Structured Drug Submissions to FDA: The Pharmaceutical Quality/ Chemistry Manufacturing and Controls Project

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Summary

- Goals, Objectives & Scope
- Expected Benefits
- Progress to Date
- Public Comment Summary
- Stakeholder Collaboration
- Next Steps
- Overall Timeline

PQ/CMC Project

Goal:

- Establish electronic standards for submitting Pharmaceutical Quality (PQ) and Chemistry & Manufacturing Controls (CMC) data

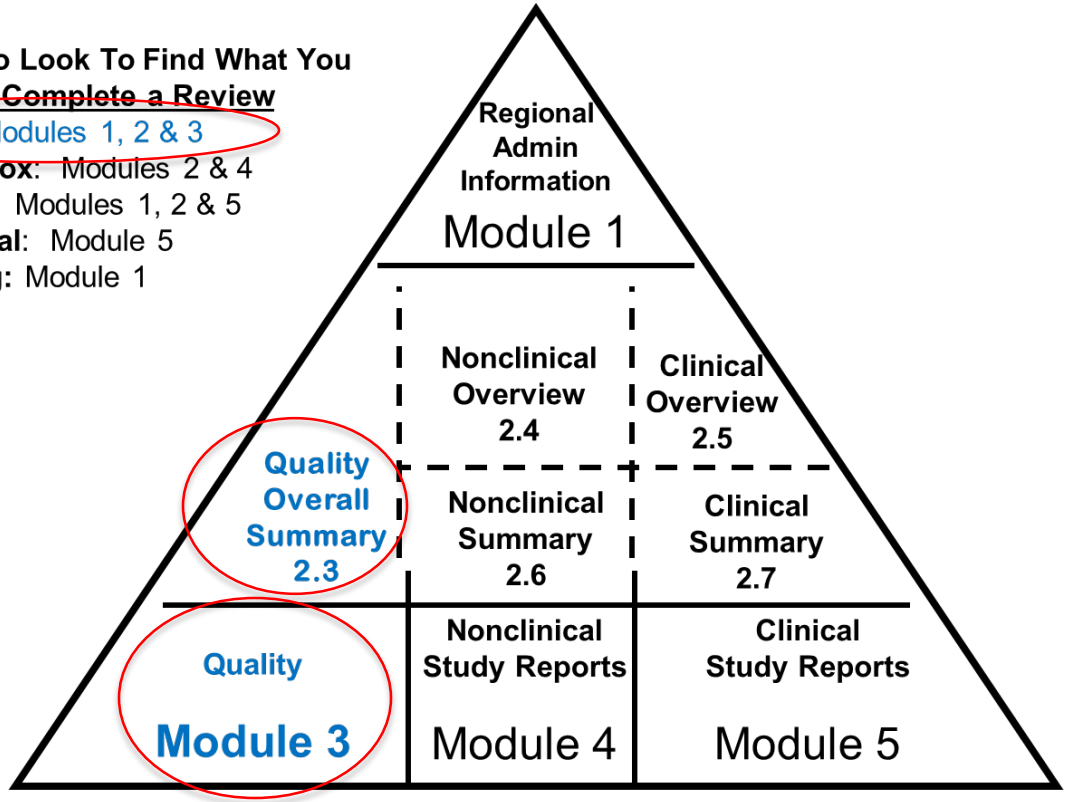
Objectives:

- Develop structured data standards for PQ/CMC
- Implement a data exchange standard for submitting PQ/CMC data

PQ/CMC Scope: Module 3 of eCTD

Where to Look To Find What You Need to Complete a Review

CMC: Modules 1, 2 & 3
Pharm/Tox: Modules 2 & 4
Clinical: Modules 1, 2 & 5
Statistical: Module 5
Labeling: Module 1



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

- Specification(drug substance/drug product/excipients)
- Batch Analysis (drug substance/drug product)
- Stability(drug substance/drug product)
- Nomenclature of Drug Substance
- Composition of Drug Product
- Batch Formula
- Impurities
- Manufacturing Process
- Annual BLA Lot Distribution Report
- CMC Changes in Annual Report – NDA/ANDA/BLA/NADA/ANADA
- Analytical Procedure Validation
- Facility Information

Note:
- Stability Analysis supported by extant HL7 eStability message (to be revised)
- Deferred to next version of PQ/CMC

