U.S. FOOD & DRUG ADMINISTRATION

Public Meeting on

Standardized Data for Pharmaceutical Quality/Chemistry Manufacturing and Control (PQ/CMC)

White Oak Campus
Silver Spring, MD

October 19, 2018

PQ/CMC Public Meeting Goals

- Share goals, objectives & progress on PQ/CMC standardization effort
- Provide perspective on public comments received on the Federal Register Notice (FRN)
- Solicit stakeholder input on the standardization effort

How to submit comments to the docket

Stakeholder input is essential and valued!

- Submit electronic comments to https://www.regulations.gov/
- All comments should be identified with the docket number FDA-2018-N-2608
- Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Comments are due by November 16, 2018

- Send questions to the PQ/CMC mailbox: PQ-CMC@fda.hhs.gov

Meeting Logistics

- **Housekeeping**
  - Pre-ordering your lunch (on your own)
    - Turn in order forms at Sodexo counter by 11:15 AM; pay with cash or credit
  - Restroom directions
  - Guest WiFi
    - WiFi Name: FDA Public
    - You will be directed to a page for a password: publicaccess
  - Please go to microphone stations for all questions
  - Webinar Participants: Type questions in Adobe chat box
- **Reminder: This webinar is being recorded**
- **Please put your cell phones on mute. Take calls outside of meeting room.**

Agenda

- Agenda Structure
  - 2 Sessions: Presentations by (1) FDA and (2) Industry
  - Question and Answer Panel at the end of each session
    - **Please hold questions until the end-of-session panel**
    - Submit unanswered questions to the docket
  - Open Public Comment session at end of meeting

Thank you

Session 1. PQ/CMC Standardization Activities at FDA

The Pharmaceutical Quality/Chemistry Manufacturing and Controls (PQ/CMC) Overview

Mary Ann Slack
Director
Office of Strategic Programs (OSP)
Center for Drug Evaluation and Research (CDER)
October 19, 2018

PQ/CMC Agenda

- 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

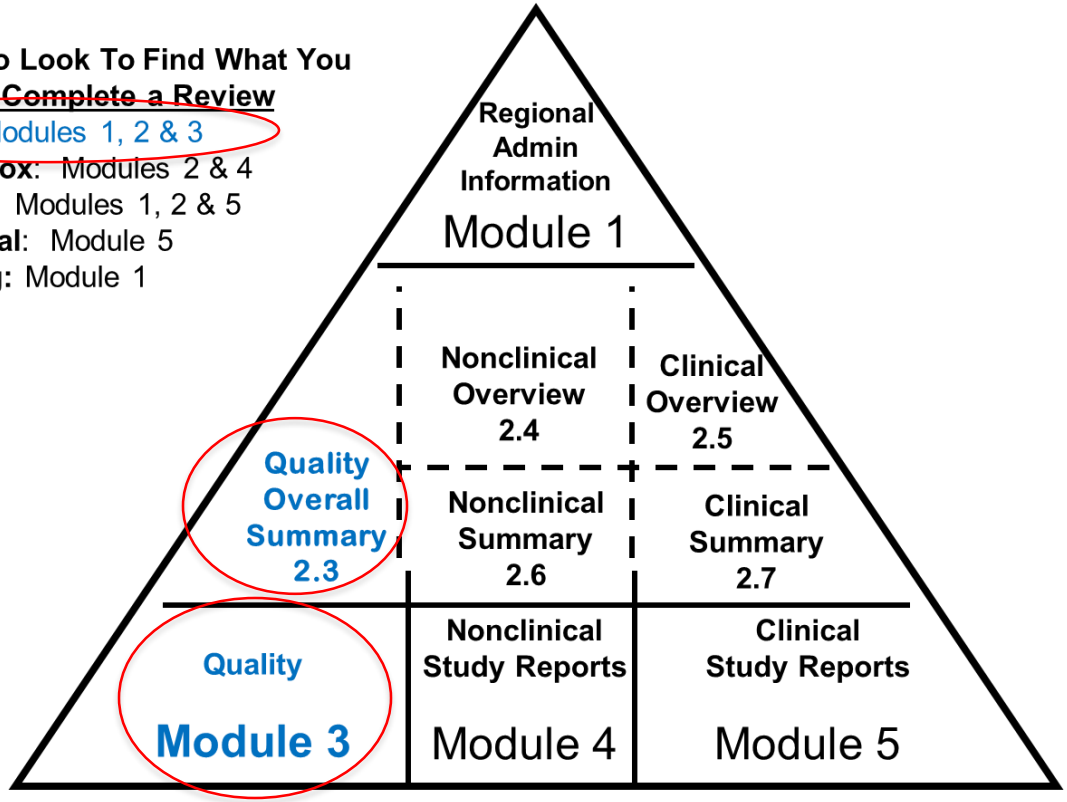
Objectives:

- 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

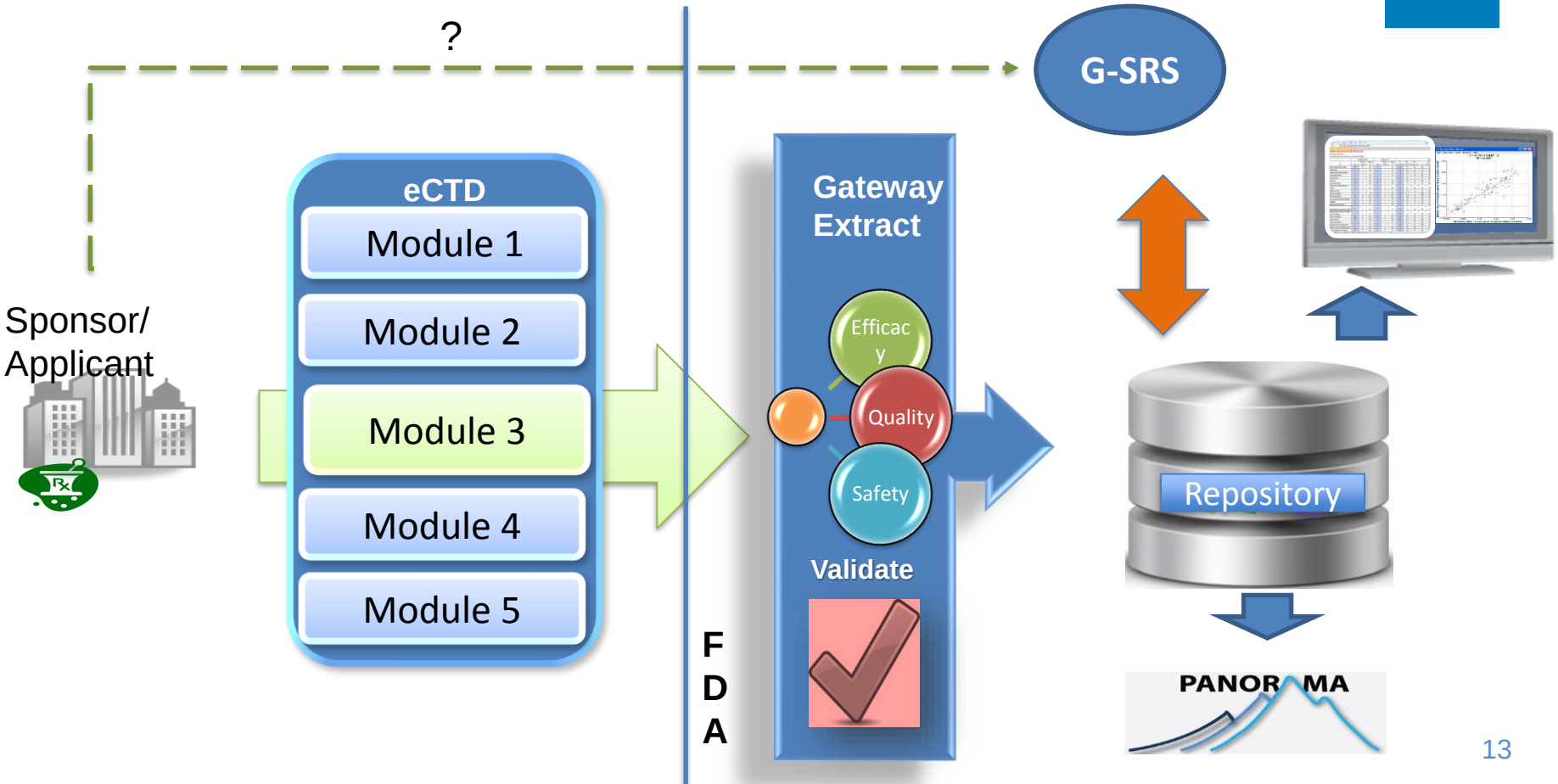
CMC: Modules 1, 2 & 3
Pharm/Tox: Modules 2 & 4
Clinical: Modules 1, 2 & 5
Statistical: Module 5
Labeling: Module 1



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
  - 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



Where We Are (1 of 4)

