WCBP 2023, Washington DC

U.S. FOOD & DRUG ADMINISTRATION

FDA's Current Effort in Structured Product Quality Submission (aka PQ/CMC)

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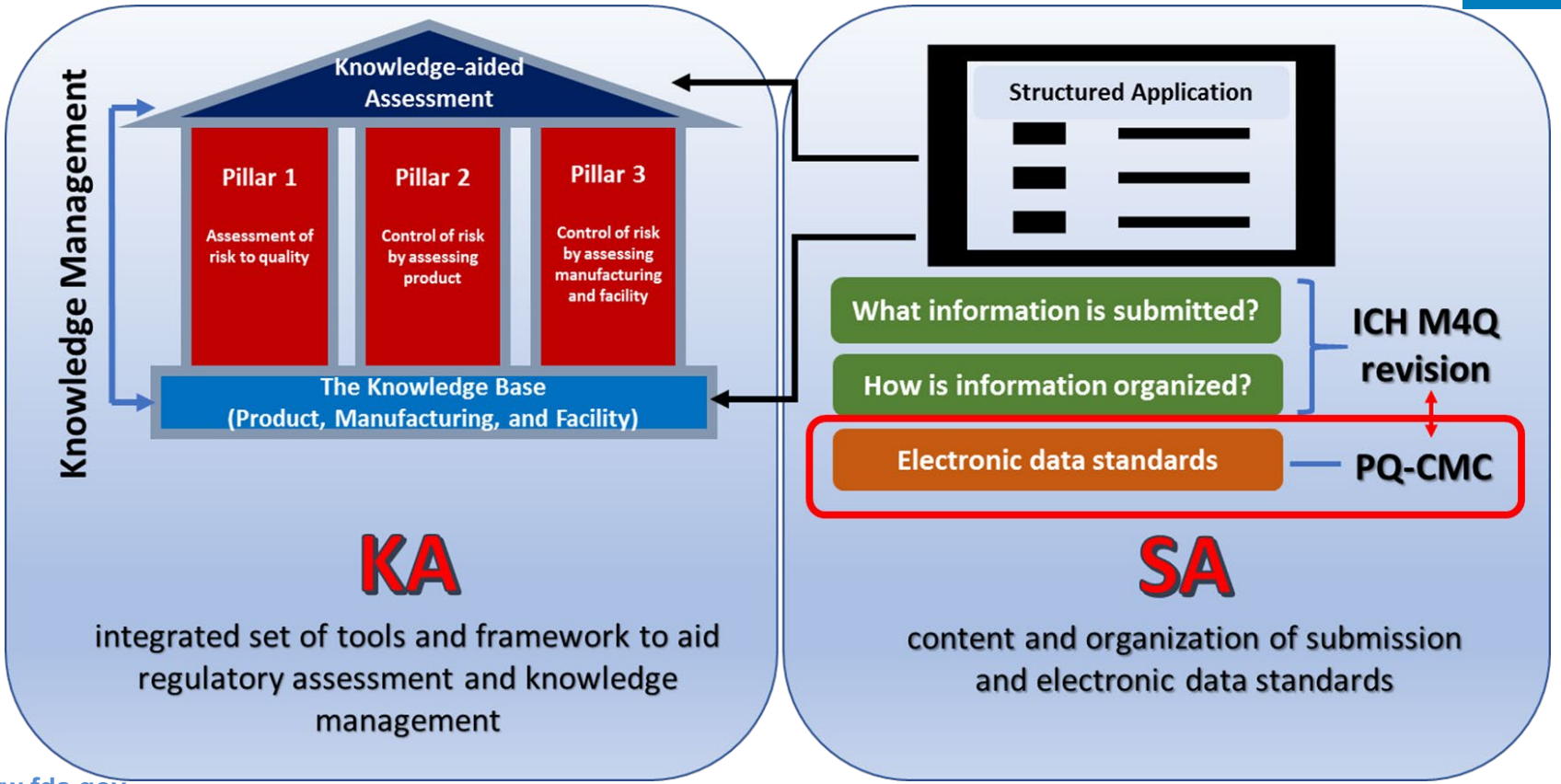
Office of Lifecycle Drug Products, OPQ
Chair, OPQ PQ/CMC Workgroup