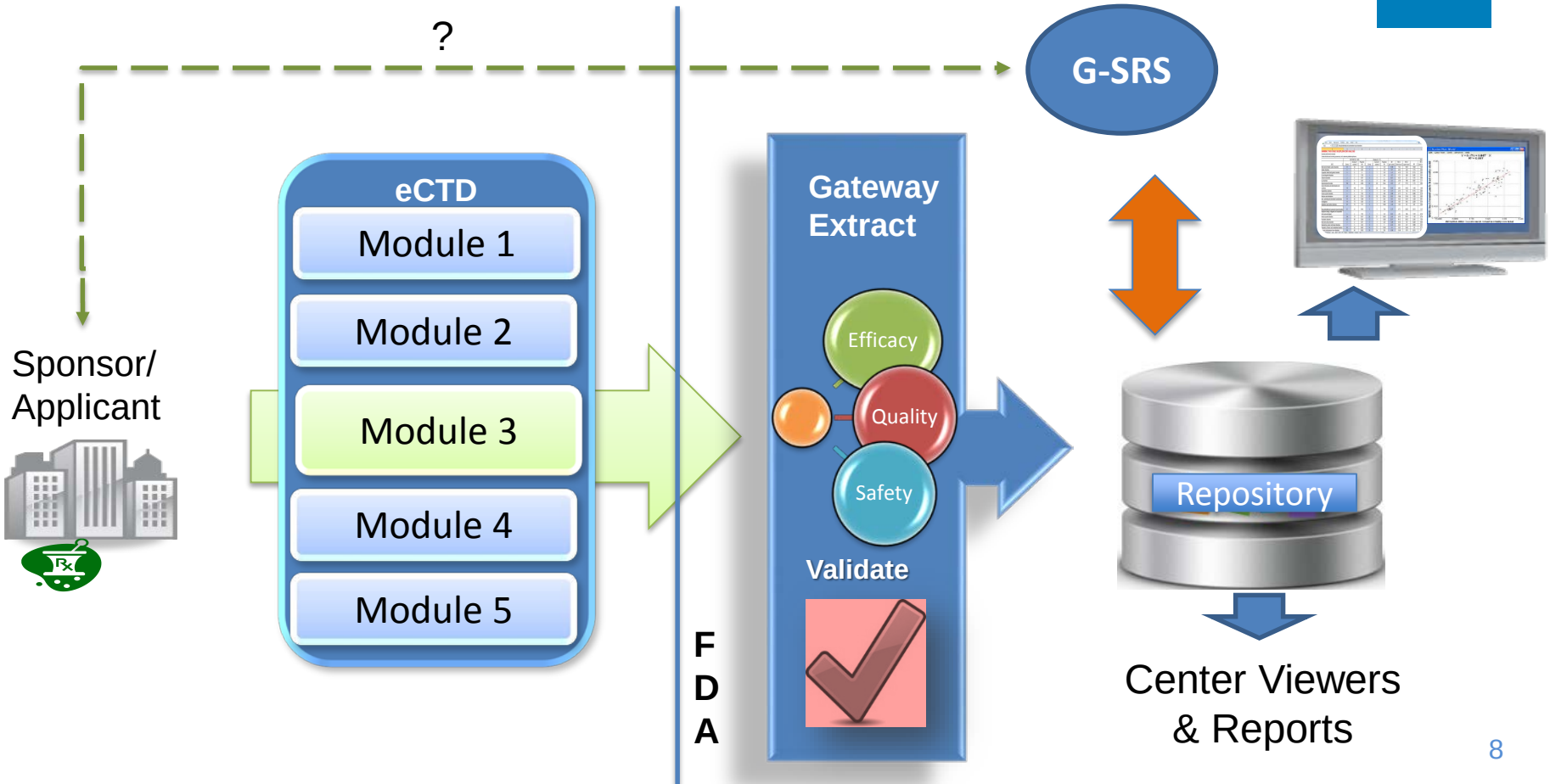
PQ/CMC Scope

- Module 3 & Module 2 QOS submissions including supplements & amendments
  - Human drugs
    - IND
    - BLA
    - NDA
    - ANDA
    - MF/DMF
  - Veterinary drugs
    - INAD
    - JINAD
    - VMF
    - ANADA
    - JINAD

