	Initial	1	3	6	12
25°C/60% RH	NMT 1.0% w/w	0.30%	0.33%	0.37%	0.41%	0.45%
25°C/60% RH	NMT 1.0% w/w	0.30%	0.32%	0.38%	0.40%	0.46%
25°C/60% RH	NMT 1.0% w/w	0.30%	0.32%	0.38%	0.41%	0.47%
40°C/75% RH	NMT 1.0% w/w	0.30%	0.35%	0.40%	0.51%	
40°C/75% RH	NMT 1.0% w/w	0.30%	0.36%	0.40%	0.52%	
40°C/75% RH	NMT 1.0% w/w	0.30%	0.37%	0.41%	0.50%	



Output - Impurity 1 is expected to be within specification when product is stored at 25°C/60% RH for 24 months

Cytotoxin Impurity 1

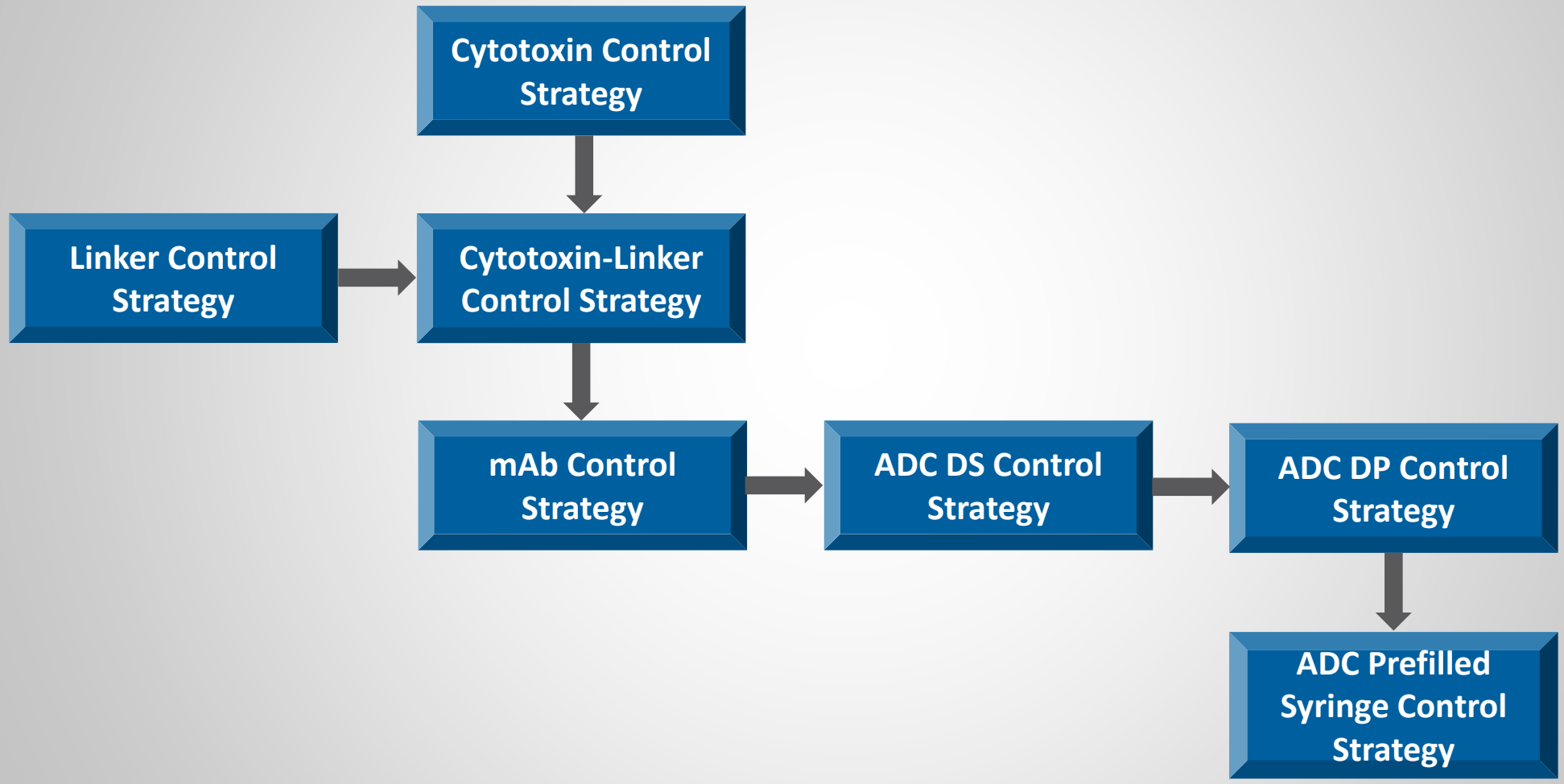
Linker Batch Analysis

Linker Control Strategy

mAb Control Strategy

Overall Control Strategy

ADC Overall Control Strategy Concept



MINI CASE STUDIES SESSION 2

COMBINATION PRODUCT CMC USE CASE

PRESENTERS: RODRIGO PALACIOS (ROCHE)

WCBP 2026

Two-in-one TRS publishing of a combination product in M4Q(R2)

A combination product use case

Roche + Boehringer Ingelheim

Device + Drug

Published in M4Q(R2)

Executed in the DNAnexus TRS cloud in Lorenz docuBridge

DNAnexus® LORENZ docuBridge

One global submission

Imagine a world where you be able to compile and do your product submission once, across countries.

…to one central location…

Data would be stored in one central location, accessible to a predefined number of regulators globally.

…reviewed across…

Health authorities would collaborate in real-time review, with common Q&A and interactions.

…bringing drugs faster to patients

Ultimately bringing drugs faster to market, democratizing access to drugs across regions and countries

Proof of Concept - Performing an M4Q(R2) submission for a drug-device combination product with two sponsors in one common cloud platform, with real-time agency review