January 24, 2023

Future KASA System

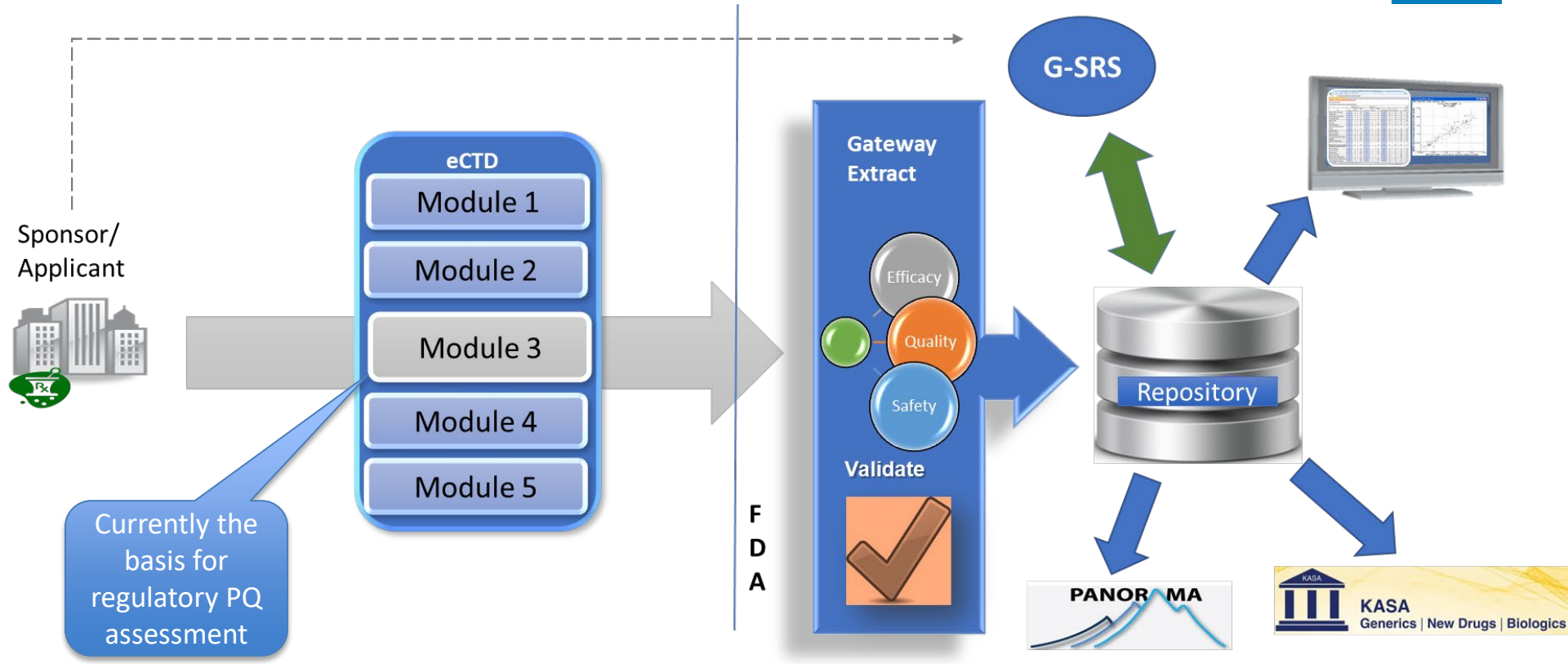


The Challenge

Currently Module 3 body of data submitted in PDF format with unstructured pharmaceutical quality data. Significantly hinders the efficiency of data exchange, quality assessment, and lifecycle knowledge management.

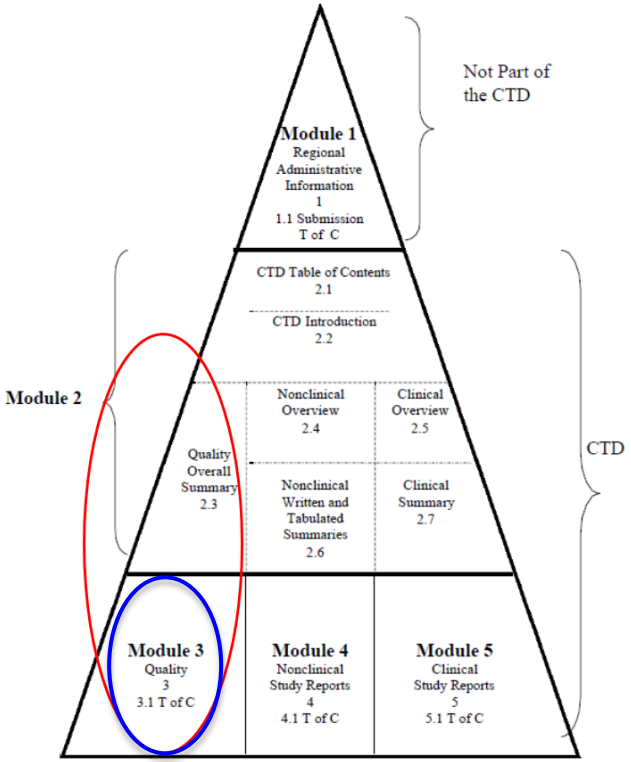
Test	*Limit*
Description	White or almost white, crystalline powder.
Identification . *Test A:* . *Test B:*	The I.R. spectrum is concordant with the *reference spectrum* [redacted] It meets the requirements of the test for [redacted]
(+)-*trans* –paroxetine (corresponding to RC C of USP)	Not more than 0.1%
Related substances: . **Impurity I** (corresponding to RC B of USP) . **Impurity II** . **Impurity III** (corresponding to RC F of USP) . **Any other ind. impurity** . **Total impurities**	 Not more than 0.30% Not more than 0.15% Not more than 0.15% Not more than 0.10% Not more than 0.50%
Heavy metals	Not more than 20 ppm (Pb)
Water	2.2 – 2.7%
Residue on ignition	Not more than 0.1%
Assay	98.5 – 102.0% *(on anhydrous and solvent-free substance)*
Residual solvents: . **Isopropanol**	 Not more than 0.2%
Additional test	
Particle size (laser)	D(v,0.1): NMT 10 μm D(v,0.5): NMT 30 μm D(v,0.9): NMT 60 μm
Polymorphic Form	The x-Ray powder diffractogram is consistent with the reference diffractogram of [redacted] Characteristic XRD peak positions are: 7.1, 10.8, 14.2, 16.7, 17.2, 18.5, 21.4, 21.8, 22.6, 23.2, 23.5, 24.0, 24.2, 28.5, 32.5 within ±0.3 degrees.