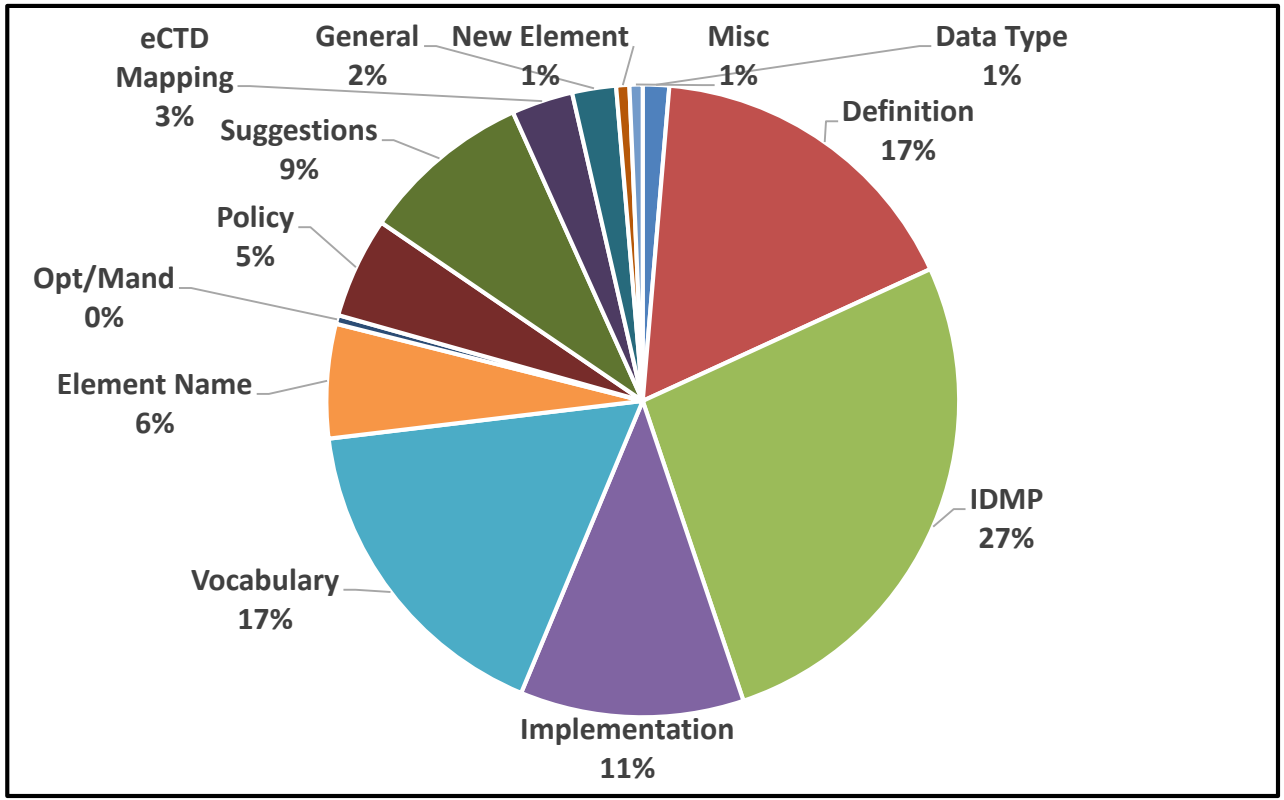
- The cross-center initiative involves FDA reviewers from CDER, CBER and CVM
- Over 150 data elements within eCTD Module 3 (CMC) were analyzed, definitions identified, and controlled terminologies developed where appropriate
- PQ/CMC Data Elements & Controlled Terminology was published for public comment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

Where We Are (2 of 4): Public Comments Summary

- 11 Organizations provided over 480 comments
  - Overall a positive response to structuring and standardization of CMC data
  - Detailed review of comments resulted in a number of changes

- Some general themes:
  1. Need FDA's overall strategic plan
  2. Avoid duplication of effort and submission
  3. Plans for global harmonization for regulators
  4. Harmonize with IDMP
  5. FDA asking for more than what is in the dossier
  6. Terms are small molecule centric
  7. Provide flexibility in adding new data elements and terminology
  8. Collaborate with Allotrope and leverage that work, where relevant

Where We Are (3 of 4): Public Comments by Categories



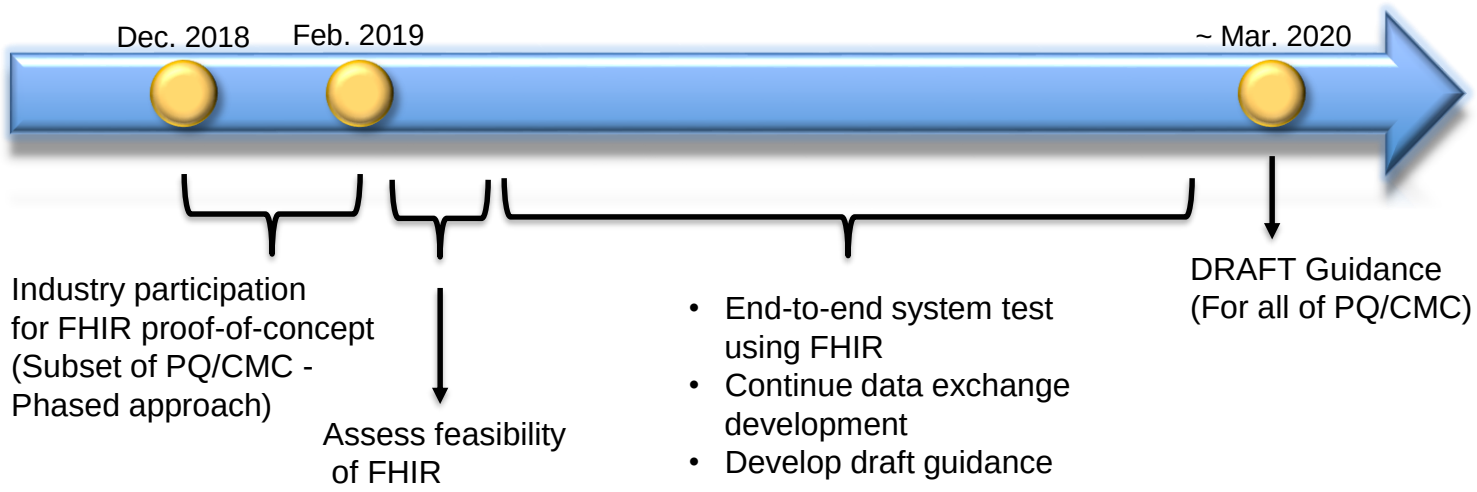
Where We Are (4 of 4)

- 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

Next Steps

- Reconcile PQ/CMC with IDMP where possible
- Develop & test PQ/CMC Data Exchange Standard
  - Originally considered HL7 SPL but unable to address full requirements
  - Evaluated HL7 FHIR as an alternate option
  - Proof of concept using Quality Specification will inform next steps for rest of PQ/CMC
- Develop draft guidance

Draft Timeline for PQ/CMC



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

Thank you

The Pharmaceutical Quality/Chemistry Manufacturing and Controls (PQ/CMC) Project

Norman R. Schmuff, Ph.D.
CDER, Office of Pharmaceutical Quality
Office of Process and Facilities
October 19, 2018

PQ/CMC – Some Details

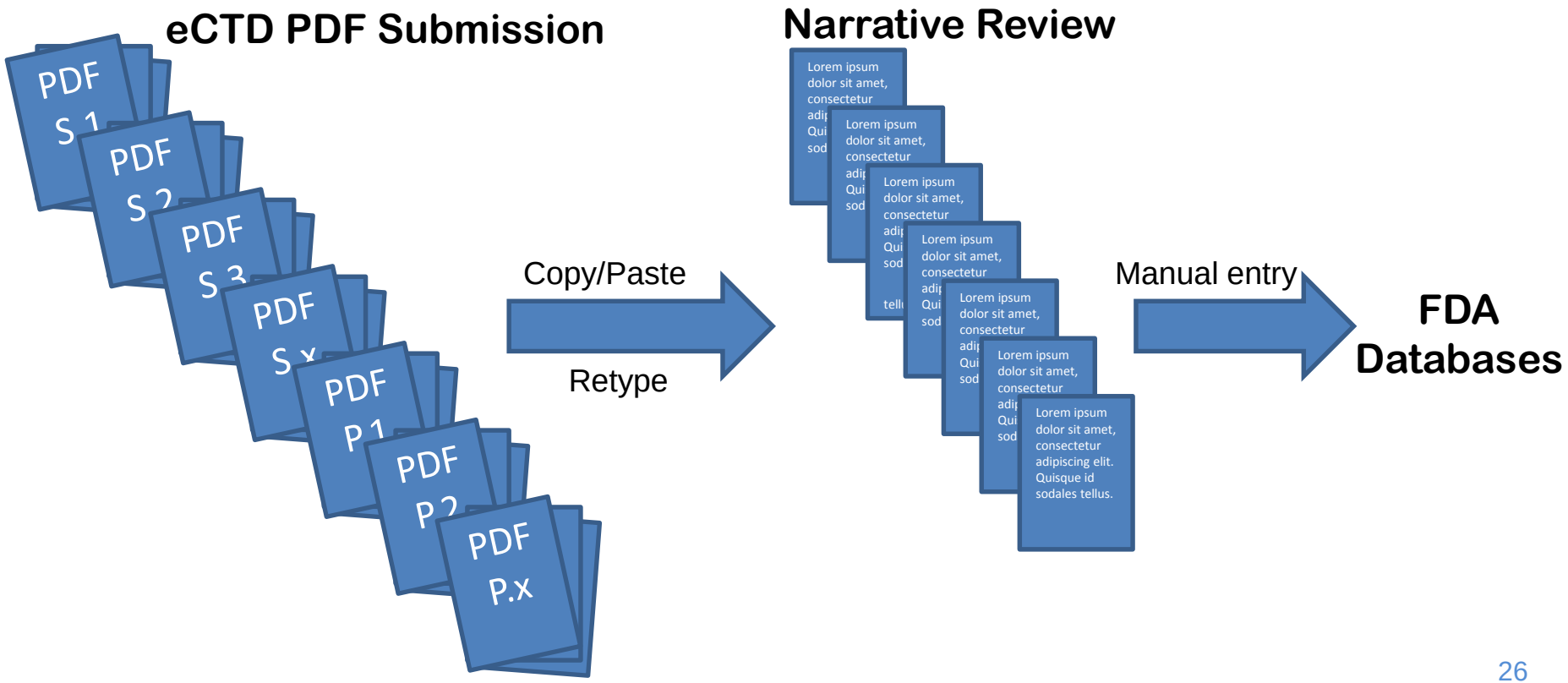
- Goals, Objectives & Scope: Another View
- Progress to Date: Some Details
- Next steps