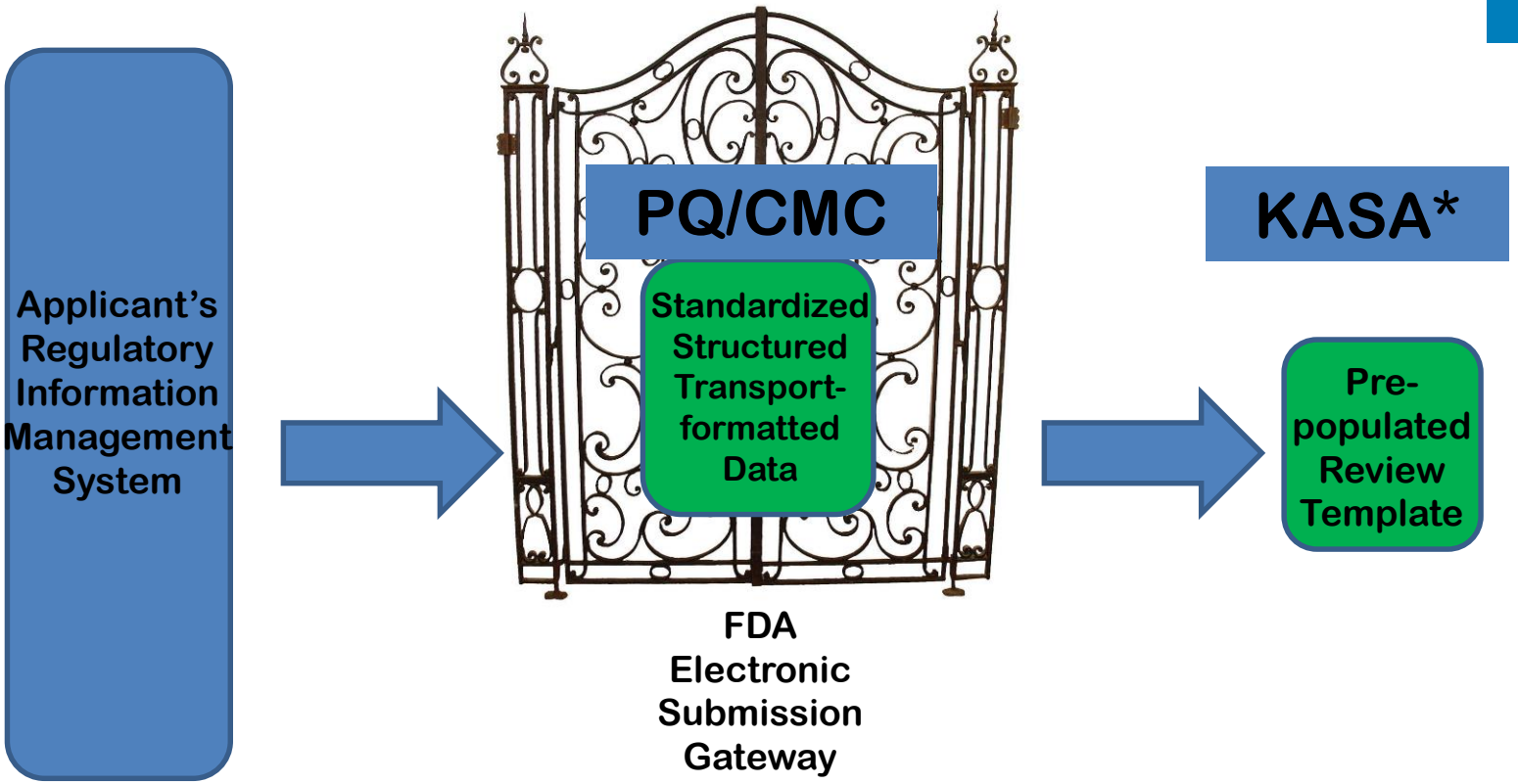
Expected Benefits

- FDA
  - Receives consistent high-quality data that can be consumed by computer systems without data entry and interpretations
  - Enables much-needed technology improvements to support quality assessments (Narrative Reviews→ Structured Assessments)
  - Improves crisis response
- Stakeholders
  - Provides consistent formats for:
    - Internal data management & storage (e.g. in LIMS)
    - Data exchange with CMOs (Contract Manufacturing Organizations)
  - Ensures industry and FDA are using the “same data”

Future State with Structured Data



Future State: Information Flow



* "Knowledge-Aided Assessment and Structured Application" Pharmaceutical Advisory Committee, September 20, 2018

The KASA System

- The KASA system is designed to:

  1. Capture and manage knowledge such as established conditions 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;

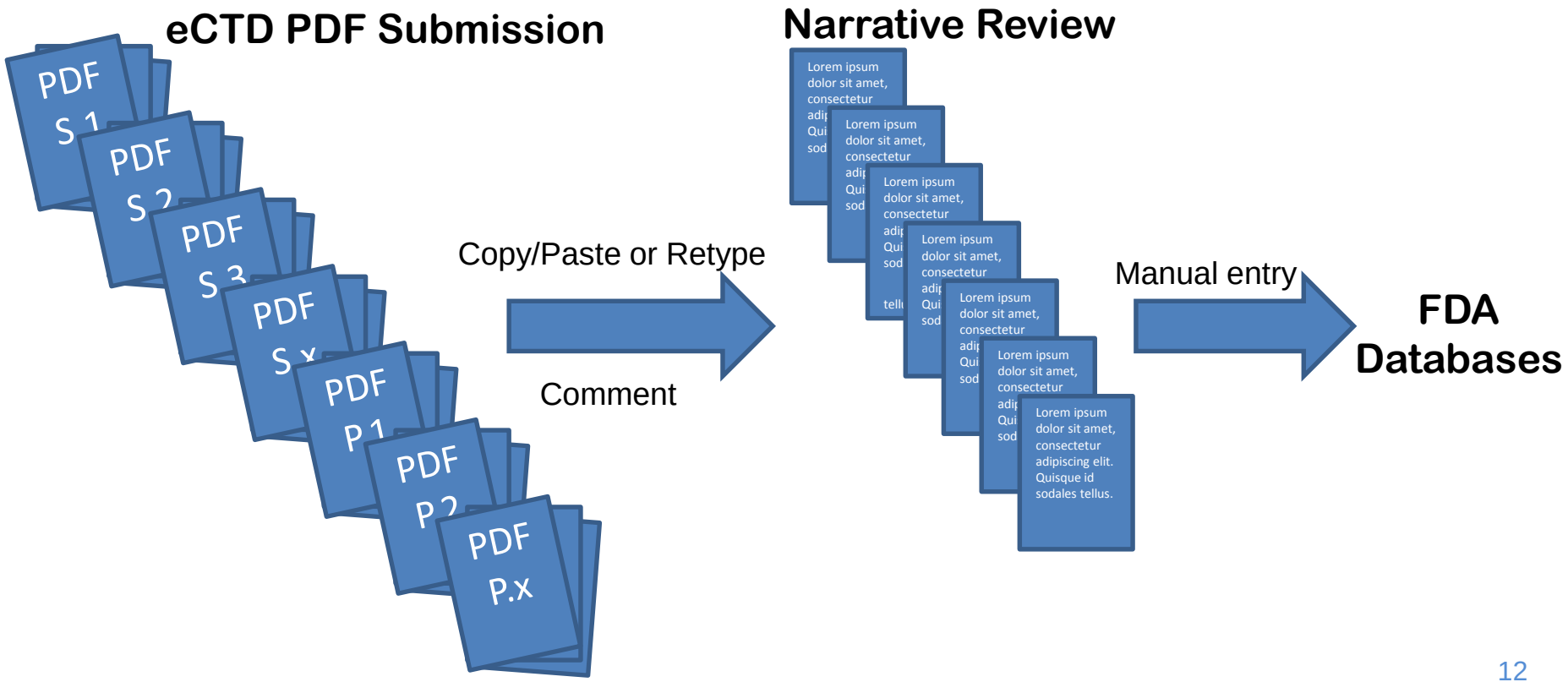
The KASA System

- The KASA system is designed to:

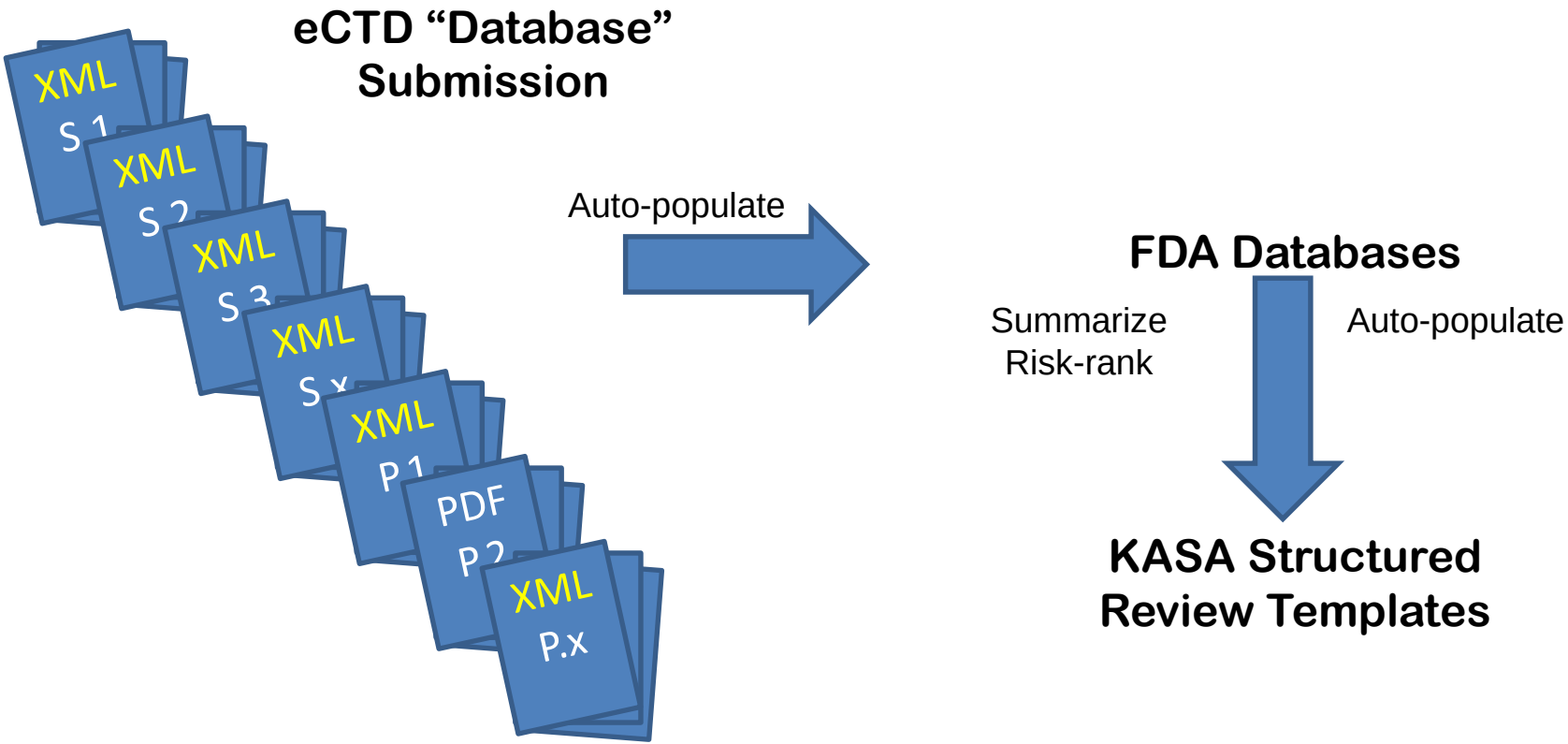
3. Perform computer-aided analyses of applications for a comparison of regulatory standards and quality risk across the repository of approved drug products and facilities