Our Vision with Structured Data



Pharmaceutical Quality Chemistry Manufacturing & Controls (PQ/CMC)

- A cross-Center effort to establish content standards and electronic exchange standards for submitting PQ/CMC data, predicated on eSubmission requirements of FD&C Act 745A(a) (NDAs, ANDAs, BLAs, and certain INDs)
- Focus on Module 3 (Body of Data) of the eCTD
- Participating Centers: **CDER**, **CBER** and **CVM**
- Led and sponsored by **CDER/Office of Strategic Programs (OSP)**
- Initiated ~ 2014

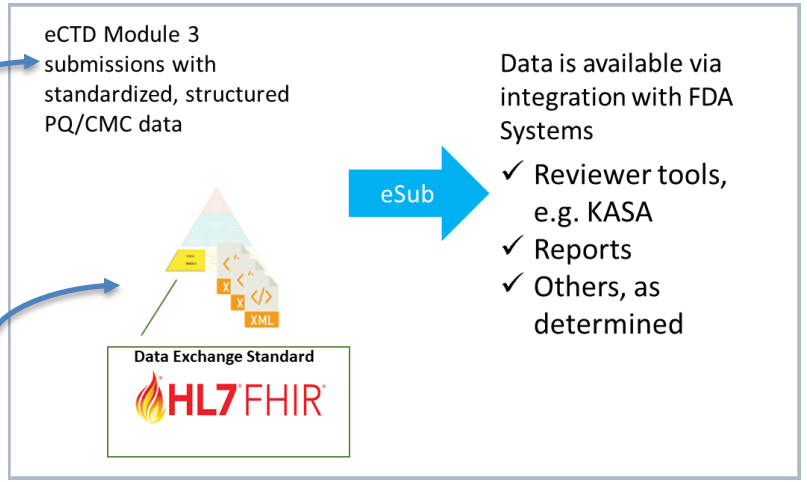


https://www.fda.gov/industry/fda-data-standards-advisory-board/pharmaceutical-qualitychemistry-manufacturing-controls-pqcmc

The Objectives

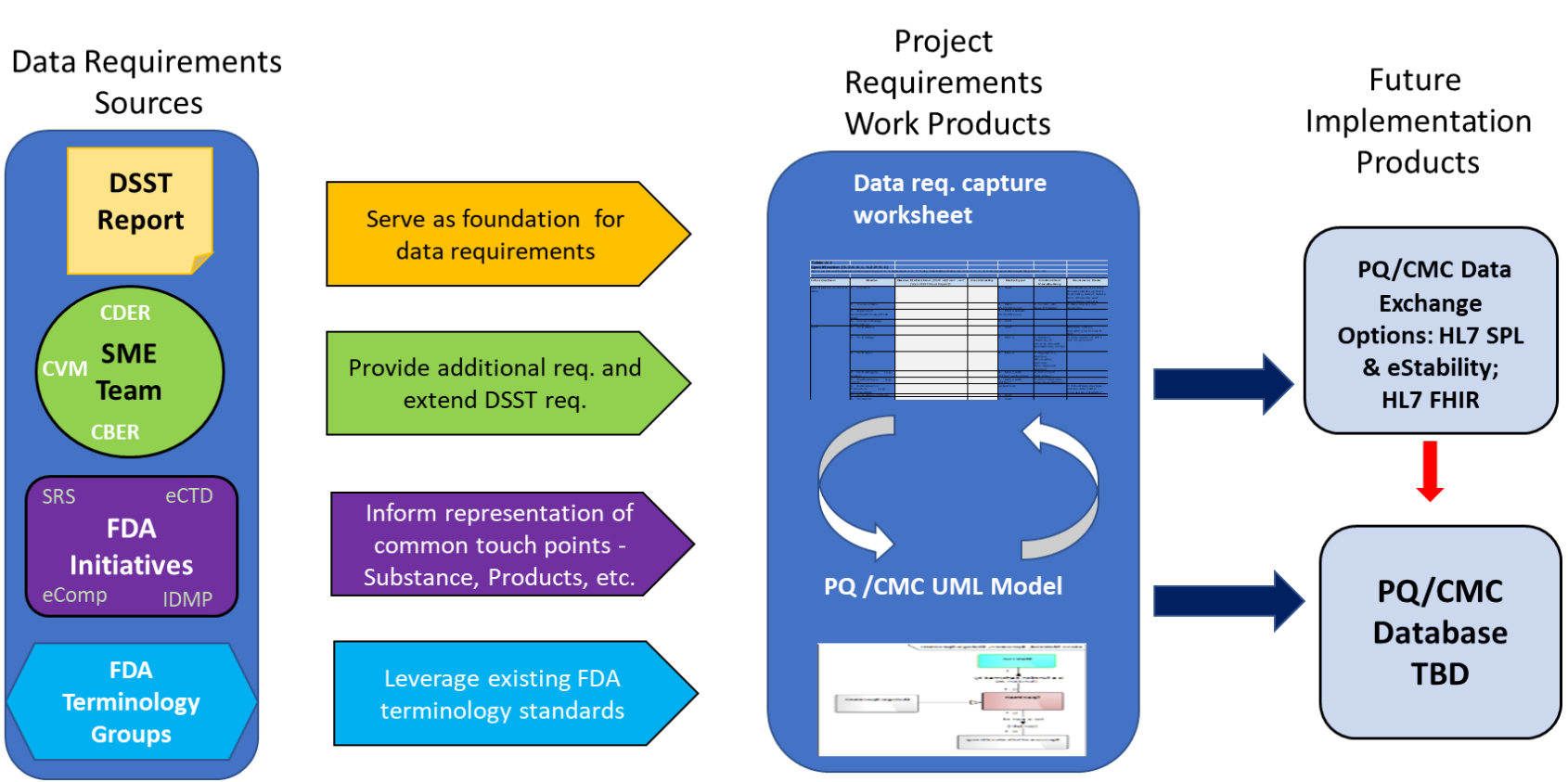
Objective 1: To develop structured and computable data standards for PQ/CMC