Roche TRS Private Space / BI TRS Private Space

BI-TRS Cloud

Roche

Submission Specialist

Device documents

1. We uploaded device and drug documents for the M4Q(R2) combination product submission

Boehringer Ingelheim

Submission Specialist

Drug documents

2. Assembled application sequence(s) for M4Q(R2) as required in eCTD 4.0

LORENZ docuBridge

Publisher

3. Reviewed content and published to regulator space

4. M4Q(R2) was made available for real-time review to regulators, incl. HAQs

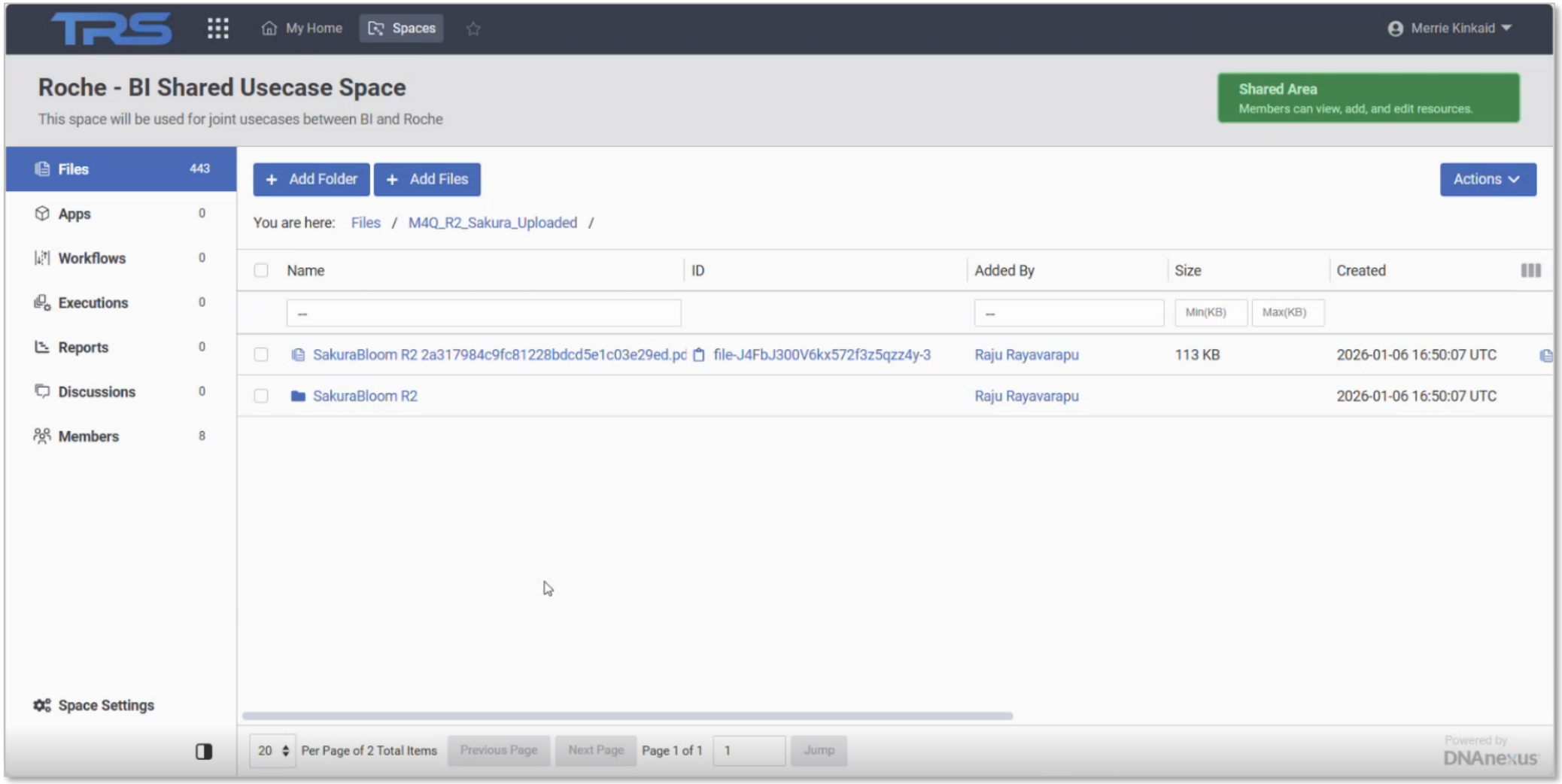
Regulators

5. Submission approval

Showcasing the combination product in M4Q(R2) using docuBridge via the TRS cloud

Uploaded device and drug documents for the M4Q(R2) combination product submission

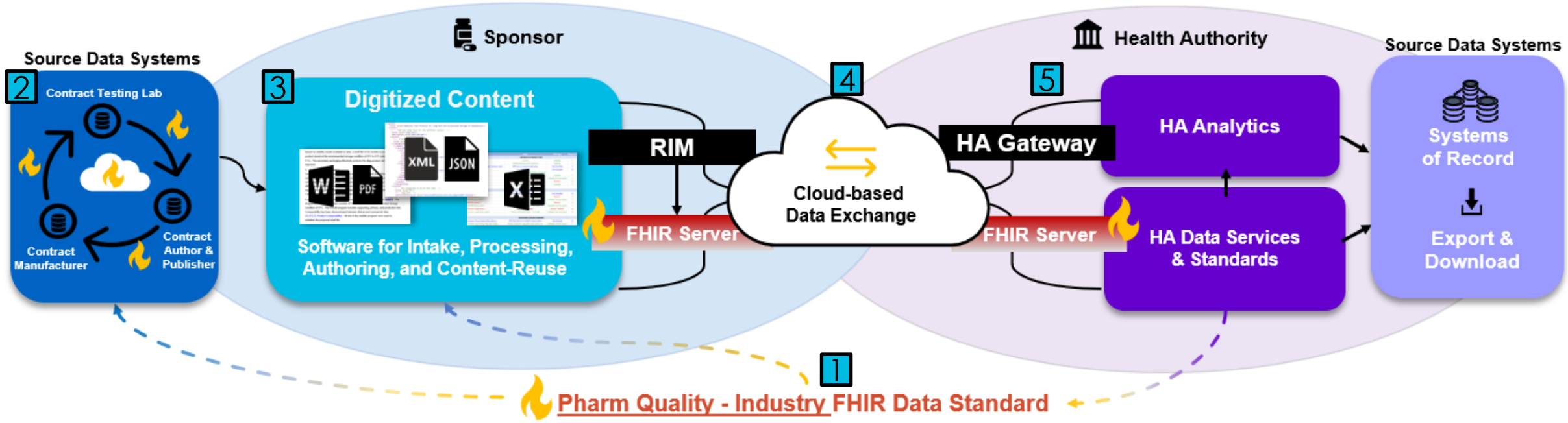
Assembling appli[illegible]duct in M4Q(R2)