Goals, Objectives & Scope: Another View

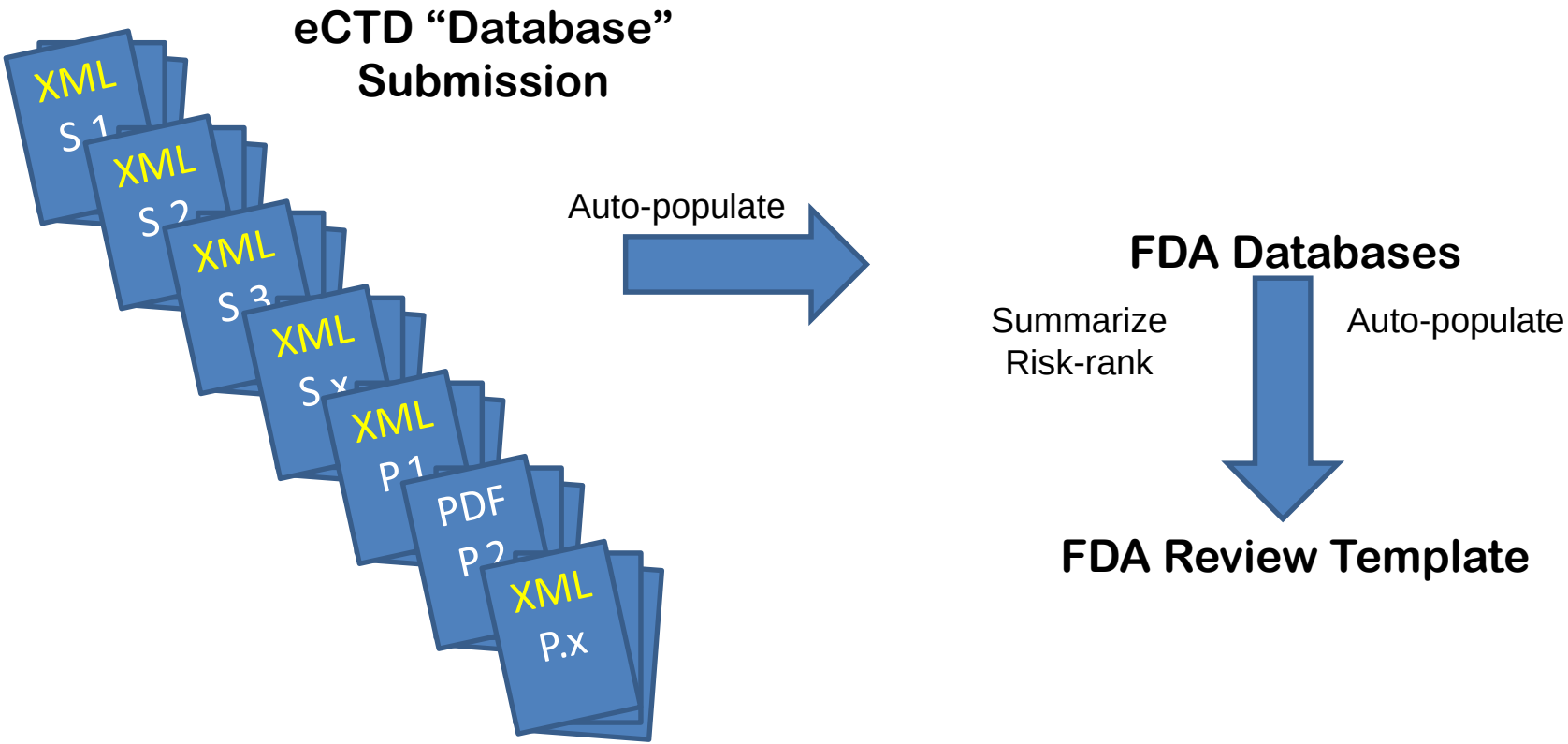
PQ/CMC Scope

- Submissions including supplements & amendments
  - Human drugs
    - IND
    - BLA
    - NDA
    - ANDA
    - MF/DMF
  - Veterinary drugs
    - INAD
    - JINAD
    - VMF
    - ANADA
    - NADA