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

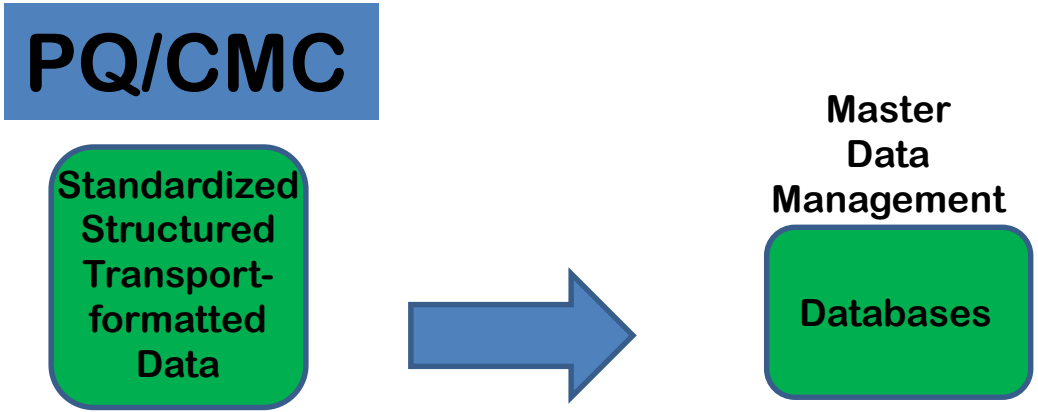
Current Module 3 Submission Model



Future Module 3 Submission Model

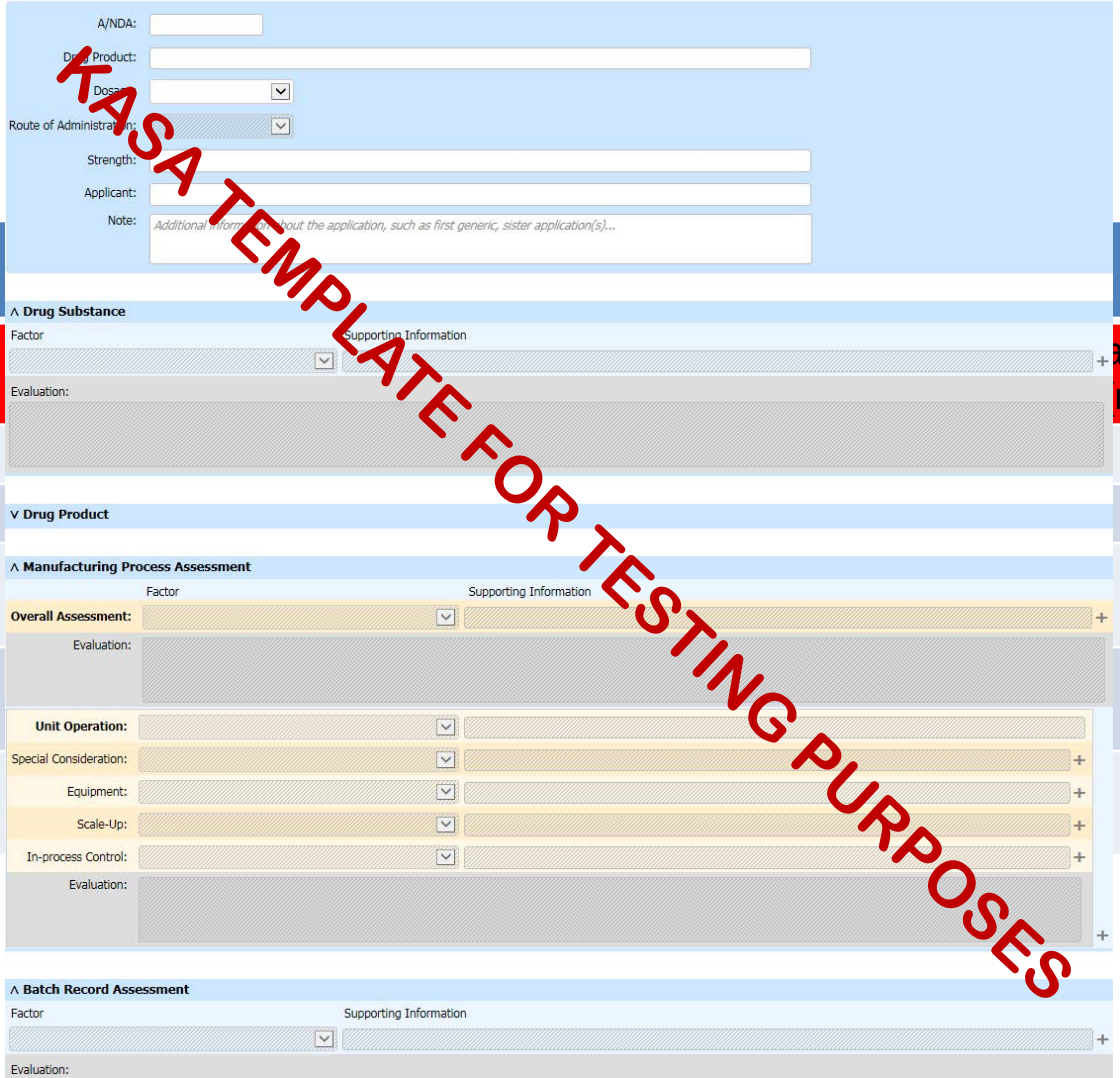


Future State: Data Flow



Master data management (MDM) is the effort made by an organization to create one single master reference source for all critical business data, leading to fewer errors and less redundancy in business processes.

Informatica:
https://www.informatica.com/services-and-training/glossary-of-terms/master-data-management-definition.html



KASA TEMPLATE FOR TESTING PURPOSES

Proposed Commercial	ax time mos)
No	36
No	42
Yes	12
Yes	12
Yes	12

From Roche/Genentech

Example:
Tabular over Narrative

Example: Narrative vs. Table

From Roche/Genentech

Narrative

32P1 India (where it is packed in blisters)

The drug product, ProduQt (Number-123) is a blue oval film-coated tablet containing 50 mg Qdrug.

The film-coated tablet is packed in an alu/pvc b
containing 10 tablets each.

One or more blisters are packed in a carton box.

32P1 Dutch (where it is packed in blisters)

Geneesmiddel, ProduQt (Number-123) is een blauwe ovale filmomhulde tablet dat 50 mg Qdrug bevat.

De filmomhulde tablet is verpakt in een alu/pvc blisterverpakking die elk 40 tabletten bevat.

Een of meerdere blisterverpakkingen zijn verpakt in een in een kartonnen doos.