Revolutionizing Regulatory Submissions Through Digital Innovation

Michael Abernathy
WCBP Mini-Case Study Session
29 January 2026

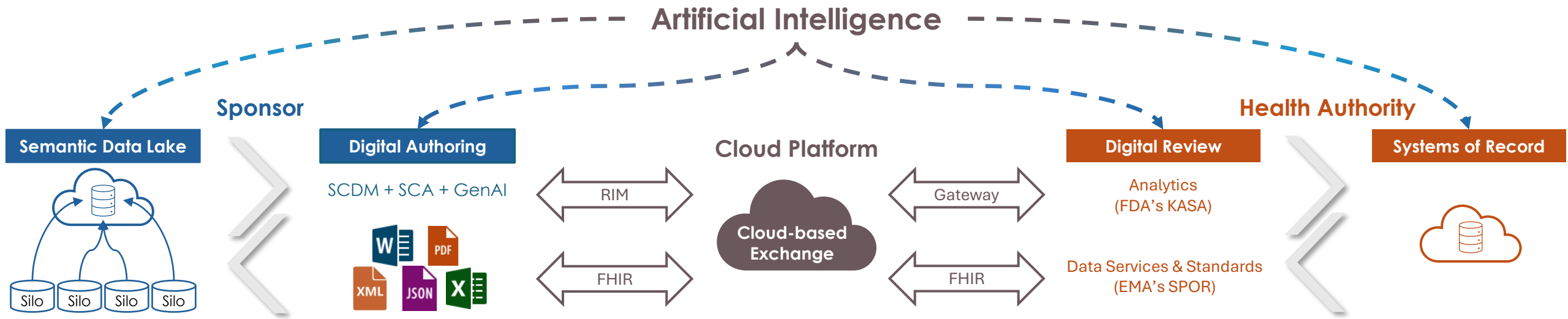
Future State Vision for Regulatory Exchange Published in 2023



1. Health authority and industry FHIR standards are used to standardize data at the source
2. Sponsor Source data systems are connected through structured, standardized data
3. Digital content management systems render data in the required format
4. A cloud-based data exchange system connects the sponsor and regulator environments
5. Regulators receive structured, standardized data that can be used in analytics software