Objective 2: To design and develop data exchange standard for submission of PQ/CMC data



- FHIR® – Fast Healthcare Interoperability Resources – is a next generation standards framework created by Health Level Seven International (HL7).
- www.hl7.org

Data Standards Development Strategy



Data Element Categories

Categories of PQ/CMC data in eCTD Module 3 and Module 2 QOS

1. Specification(drug substance/drug product/excipients)
2. Batch Analysis (drug substance/drug product)
3. Stability(drug substance/drug product)
4. Nomenclature of Drug Substance
5. Composition of Drug Product
6. Batch Formula
7. Impurities
8. Manufacturing Process
9. Annual BLA Lot Distribution Report
10. CMC Changes in Annual Report – NDA/ANDA/BLA/NADA/ANADA
11. Analytical Procedure Validation
12. Facility Information

Categories 1 -7

PHASE 1

2014-2020

Categories 8 -12

PHASE 2

2021- now

Phase 1: 2014-2020; ~ 33% of Module 3

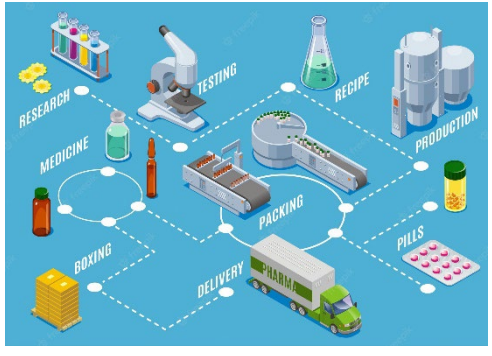
Section	Coverage	# of elements
1. Drug Substance	Nomenclature, characterization, control of materials and impurities	40
2. Drug Product	Component & composition, control of excipients and impurities	37
3. Batch Formula	Properties of batch formula	11
4. Quality Specification	Properties of a quality specification	26
5. Batch Analysis	Properties of a batch analysis	50
6. Stability data	Properties of a stability study	21
7. Terminology	Controlled terminology (31), CCS & component function (153), units of measure (70)	

- 2017 PQ/CMC FRN
- 2018 Public Meeting
- 2022 PQ/CMC FRN – updated Phase 1 data elements for comments

Phase 2: 2021 – now;

- Manufacturing:
  - Manufacturer info
  - Equipment
  - Manufacturing process
  - Unit operations
  - Process parameters
  - In-process controls/tests

- Solid oral drug products – completed
- Drug substance – on-going
- Liquid-based drug products – upcoming



A Demonstrative Example

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Currently unstructured Specification Table

A Demonstrative Example

Table	Data Element Name	Data Element Name Definition	Data type	Terminology	Controlled Vocabulary	Conformance
01-Specification	**Specification Title**	The textual identification for the specification.	Text		0	M
01-Specification	**Specification Subtitle**	An additional textual identification for the spe	Text		0	O
01-Specification	**Specification Type**	A classification of specification related to the	Code	Drug ProductDrug Su	See Controlled Terminology sheet	M
01-Specification	**Specification Version**	The alphanumeric text assigned by the spons	Text		0	M
01-Specification	**Specification Version Date**	The date when the sponsor assigned a date to	Date		0	M
01-Specification	**Specification Status**	The current FDA regulatory status of the spec	Code	ApprovedTentatively A	See Controlled Terminology sheet	M
01-Specification	**Specification Status Date**	The date on which the FDA approval status fo	Date		0	M
01-Specification	**Specification Additional Information**	Placeholder for providing any comments that	Text		0	O
02-Test	**Test Name**	The textual description of a procedure or anal	Text		0	M
02-Test	**Test Method Origin**	A coded value specifying the source of the me	Code	CFRProprietaryComp	See Controlled Terminology sheet	M
02-Test	**Test Category**	A high level grouping of quality attributes for	Code	AssayBiological Prope	See Controlled Terminology sheet	M
02-Test	**Analytical Procedure**	The name of the technique used to determine	Text		0	M
02-Test	**Reference to Procedure**	A sponsor/applicant provided alphanumeric c	Text		0	M
02-Test	**Relative Retention Time**	The ratio of the retention time of a componer	Text		0	O
02-Test	**Test Additional Information**	Placeholder for providing any comments that	Text		0	O
02-Test	**Test Order**	The sequential number assigned to each Test	Numeric		0	M
02-Test	**Stage Name**	A textual description and/or a number that ic	Text		0	M
02-Test	**Stage Sequence Order**	The order of the stages in regular succession.	Numeric		0	M
02-Test	Stage Additional Information	Placeholder for providing any comments that	Text		0	O
03-Acceptance Criteria	**Value**	The acceptable qualitative or text value of the	Text		0	O
03-Acceptance Criteria	**ValueNumeric**	The acceptable quantitative or numeric value	Numeric		0	O
03-Acceptance Criteria	**ValueNumeric UOM**	A named quantity in terms of which other qu	Code	http://www.fda.gov/	See Controlled Terminology sheet	O
03-Acceptance Criteria	**Original Text**	The text of the acceptance criteria as provide	Text		0	M
03-Acceptance Criteria	**Acceptance Criteria Usage**	A coded value specifying when a particular an	Code	ReleaseStability	See Controlled Terminology sheet	M
03-Acceptance Criteria	**Interpretation Code**	A code that describes how to relate the given	Code	NMT (not more than)	See Controlled Terminology sheet	M
03-Acceptance Criteria	**Additional Information**	A textual field to provide any additional infor	Text		0	O