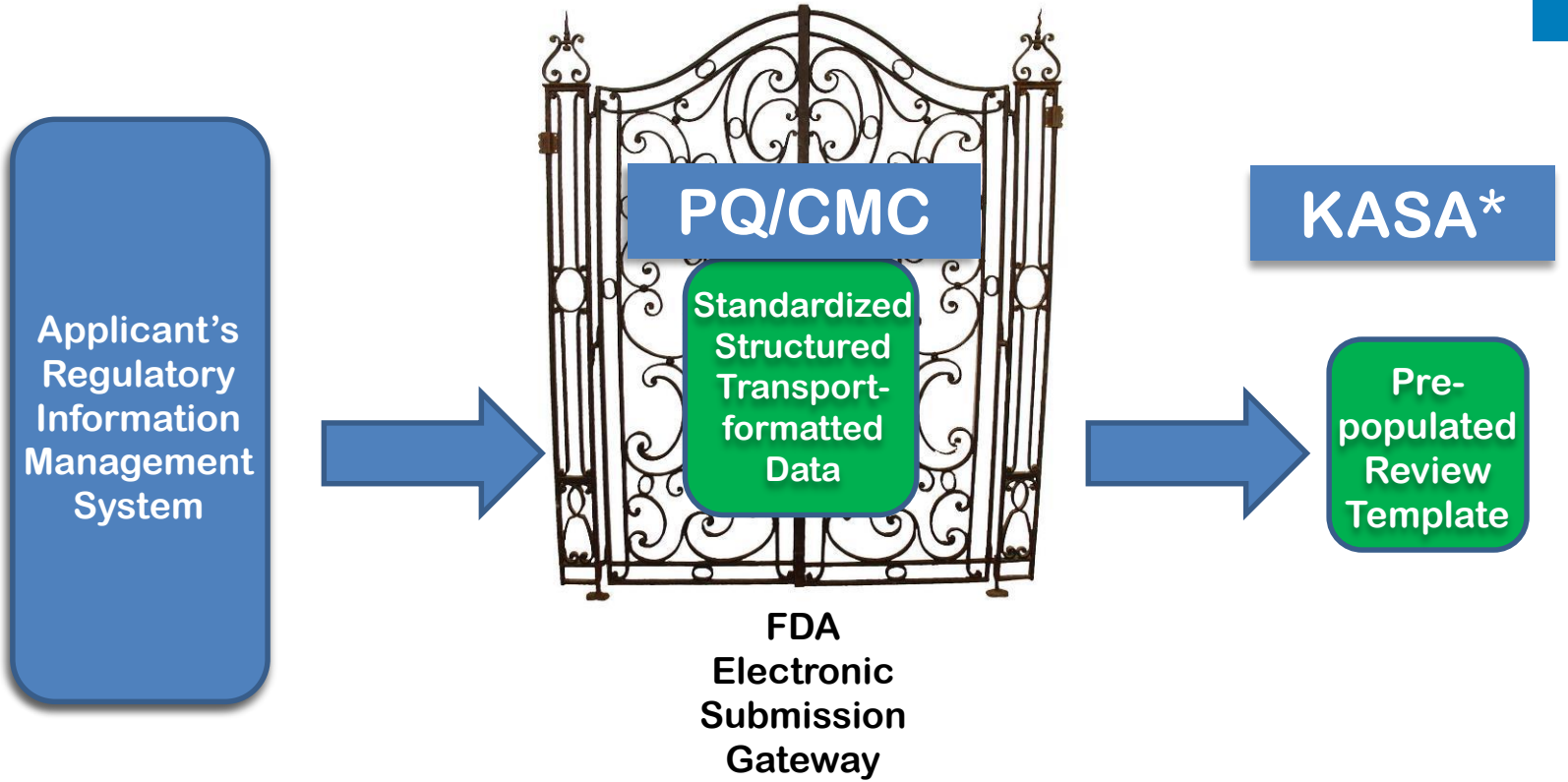
Current Module 3 Submission Model



Future Module 3 Submission Model

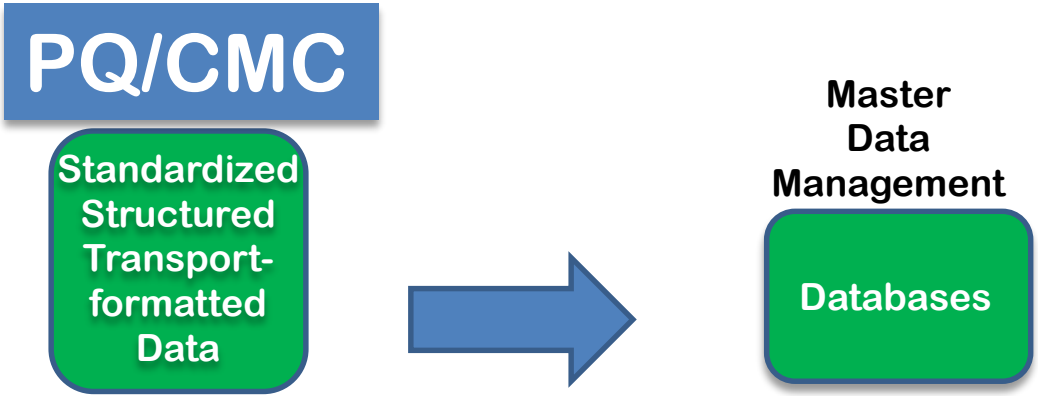


Future State: Information Flow



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

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

Potential Benefits to FDA

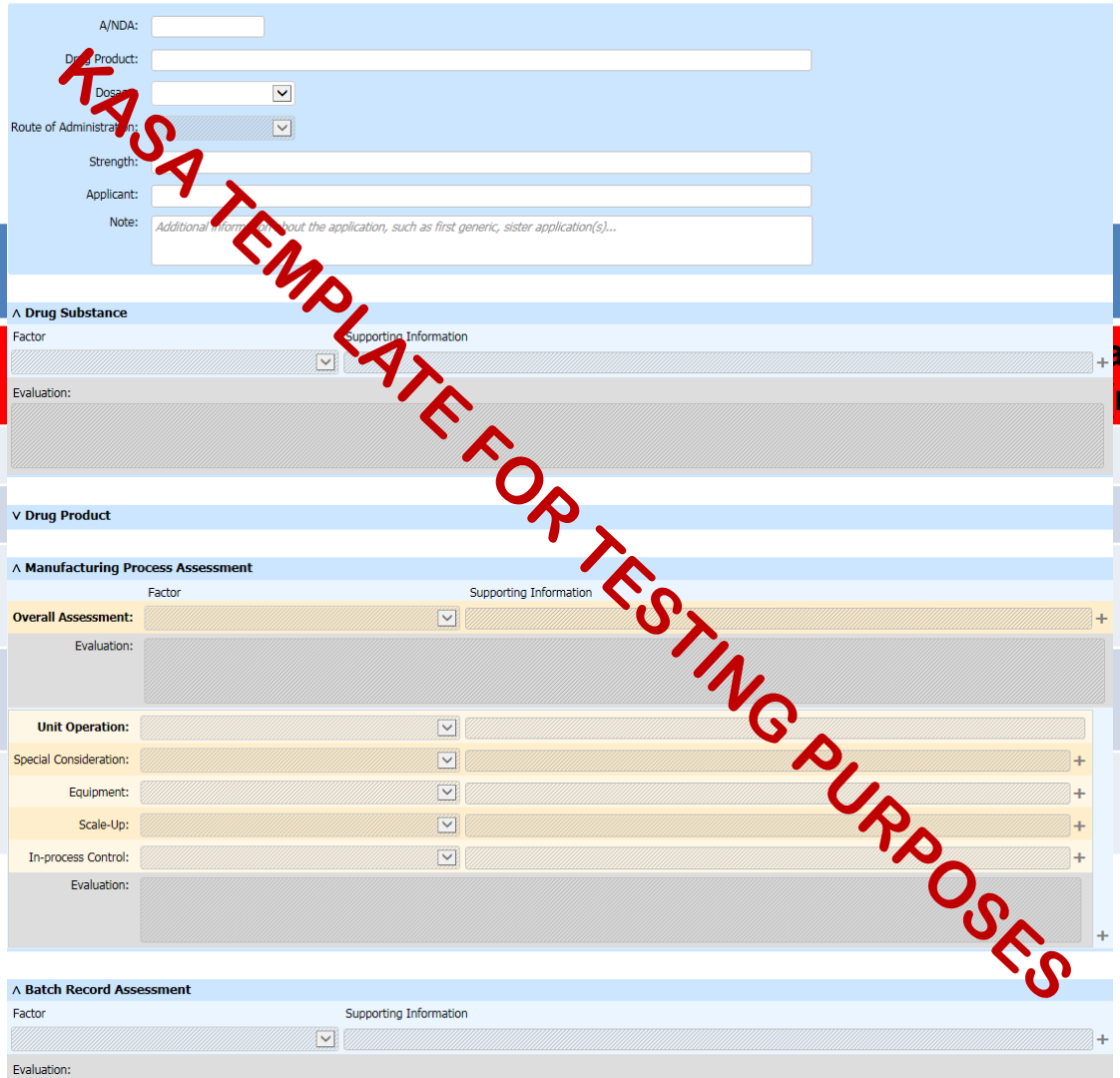
- Faster & better quality assessments
  - All applications have the same look and feel
  - Views can be customized
  - Links can be included to related data (e.g., specification for applicant's other dosage form with the same API)
  - Assessment templates can be prepopulated
  - Summary data can be pushed out in assessment templates, e.g.
    - Stability data
    - Drug product unit operations with Critical Process Parameters
- Improved crisis response
  - Database access to data, e.g.
    - Specification history
    - Current specification
    - Current expiry dating
    - Facility history

Potential Benefits to FDA

- **STABILITY SUMMARY**

Proposed Commercial	Strength	Container	Size	Closure	Count	Max time (mos)
No	50 mg	Glass	100 mL	Al screw cap	50	36
No	100 mg	Glass	250 mL	Al screw cap	50	42
Yes	50 mg	HDPE	100 mL	PP cap, LDPE seal	50	12
Yes	50 mg	HDPE	250 mL	PP cap, LDPE seal	100	12
Yes	100 mg	HDPE	250 mL	PP cap, LDPE seal	50	12

- Current expiry dating
- Facility history



KASA TEMPLATE FOR TESTING PURPOSES

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

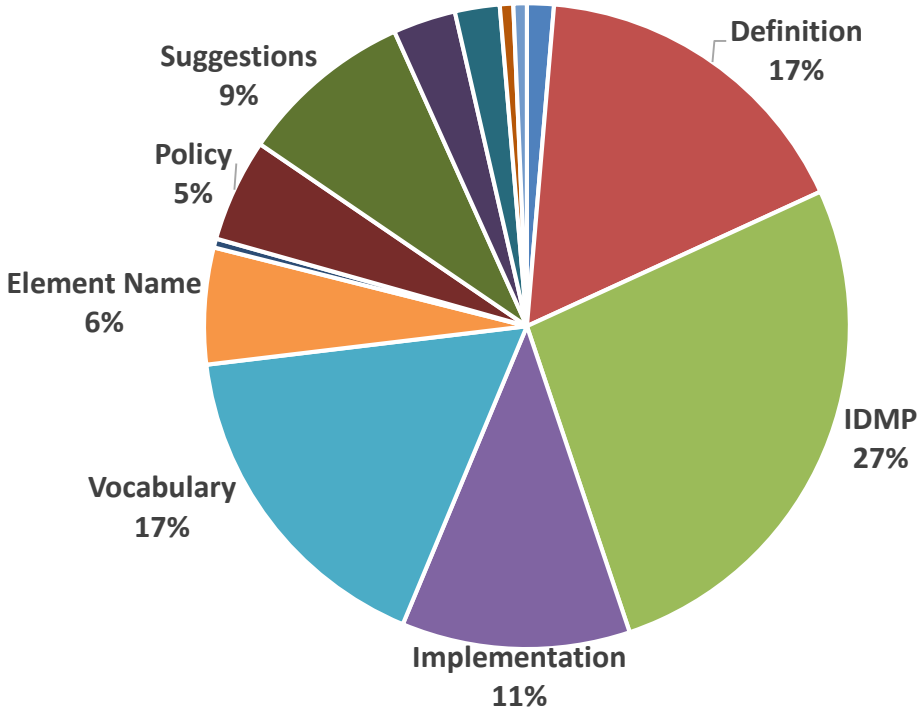
Progress to Date:
Some Details

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

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 IDMP standards
  - 11238 SSG* 4 specification use case differs from PQ/CMC
  - Not all terms are defined
  - Most controlled vocabulary code lists (CD) undefined
- PQ/CMC items not included in IDMP
  - Quality data for drug product,
    e.g. specification (may include test stages)
  - Quality data for excipients
  - Lifecycle model for specification
  - Batch Analysis Tables