Translations

ular views

32P1 English

Product name:	ProduQt
Manufactured dose form:	film-coated tablet
Strength:	50 mg
Active substance:	Qdrug
ID number:	Number-123
Colour:	blue
Shape:	oval
Primary container type:	alu/pvc blister
Quantity in primary container:	10
Seconardary container type:	carton box
Quantity in seconardary container:	one or more

32P1 Dutch

Product naam:	ProduQt
Gefabriceerde doserings vorm:	film-omhulde tablet
Sterkte:	50 mg
Actieve substantie:	Qdrug
ID nummer:	Number-123
Kleur:	blauw
Vorm:	ovaal
Directe verpakking:	alu/pvc blisterverpakking
Alu/pvc blisterverpakking inhoud:	10
Buiten verpakking:	kartonnen doos
Kartonnen doos inhoud:	een of meer

Example: Narrative vs. Table
Concentrate for solution for injection

Narrative

32P1 concentrate for solution for injection

The drug product, ProQuit (Number-456) is a colourless concentrate for solution for injection containing 5 mg/mL Qdrug.

The concentrate for solution for injection is packed in a glass vial, with a minimal extractable volume of 2 mL.

The concentrate for solution for injection is to be diluted with the solvent water for injection prior to administration.

One glass vial of the concentrate for solution for injection is co-packed with one glass vial of solvent in a carton box.

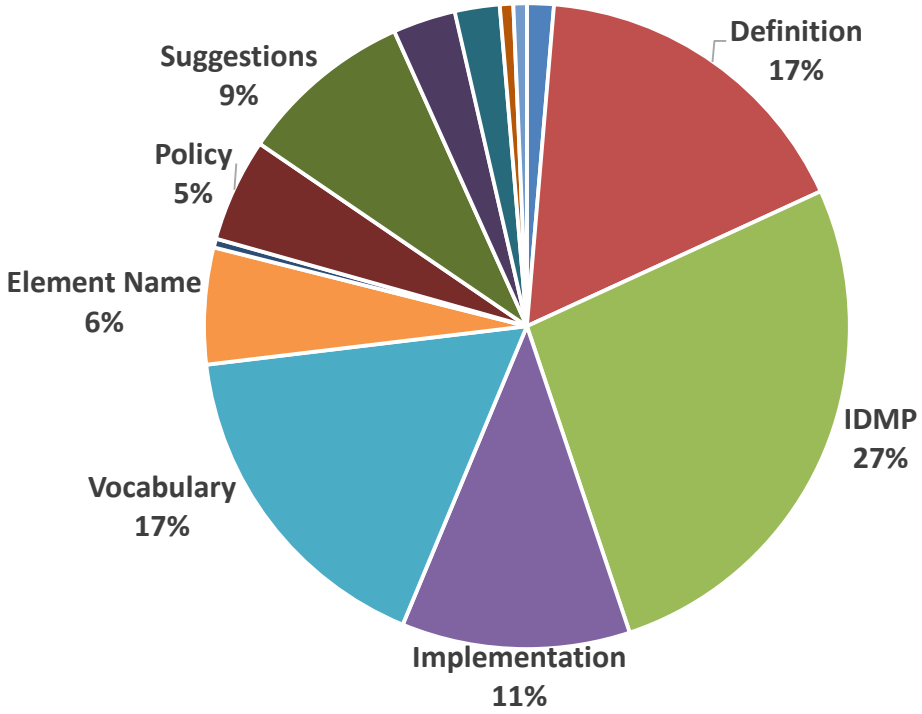
Tabular view

32P1 concentrate for solution for injection

Product name:	ProQuit
Manufactured dose form:	concentrate for solution for injection
Concentration:	5 mg/mL
Administrable dose form:	solution for injection
Strength/Concentration:	500 mcg/mL
Active substance:	Qdrug
Colour:	colourless (clear)
ID number:	Number-456
Primary container type:	glass vial
Quantity in primary container:	3 mL
Minimum extractable volume:	2 mL
Seconardary container type:	carton box
Quantity in seconardary cont.:	1

From Roche/Genentech

Public Comment by Category



- 450 comments
- 11 organizations
  - Trade organizations (2)
  - Individual PhRMA members (6)
  - Misc (3)