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01-Specifica						O
02-Test						M
02-Test						M
02-Test						M
02-Test						M
02-Test						M
02-Test	**Relative Retention Time**	The ratio of the retention time of a componer	Text		0	O
02-Test	**Test Additional Information**	Placeholder for providing any comments that	Text		0	O
02-Test	**Test Order**	The sequential number assigned to each Test	Numeric		0	M
02-Test	**Stage Name**	A textual description and/or a number that id	Text		0	M
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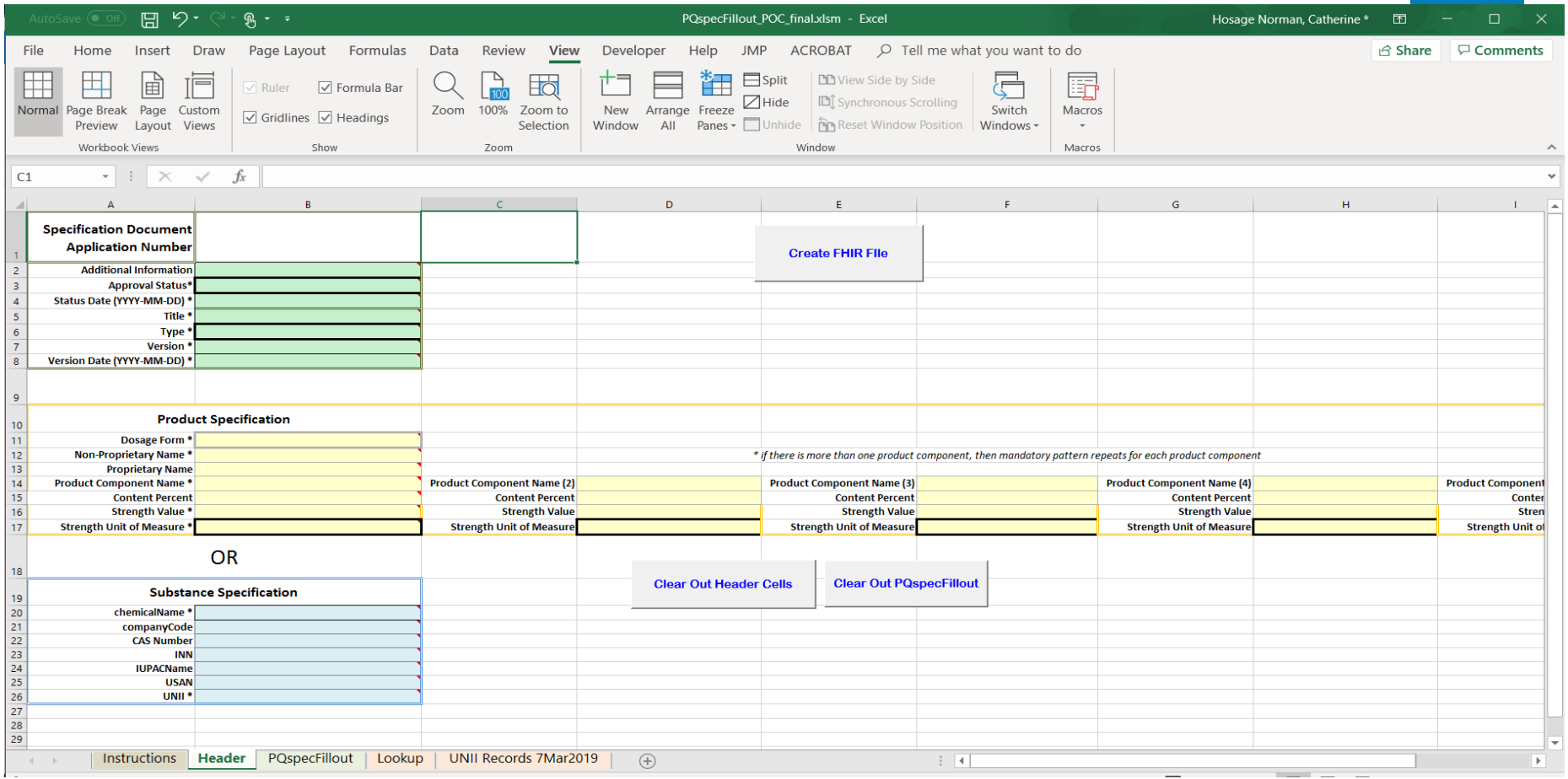
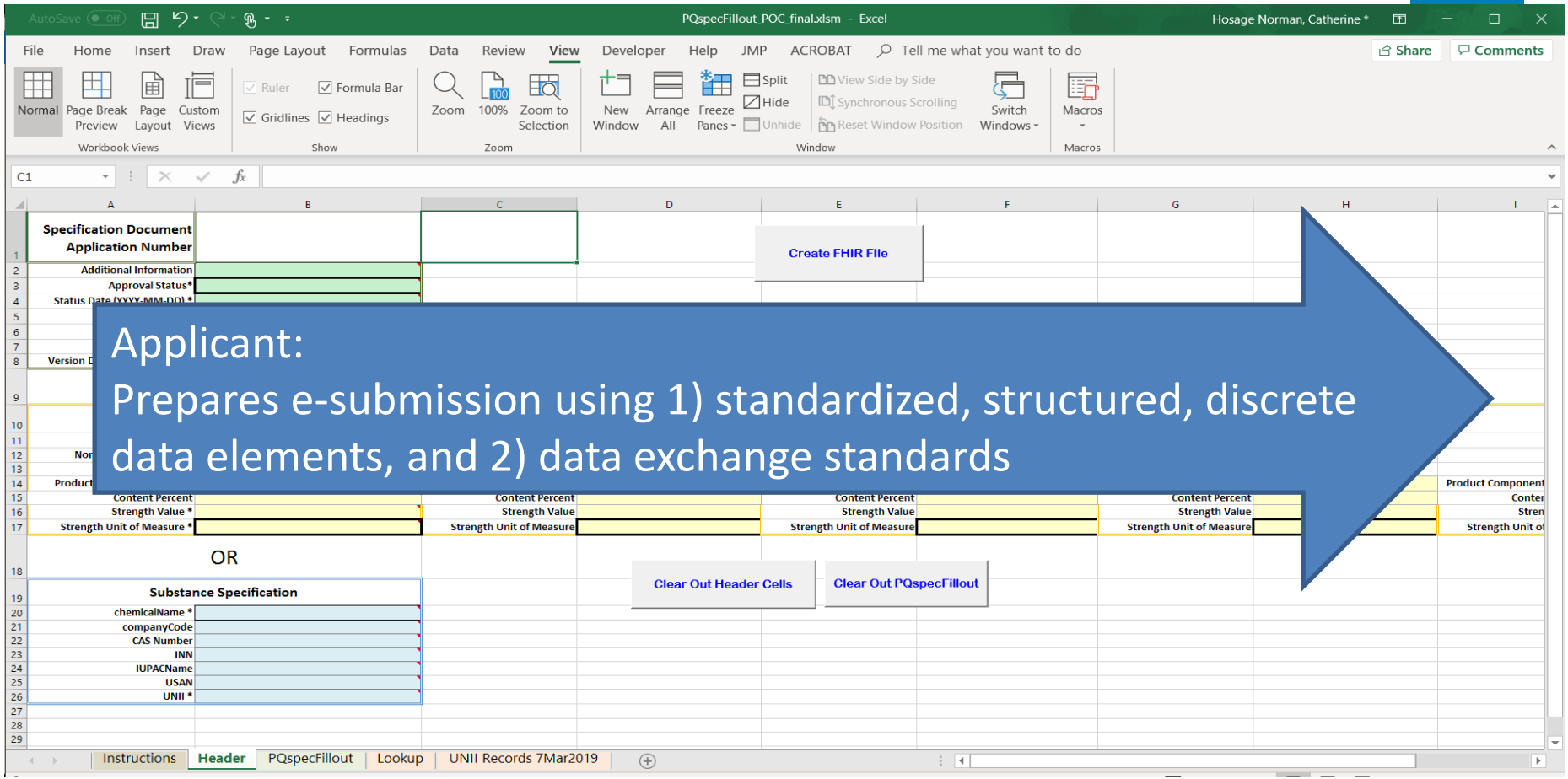
PQ/CMC effort:
Transform into standardized and structured, discrete data elements