*SSG – Specified Substance

PQ/CMC IDMP Challenges

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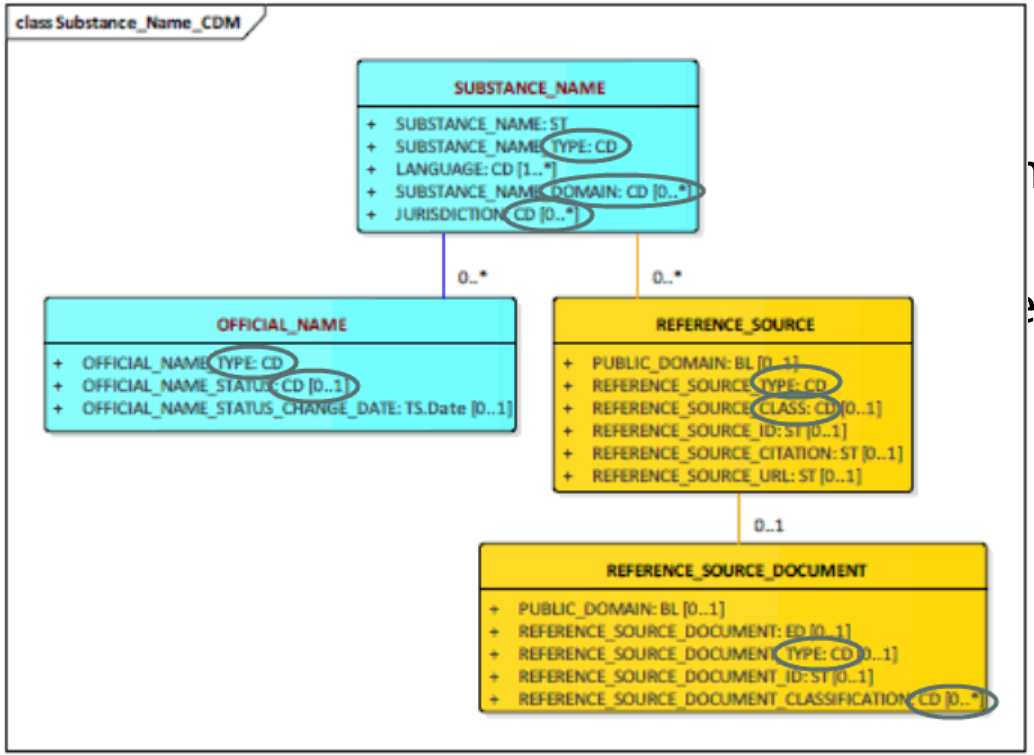
    e.
  - Q
  - Lif
  - Ba

n PQ/CMC

efined



*SSG – Specified Substance

IDMP Mapping

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

IDMP Mapping Summary (1 of 2)

#	PQ/CMC Table	ISO IDMP Mapping
1	Specification	ISO 11238 Specified Substance Group 4
2	Test	ISO 11238 Specified Substance Group 4
3	Acceptance Criteria	ISO 11238 Specified Substance Group 4
4	Batch Information	ISO 11615: PackagedMedicinalProduct, ManufacturedItem, …
5	Batch Analysis	Not Applicable
6	Stability Study	Not Applicable
7	Nomenclature & Structure of Drug Substance	ISO 11238: Substance, SubstanceName, SubstanceCode, Structure, StructuralRepresentation

Maps in concept, but different use case

IDMP Mapping Summary (2 of 2)

#	PQ/CMC Table	ISO IDMP Mapping
8	Drug Substance Characterization	ISO 11238: Substance, ReferenceSource, ReferenceSourceDocument
9	Drug Product Composition	ISO 11615: MedicinalProduct, MedicinalProductName, Ingredient
10	Batch Formula	Not Applicable
11	Drug Substance – Control of Materials	ISO 11238: Manufacturing Material, Source material, Organism, etc.
12	Drug Product – Control of Excipients	ISO 11238: Source material, Organism, etc.
13	Drug Substance Impurities	ISO 11238: Specified Substance Group 4, Impurity, Structural Representation
14	Drug Product Impurities	TBD

IDMP Docket Comment

- Batch or Lot numbers are often used interchangeably. Although synonymous, suggest some guidance be provided for the purpose of harmonization. For example, Lot is often used for bulk materials and Batch is often used for packaged products. Or define that Lot is normally used for drug substance and Batch is normally used for drug product…
- It is not clear how this element aligns with ISO 11615:2017 regarding Medicinal Products or ISO 11238:2017 regarding Substances. ISO 11615:2017 uses the term “Batch identifier” and the abbreviation “BAID”…
- Ensure alignment of PQ/CMC terms with ISO 11615:2017 or explain the mapping

IDMP Mapping Example: Batch (CFR)

- Batch means
  - a specific quantity of a drug or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture. [21 CFR § 210.3, CGMP]
  - a specific quantity or lot of a test or control article that has been characterized according to § 58.105(a). [21 CFR § 58.15, GLP]

IDMP Mapping Example: Lot (CFR)

- Lot means:
  - a batch, or a specific identified portion of a batch, having uniform character and quality within specified limits; or, in the case of a drug product produced by continuous process, it is a specific identified amount produced in a unit of time or quantity in a manner that assures its having uniform character and quality within specified limits. [21 CFR § 210.3]
  - that quantity of uniform material identified by the manufacturer as having been thoroughly mixed in a single vessel. [21 CFR § 600.3]

IDMP Mapping Example: Batch (IDMP)

- Batch
  - specific manufacturing release of a Medicinal Product or item by the manufacturer [11615, "…regulated medicinal ***product***]
  - [undefined in 11238, "…regulated information on ***substances***"]

3.1.7
batch
specific manufacturing release of a Medicinal Product or item by the manufacturer

3.1.8
batch number
identifier assigned to a specific batch of a Medicinal Product or item resulting from a manufacturing process at a specific point of time

Medicinal Product Batch Identifier (BAID)

- For each authorized Medicinal Product, a BAID_1 [2] shall [can] be assigned
- shall use the batch number … expiration date together with the PCID*
- shall use a common attribute set related to a packaged Medicinal Product, which when all of them have a value, define a specific BAID_1 [2] concept:
  a) PCID;
  b) batch number (outer [inner] packaging);
  c) expiration date (month/year) using the ISO 8601 date format.

*Packaged Medicinal Product Identifier (PCID)

Batch/Lot Conclusion

- GAP
- FDA term is a broader, more general term than the BAID, and would sit higher in a hierarchy. It is not restricted to Medicinal Product (packaged stuff), although it incorporates both BAID1 and BAID2. For an unboxed bottle or vial, it probably corresponds to BAID2 (immediate container); for a boxed container (bottle or vial) probably BAID1 (outer).
- PQ/CMC discriminates “bulk” from “packaged” and uses the term for uses other than Medicinal Product, e.g. API, other components

PQ/CMC Terminology Challenges

- Ambiguous/conflicting FDA definitions (e.g. active moiety)
- ISO Identification of Medicinal Product standards mapping
  - In IDMP standards
    - 11238 SSG 4 specification use case differs from PQ/CMC
    - Not all terms are defined
    - Most controlled vocabulary code lists (CD) undefined
  - PQ/CMC items not included in IDMP
    - Quality data for drug product, e.g. dp specification (may include test stages)
    - Quality data for excipients
    - Lifecycle model for specification
    - Batch Analysis Tables
    - Control of Excipients

Other Types of Changes Based on Public Comments

- Modified Definitions
- Updated Valid Values
- Changed Element Names
- Changed Data Types
- Added Examples
- Added New Data Elements
- Added Notes to the several Definitions
- Added Business Rules

Modified Definitions

- Example: Batch Information.Expiration Date
  - Old Definition: *The date placed on the container label of a drug product (and/or drug substance) designating the time prior to which a batch of the product is expected to remain within the approved shelf-life specification if stored under defined conditions, and after which it must not be used. [Source: Adapted from Q1A(R2)]*
  - New Definition: *The date the manufacturer guarantees the full potency and safety of a particular batch/lot of medicinal product. The complete point in time date consisting of day, month and year shall be specified using the ISO 8601 date format. [Source: ISO IDMP 11615-2017]*

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Data Element Name Change

- Few examples where the data element name was changed based on public comments:
  - Chemical Name -> Substance Name (IDMP)
  - Quality Benchmark -> Quality Standard
  - Amount -> Quantity
  - Source Organism Subsource -> Source Organism Part (IDMP)
  - Release Date -> Batch Analysis Release Date
  - Literal Text -> Original Text

New Data Elements

- Some new data elements were added based on public comments:
  - Drug Product Component Function Category
  - BatchFormula.QuantityPercent
  - Process Related Impurity Category
  - Product Related Impurity Category
  - Co-Packaged Indicator

Future Plans

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

FDA Presenter Panel

BREAK

(Turn in lunch order forms at Sodexo Counter)

Session 2. Industry Perspectives

Business Case for Structured Submissions

Charles Morgan,
Regulatory Group Director & IDMP-MDA PT Lead
Pharma Technical Regulatory,
Genentech Inc., A Member of the Roche Group
South San Francisco, CA, USA

Rodrigo Palacios,
Global Head for Business Systems,
Pharma Technical Regulatory,
F. Hoffman-La Roche Ltd
Basel, Switzerland

Agenda

1. Introduction
2. Current State
3. Future State
4. Use Cases and Benefits
5. The Path Forward
6. Examples
7. Conclusion

Disclaimer

The views and opinions presented here represent those of the speakers and should not be considered to represent formal guidance on behalf of Roche.