From Anderson, Algorri, Abernathy 2023

Practical Application of Regulatory Exchange



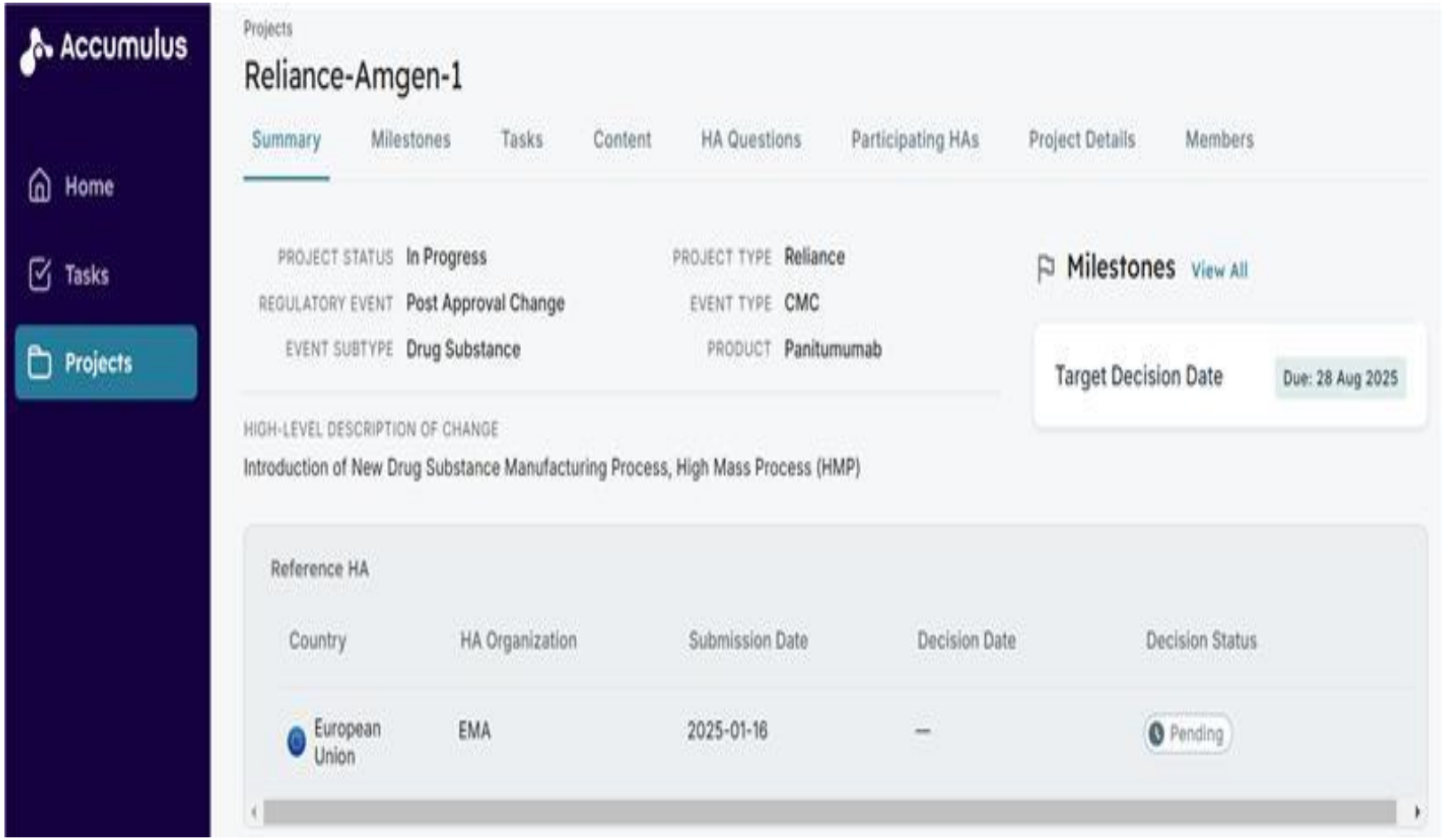
Foundational End-to-End Data Standards (PQ-CMC, ISO IDMP, HL7 FHIR Pharm Quality - Industry)

Benefits of Digitalization

- Time Efficiency & Optimization
- Manual Error Reduction
- Increased Manufacturing Capacity
- Reduced Medicinal Waste
- Real-time Collaboration
- Accelerated Approvals
- Global Patient Access

Figure from "The Future of Regulatory Filings: Digitalization," Ahluwalia et al., 2025, doi: 10.1186/s41120-025-00113-7

Leading the Way in Cloud-Based Exchange
Amgen's Vectibix High Mass Process (HMP) Pilot



84%
COUNTRY ENGAGEMENT

73%
NRA PARTICIPATION

- **53 of 63 Vectibix licensed countries participating in PAC Reliance -** enhancing efficiency, collaboration, and accelerating patient access
- **27 out of 37 National Regulatory Authorities participating in PAC Reliance**
- **Of those 27 NRAs, 25 are are using Accumulus** to access the Vectibix PAC dossier, the EMA Assessment Report, and other regulator questions and Amgen responses **in real time**.

* Platform Demonstration