Reference: Federal Register Notice Draft PQ/CMC Data Elements and Terminologies; Request for Comments (07/11/2017)

A Demonstrative Example



A Demonstrative Example



A Demonstrative Example

U.S. FOOD & DRUG ADMINISTRATION

PHARMACEUTICAL QUALITY
CHEMISTRY, MANUFACTURING, AND CONTROLS (PQ/CMC)

Application Sequence .. ATZN32801 0001 Spec. Ver...
Test Category: (All)

Drug Product Specification [redacted]
Specification .

Type: Drug Product
Approval Status: Not Approved
Additional Information: Test example specification

Version: 2.0

Version Date: 2018-04-27
Approval Date: 2019-05-23

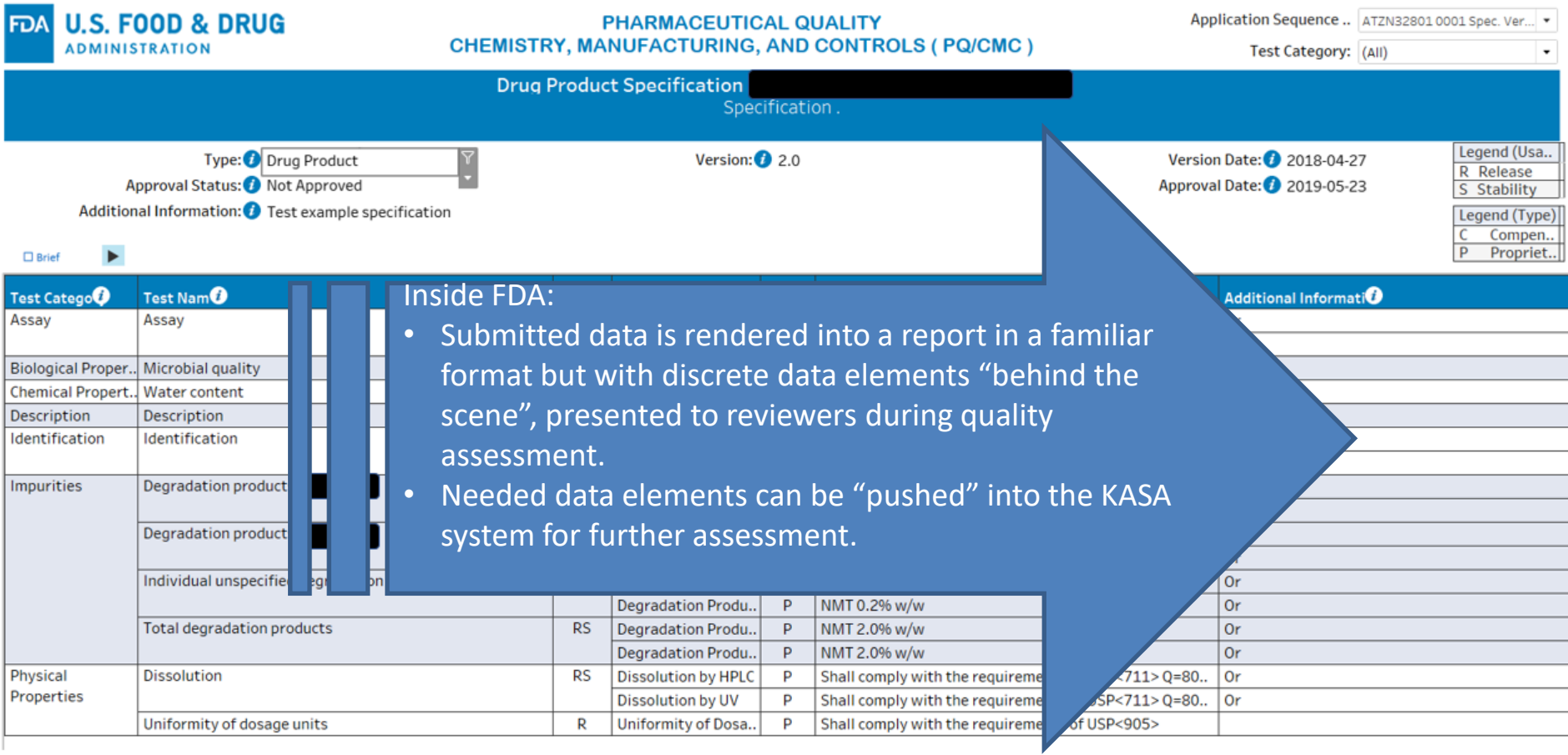
Legend (Usa..
R Release
S Stability

Legend (Type)
C Compen..
P Propriet..

Brief

Test Catego	Test Nam	Usag	Metho	Typ	Acceptance Crite	Additional Informati
Assay	Assay	RS	Assay by HPLC	P	90% to 110% of label claim	Or
			Assay by UHPLC	P	90% to 110% of label claim	Or
Biological Proper..	Microbial quality	S	Microbial quality	C	Monitor Report	text
Chemical Propert..	Water content	S	Water Content by K..	P	Monitor Report	text
Description	Description	RS	Visual inspection	P	Size 1 hard capsule with a blue opaque cap and a yellow ..	
Identification	Identification	R	Identification by H..	P	Consistent with the retention time and UV spectrum of t..	Or
			Identification by U..	P	Consistent with the retention time and UV spectrum of t..	Or
Impurities	Degradation products [redacted]	RS	Degradation Produ..	P	NMT 0.6% w/w	Or
			Degradation Produ..	P	NMT 0.6% w/w	Or
	Degradation products [redacted]	RS	Degradation Produ..	P	NMT 0.6% w/w	Or
			Degradation Produ..	P	NMT 0.6% w/w	Or
	Individual unspecified degradation products	RS	Degradation Produ..	P	NMT 0.2% w/w	Or
			Degradation Produ..	P	NMT 0.2% w/w	Or
	Total degradation products	RS	Degradation Produ..	P	NMT 2.0% w/w	Or
			Degradation Produ..	P	NMT 2.0% w/w	Or
Physical Properties	Dissolution	RS	Dissolution by HPLC	P	Shall comply with the requirements of USP<711> Q=80..	Or
			Dissolution by UV	P	Shall comply with the requirements of USP<711> Q=80..	Or
	Uniformity of dosage units	R	Uniformity of Dosa..	P	Shall comply with the requirements of USP<905>	