Federal Register Comments

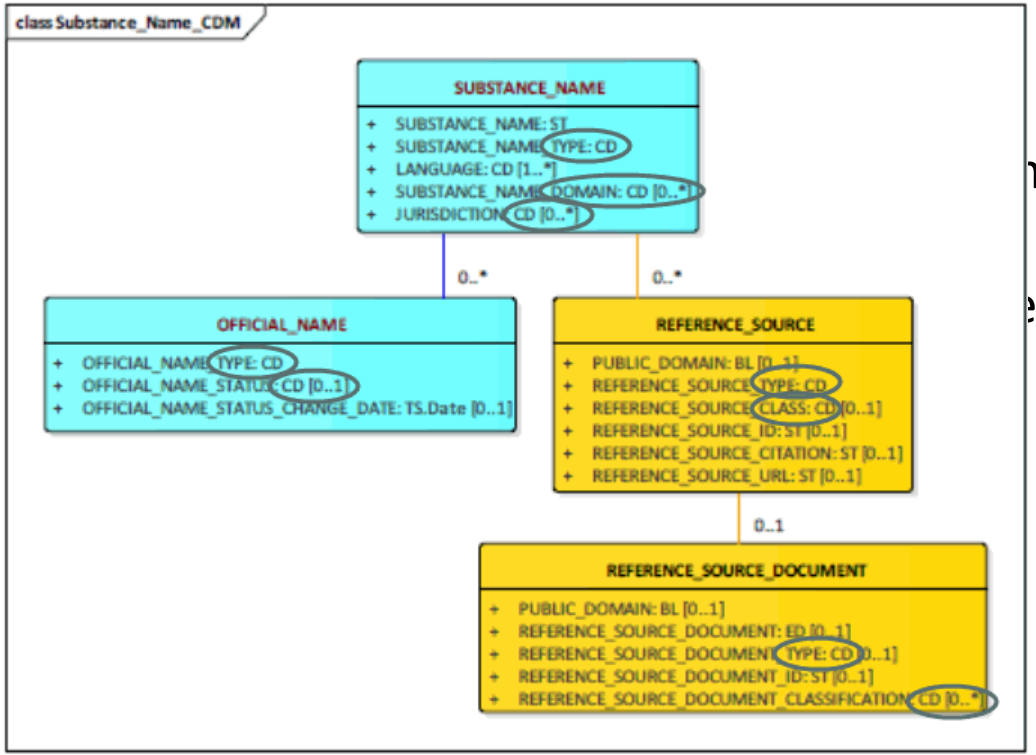
- Trade organizations (2)
  - PhRMA
  - Plasma Protein Therapeutics Assn
- Misc (3)
  - Acuta
  - Allotrope Foundation
  - IRISS
- Individual PhRMA members (6)
  - Boehringer Ingelheim
  - Johnson & Johnson
  - Merck
  - Novartis
  - Roche/Genentech
  - Sanofi

Top Three Categories (55%)

- IDMP
  - Is this the same or different as, does this map to IDMP term
- Vocabulary
  - Clarification, new valid values for controlled vocabulary list
- Definition
  - Clarification, rewording

PQ/CMC IDMP Challenges

- In ID
  - 11
  - N
  - M
- PQ/
  - Q
    e.
  - Q
  - Lif
  - Ba



*SSG – Specified Substance

IDMP Mapping

- Mapped 84 PQ/CMC term
- Resultant mapping document
  - Narrative & tables
  - 82 pages
  - Distributed to PhRMA
- Secondary interactive public review planned

GSRS Comments

- 6 organization comments on alignment
- Example of specific comments:
  - “practical experience from GSRS should also be leveraged”
  - “Requiring submission of redundant information”
  - “Table 7 appears to be entirely duplicated in … SRS”
  - “auto-population of meta data from the eCTD into downstream medicinal product databases such as G-SRS for the GINAS”

Where We Are (1)

- The cross-center initiative involves FDA reviewers from CDER, CBER and CVM
- Over 150 data elements within eCTD Module 3 (CMC) were analyzed, definitions identified, and controlled terminologies developed where appropriate
- PQ/CMC Data Elements & Controlled Terminology was published for public comment in July 2017
  - https://www.regulations.gov/document?D=FDA_FRDOC_0001-7545

Where We Are (2)

- Harmonizing with ISO IDMP, where feasible
  - Detailed mapping complete, under secondary review
- Informal discussion within ICH M2 about a potential quality topic
  - positive initial response; M2 project opportunity proposal to be developed
- Several possible electronic data exchange mechanisms evaluated

Future Plans

- Refine the model, terms and definitions
- Create & test PQ/CMC database
- Test FHIR as a transport model for substance
- Continue international collaboration
- Schedule interactive IDMP mapping with stakeholders
- Draft 745A guidance

Longer Term

- This project covers 1/3rd of submitted CMC data
- Other CMC data may be addressed in future
  - For example: manufacturing process, annual reports

Draft Timeline for PQ/CMC