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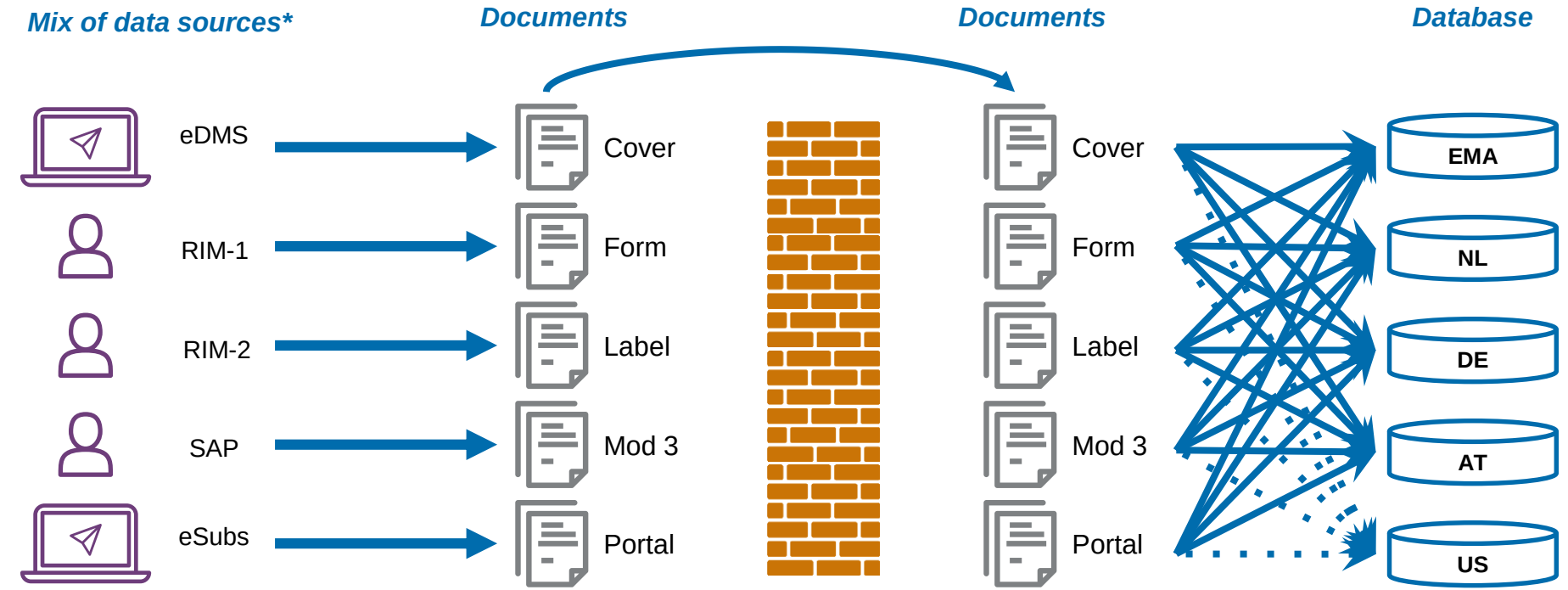
Introduction

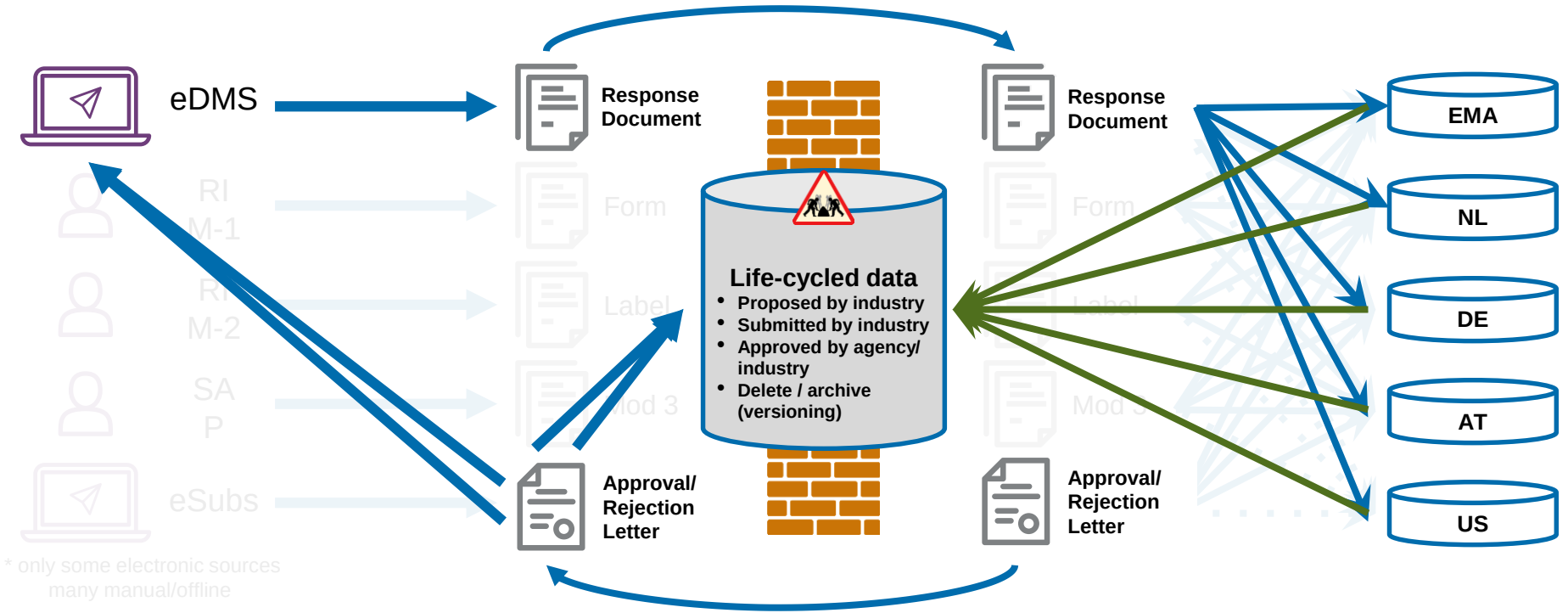
- Our global regulatory processes are highly complex and inefficient. Creation and review of dossier documents is highly manual, and regulatory data analytics are currently only available via additional submissions and high-effort transformations.
- Major gains in efficiency will be needed to sustainably meet the projected demands while at the same time resource constraints and patient access to drugs are both expected to increase in the future.
- Significant benefits can be derived by moving to an end to end, data-driven regulatory model. We need one model, based on common standards, utilized across the entire product lifecycle - from development, to manufacturing, to the patient.

Current State



* only some electronic sources
many manual/offline

Future State



Many Health Authorities are Moving to Receiving Data

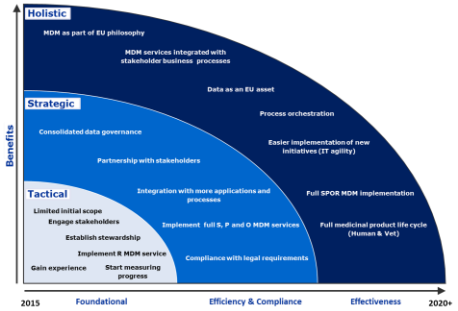
EMA: XEVMPD, IDMP, SPOR, CESSP, CTR

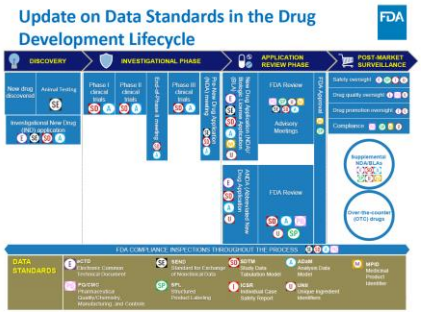
FDA: SPL, PQ/CMC, GSRS

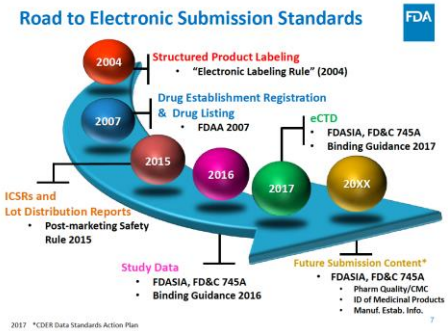
Others: Japan (PDMA)

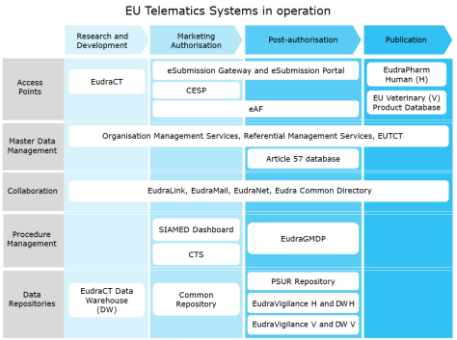
Next set of structured CMC data appears to be Manufacturers information:

- *EMA OMS implementation*
- *FDA draft guidance (2016) on MEI*









Benefits of Moving to Data-Based Submissions

Efficiency, Compliance & Speed

	Industry	Health Authorities	Patients
Efficiency	• Reduction in manual work and rework • Innovation focus versus administrative activities	• Increase efficiency of review • Resources scaled with medicinal value (e.g. get right therapies to market)	• Lower overhead in overall system, leading to lower cost
Compliance	• Increased ability to sustain compliance through changes and innovation • Less effort and higher confidence	• Improved oversight in quality and real world evidence impact, (recognition of issues impacting multiple products, indications, etc.)	• Safer medicines
Speed	• Faster to market • Improved revenue capture • Improved reputation	• Provide access to therapies sooner with improved oversight • Faster response to address shortages	• Faster access to medicines

Use Cases

Examples from EMA - why do we need standardization?