A Demonstrative Example



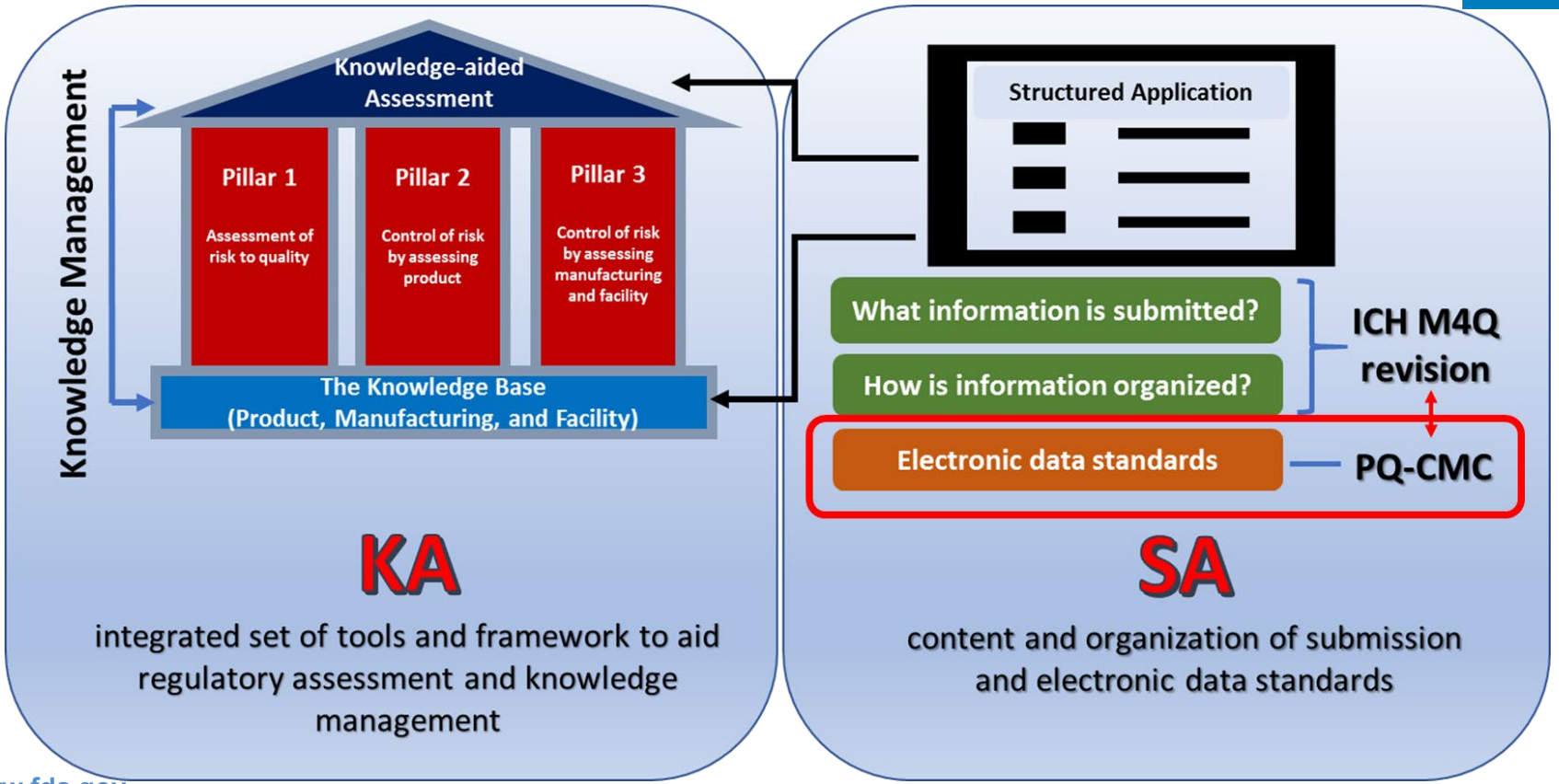
Inside FDA:

- Submitted data is rendered into a report in a familiar format but with discrete data elements “behind the scene”, presented to reviewers during quality assessment.
- Needed data elements can be “pushed” into the KASA system for further assessment.

Envisioned Benefits

- Ensures Industry and FDA are using the “same data”
- Industry
  - Could provide consistent formats for internal and external data management & storage (e.g. in LIMS), and data exchange with CMOs (Contract Manufacturing Organizations)
- FDA
  - Receives consistent high-quality data that can be consumed by computer systems without data entry and interpretations
  - Operationalize submitted data to enhance the effectiveness of quality assessment – a significant enabler for KASA
- Facilitates the M4Q implementation and enhances global regulatory convergence
- Accelerates the digitization efforts in both Industry and FDA, eventually enhances lifecycle knowledge management (e.g., for crisis response)

Future KASA System



Acknowledgment

FDA PQ/CMC SME Group:
- Norman Gregory (CVM)
- Frank Holcombe, Jr. (CDER)
- Michael Kerrigan (CVM)
- Ze Peng (CBER)
- Andre Raw (CDER – for KASA)
- Norman Schmuff (CDER)
- Chikako Torigoe (CBER)
- Geoffrey Wu (CDER)

OPQ PQ/CMC Workgroup:
- **Chair:** Geoffrey Wu
- **Technical Lead:** Norman Schmuff
- **Project Manager:** Mihir Jaiswal
- **Members:**
  - Ted Carver
  - Ee-Sunn (Joanne) Chia
  - Bazarra Damdinsuren
  - Frank Holcombe, Jr.
  - Susan Zuk


FDA
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