Standardised data will…

Pharmacovigilance	…improve signal detection and speed of response for authorized products, thus improving protection of public health in EU
ePrescription	…support cross-border electronic prescription of medicines in EU enabling patients to obtain right product(s) when outside their home country based on standardized data
Falsified Medicines	…support the mechanism for controlling authenticity of medicine
Shortages	…allow substances and products to be identified across countries enabling faster response to address shortages
Batch recalls	…allow substances and products to be identified across countries enabling faster response to address shortages
Inspections	…improve link between Supply Chain and regulatory dossier since inspectors will have better records available to support their findings in Manufacturing sites
Regulatory activities	…facilitate process efficiencies in regulatory activities e.g. submission of regulatory applications and variations

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Reference:

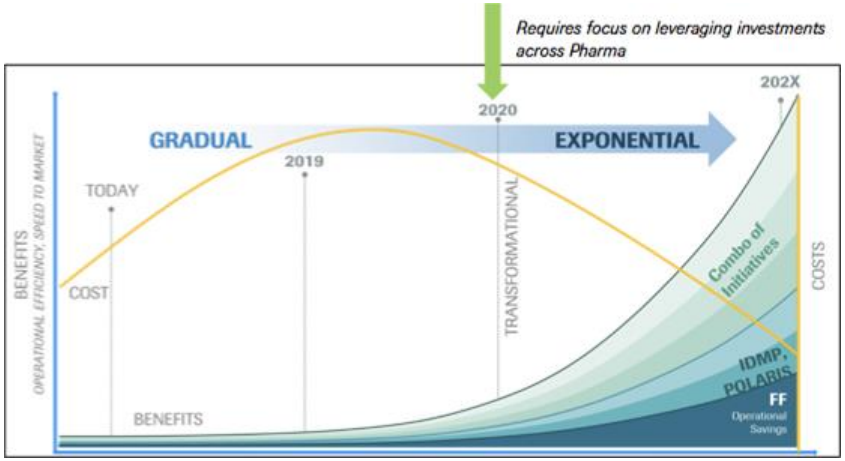
Implementation of ISO IDMP standards within the European Medicines Regulatory Network

EMA SPOR Roadmap, iterations and target operating model for medicinal products and substances

Paolo Alcini, Head of Data Standardisation and Analytics 09 November 2016

Value Drivers for Industry (Roche Example)

Key Value Drivers We are Pursuing



Transformational benefits are more likely with **a Pharma level initiative**. Additional work will be undertaken to build out ROI analysis

2x Productivity gains by Roche DIA (diagnostics) for labeling, post SCM adoption

Peers see **40-60% increased efficiency**

25% of time and cost of clinical study lost to document & compliance issues (industry average) – **what if we could change that?**

Faster to Entry in Human (EIH), Faster to Market

Sources: DIA interviews, Author-IT, Schema, IDC, DIA, Rockley Group

!

Risk of Doing Nothing

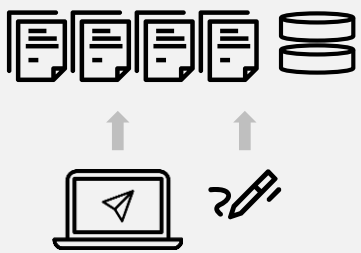
- **Misaligned content:** the same piece of content (e.g. ADR) is created using different processes and technologies, limiting reuse and increasing complexity
- **Increased cost:** Costs to produce and manage content continue to increase
- **Later to Market:** Recent IDC study found industry average of 25% of time and cost of clinical study is lost to document and compliance issues

The Path Forward

Proposal: Implement a Stepwise Approach to the Data-Centric Future

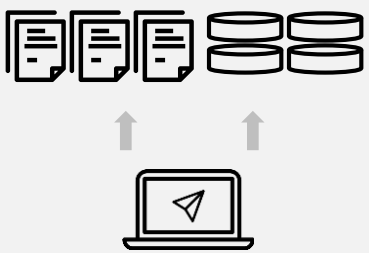
Guiding principle: Value must be realized at each step

Today



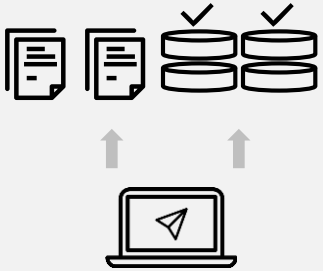
1 Additional Submission of Data

- Manually write unstructured documents (sections)
  e-paper submission (eCTD 3)
- Parallel integration of data from databases into a data feed for XEVMPD, SPL



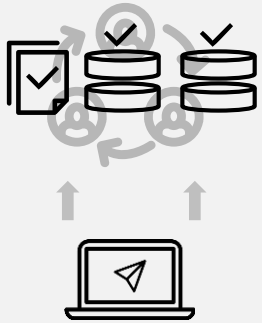
2 Automatic Generation of Submission Documents

- Instead of people, technology creates documents from data
- Removes manual activity for Sponsor / Industry
- Need to prepare information in tabular rather than narrative form



3 Reduce Submission of Documents (specific sections or subm. types)

- Reduce number of documents that are sent to HA
- HA starts to analyze the database content instead of reviewing documents



4 Data-Centric Regulatory

- Only submit narratives for justifications and conclusions
- Opportunity to share across HA's (enable interoperability)

Getting Started

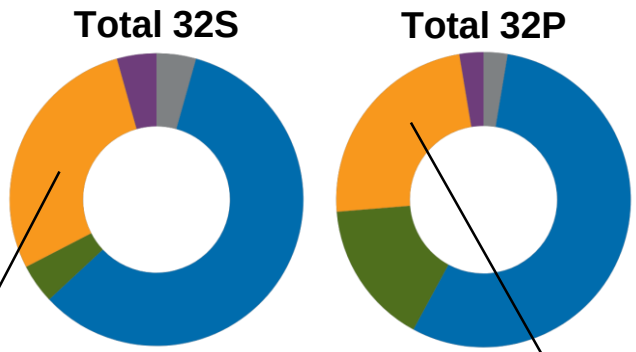
Estimated Distribution - Component vs. Tabular vs. Narrative

Potential ideas:

- Lay the foundation - e.g. implement Data Standards & Controlled Vocabularies/List of Values (CV/LOV)
- Establish uniform data standards used across all products (content can vary per product & per regulations) leading to structured content management (re-use and automation)
- Focus on Structured Submissions: regulators and industry switch a subset of M3 sections to structured form. CMC information is shared across modules/label.

32S (as received)	
S.6	
Component	
S.2.2	S.4.2
S.2.4	S.4.3
S.2.5	S.4.5
S.2.6	S.7.1
S.3.2	S.7.2
Narrative	
S.3.1	
Tabular	
S.1.1	S.2.2
S.1.2	S.2.3
S.1.3	S.4.4
S.2.1	S.7.3
Tabular + Component	
S.5	

Also consider cover letter, application form label, PACMP, 32A tables and 32R PACMP, Process validation package etc.



M3 transformation section by section

32P (as received)	
P.7	
Component	
P.2.0	P.4.5
P.2.1	P.4.6
P.2.2	P.5.2
P.2.4	P.5.3
P.2.5	P.5.5
P.2.6	P.5.6
P.3.3	P.6
P.4.2	P.8.1
P.4.3	P.8.2
P.4.4	P.9
Narrative	
P.2.2	P.2.6
P.2.3	P.3.3
P.2.4	P.3.4
P.2.5	P.3.5
Tabular	
P.1	P.4.1
P.3.1	P.5.1
P.3.2	P.6
P.3.3	P.8.3
Tabular + Component	
P.5.4	

Example:
Tabular over Narrative

Example: Narrative vs. Table

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 blister, 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

Tabular 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

Implementation Risks and Barriers

Risks & Barriers	Potential Solution
Workforce capabilities within regulators & industry Change resistance/ adherence to status quo	Training & Governance; address leadership and culture shifts needed
Status of technology, status of data	Pilot and proof of concept (POC)
Divergent standards and local variants across HAs	Confirm mechanisms to drive harmonization across HAs
Multiple implementation projects: IDMP, PQ/CMC, SPOR, FMD	Aligned strategies and data standards
Duplication - submitting both documents and structured data means the gains are lost	Confirm mechanisms to drive harmonization across HAs

Conclusion

Significant benefits can be derived by moving to an end to end, data-driven regulatory model.

We need one model, based on common standards,
utilized across the entire product lifecycle - from development, to manufacturing,
to the patient.

We can start now… **and we have to**

Acknowledgements

Hans van Bruggen	eCTDconsultancy
Lorrie Dixon	Roche

Doing now what patients need next

LUNCH

Session 2. Industry Perspectives (continued)

PQ/CMC Standardized Data Approaches and the Impact on Global Harmonization

October 19, 2018

Presenters

Andy Chu

Director, Global Safety & Regulatory Sciences

Regulatory Systems Strategy – Regulatory Quality & Operations

Biogen

John Groskoph

Executive Director New Products CMC

Global Chemistry Manufacturing & Controls

Pfizer

PQ/CMC Standardization Initiative

- Operational Model of PQ/CMC
- Identification of Medicinal Products
- KASA Review Initiative
- Harmonization Activities

Operational Model of PQ/CMC

Opportunities

- CDER / CBER Data Standards Action Plan
- Streamlining submission of structured product information
- Quality across product lifecycle
- Improved communication and information sharing within FDA
- Consistent definitions and integrated data structure

Challenges / Questions

- Overarching strategic plan and roadmap
- Duplication of effort for sponsors and Agency
- Impact to current submission practices
- Fixed definitions and data elements
- FHIR

Identification of Medicinal Products

- Understanding of how PQ/CMC initiative connects to the Agency's overall plan for all structured product information initiatives
- Ensuring that all appropriate audiences at the Agency have access to the data to prevent any duplication of efforts for both sponsors and Agency staff (e.g., entering data into a single repository such as the Global Substance Registry System)
- Mapping of substance information between GSRS and PQ/CMC
- Addressing potential increase in controlled vocabularies

KASA Review Initiative

Opportunities

- Structured collection of data
- Product lifecycle
- Facilitates risk assessment
- Streamlining of text-based narratives

Challenges / Questions

- Alignment / Connection with PQ/CMC and other data standardization initiatives
- Information flow between eCTD and KASA
- Timeline for expansion to NDAs and BLAs
- Alignment of data standards with other ICH regions

Harmonization Activities

Opportunities

- Value of eCTD standard
- CDER / CBER Data Standards Program Action Plan
- Mutual Reliance on ICH Partners
- Alignment of submission vs inspectional data elements

Challenges / Questions

- Region-specific content placement and terminologies
- Supported versions of eCTD should support all requested data elements and terminologies
- Impact on ICH Q12
- Alignment with Established Conditions
- Potential expansion of NDA data requirements vs ICH

Plasma Protein Therapeutics Association

PPTA Presentation at Public Meeting: Standardized Data for Pharmaceutical Quality/Chemistry Manufacturing and Control

Christopher Leonienco, Emergent BioSolutions
Speaking on behalf of PPTA
October 19, 2019

Agenda

- Who is PPTA
- Review of Critical Comments
  - Comment
  - Proposed Solution
- Closing thoughts

PPTA
Plasma Protein Therapeutics Association

WHAT IS PPTA

A trade and standards-setting organization representing private sector plasma collectors and producers of plasma-based and recombinant biological therapeutics. PPTA members:

- Provide more than 80% of the world's Source Plasma for fractionation
- Provide the majority of the world's life-saving plasma protein therapies
- PPTA and its members take an active role in the areas of pathogen safety, health policy, patient advocacy, awareness and standards setting

North America Members

- Bio Products Laboratory
- CSL Behring
- Emergent BioSolutions
- Grifols, Inc
- Kedrion SpA
- Shire

PPTA Comments

- **FDA issued draft Guidance in Federal Register Notice/ Vol.82, No. 11/ July 11, 2017**

- **PPTA submitted comments on September 11, 2017**

Comment # 1

- FDA should clarify a system in which sponsors/license holders can add new data elements and/or acronyms/terms when developing submissions in the instance they have a product or need that has not been contemplated before and that those issues can be addressed in a timely manner

Proposed Solution

- *Data Standards must be able to accommodate innovative and unique technology and products*
  - *Phased approach focusing on easily defined processes from synthetic products initially and then moving to complex substances and products*
  - *Can a solution be taken from what we learn from the implementation of SPL, focusing on one core product (Content of Labeling) and then broadening the scope as the impact of the change becomes evident*

Comment # 2

- FDA should clarify how sponsors/license holders can address existing CTDs that do not necessarily reflect FDA's current proposal

https://stock.adobe.com

Proposed Solution

- A transition plan to update existing applications should be created and include a mapping type document to align existing metadata and application lifecycling

Comment # 3 & 4

- The FDA should define the requirements vs. recommendations for each Data Element

- In the implementation plan for this Controlled Vocabulary, FDA should ensure flexibility in their use

Proposed Solution

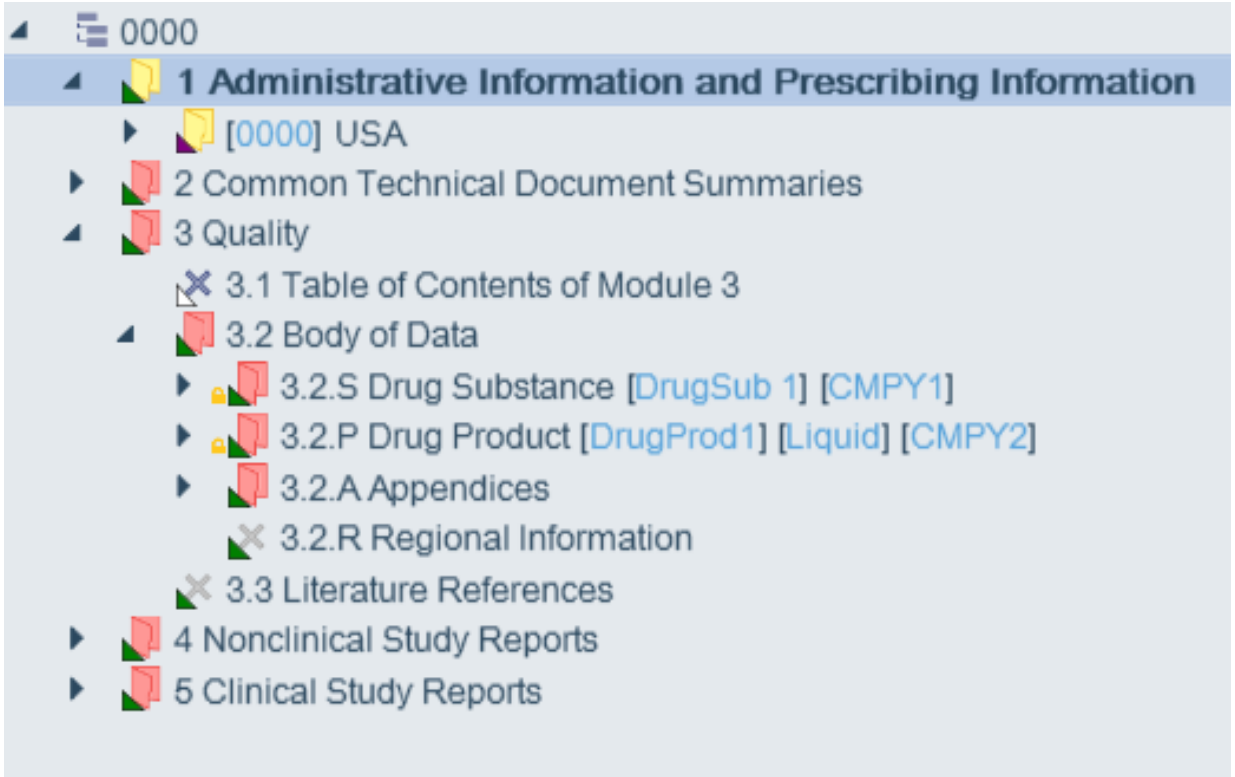
- Key data elements should be identified as part of the initial implementation of the guidance and provide a timeline for full compliance

Comment # 5

- FDA must provide an implementation plan in order to ensure that Controlled Vocabularies do not create validation conflicts with existing metadata

Proposed Solution

- For industry:
  - education and training needs to be conducted in-house in order to understand how changes will affect existing content
  - an application by application transition plan should be established in order to implement new data standards


0000
1 Administrative Information and Prescribing Information
[0000] USA
2 Common Technical Document Summaries
3 Quality
3.1 Table of Contents of Module 3
3.2 Body of Data
3.2.S Drug Substance [DrugSub 1] [CMPY1]
3.2.P Drug Product [DrugProd1] [Liquid] [CMPY2]
3.2.A Appendices
3.2.R Regional Information
3.3 Literature References
4 Nonclinical Study Reports
5 Clinical Study Reports

Comment # 6

- The FDA should harmonize the Data Elements and Controlled Vocabulary with other jurisdictions, in particular ICH and the IDMP initiative

Proposed Solution

- Consideration should be given to the concept that components of applications may be used in another jurisdiction.
- Alignment should be sought with other initiatives such as IDMP in order to ensure that data and content can be shared across regions

Comment # 7

- In general, it is noted that the terminologies proposed are more commonly used terms and aligned with small molecule pharmaceuticals
- FDA should confirm that biologics and products approved via unique mechanisms (e.g. Animal Rule products) should be captured

Proposed Solution

- FDA should create a Pilot project consisting of Industry members and software vendors in order to ensure that the implementation of data standards is well understood

Closing Thoughts

- Phased approach
- Continued collaboration with Industry and software vendors
- Education within FDA and Industry

PPTA
Plasma Protein Therapeutics Association

Thank you

Industry Presenter Panel

OPEN PUBLIC COMMENT

Closing Remarks

- **Thank you for attending today's PQ/CMC Public Meeting!**
- Submit electronic comments to https://www.regulations.gov/
- All comments should be identified with the Docket Number FDA-2018-N-2608

Comments are due by November 16, 2018

- Website for all meeting materials and recording

Send questions to the PQ/CMC mailbox: PQ-CMC@fda.hhs.gov