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
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

Sponsor/Applicant

eCTD
Module 1
Module 2
Module 3
Module 4
Module 5

Gateway
Extract
Efficacy
Quality
Safety
Validate

F D A

? G-SRS

Repository

PANOR MA
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
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

- **Dec. 2018**
  - Industry participation for FHIR proof-of-concept (Subset of PQ/CMC - Phased approach)
  - Assess feasibility of FHIR

- **Feb. 2019**
  - • End-to-end system test using FHIR
  - • Continue data exchange development
  - • Develop draft guidance

- **~ Mar. 2020**
  - DRAFT Guidance (For all of PQ/CMC)
Longer Term

• This project covers 1/3\textsuperscript{rd} 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
Future Module 3 Submission Model

eCTD “Database” Submission

Auto-populate

FDA Databases
Summarize Risk-rank
Auto-populate

FDA Review Template

XML S1
XML S2
XML S3
XML S4
XML P1
PDF P2
XML P.X
Future State: Information Flow

Applicant’s Regulatory Information Management System

PQ/CMC

Standardized Structured Transport-formatted Data

FDA Electronic Submission Gateway

KASA*

Pre-populated Review Template

* “Knowledge-Aided Assessment and Structured Application” Pharmaceutical Advisory Committee, September 20, 2018
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.

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
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### STABILITY SUMMARY

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<th>Proposed Commercial</th>
<th>Strength</th>
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<th>Size</th>
<th>Closure</th>
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<td>HDPE</td>
<td>250 mL</td>
<td>PP cap, LDPE seal</td>
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<th>Proposed Commercial Strength</th>
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<th>Count</th>
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</table>
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
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*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
<table>
<thead>
<tr>
<th>#</th>
<th>PQ/CMC Table</th>
<th>ISO IDMP Mapping</th>
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<tr>
<td>1</td>
<td>Specification</td>
<td>ISO 11238 Specified Substance Group 4</td>
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<tr>
<td>2</td>
<td>Test</td>
<td>ISO 11238 Specified Substance Group 4</td>
</tr>
<tr>
<td>3</td>
<td>Acceptance Criteria</td>
<td>ISO 11238 Specified Substance Group 4</td>
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<tr>
<td>4</td>
<td>Batch Information</td>
<td>ISO 11615: PackagedMedicinalProduct, ManufacturedItem, ...</td>
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<tr>
<td>5</td>
<td>Batch Analysis</td>
<td>Not Applicable</td>
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<tr>
<td>6</td>
<td>Stability Study</td>
<td>Not Applicable</td>
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<tr>
<td>7</td>
<td>Nomenclature &amp; Structure of Drug Substance</td>
<td>ISO 11238: Substance, SubstanceName, SubstanceCode, Structure, StructuralRepresentation</td>
</tr>
<tr>
<td>#</td>
<td>PQ/CMC Table</td>
<td>ISO IDMP Mapping</td>
</tr>
<tr>
<td>----</td>
<td>-----------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>9</td>
<td>Drug Product Composition</td>
<td>ISO 11615: MedicinalProduct, MedicinalProductName, Ingredient</td>
</tr>
<tr>
<td>10</td>
<td>Batch Formula</td>
<td>Not Applicable</td>
</tr>
<tr>
<td>11</td>
<td>Drug Substance – Control of Materials</td>
<td>ISO 11238: Manufacturing Material, Source material, Organism, etc.</td>
</tr>
<tr>
<td>12</td>
<td>Drug Product – Control of Excipients</td>
<td>ISO 11238: Source material, Organism, etc.</td>
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<tr>
<td>13</td>
<td>Drug Substance Impurities</td>
<td>ISO 11238: Specified Substance Group 4, Impurity, Structural Representation</td>
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<tr>
<td>14</td>
<td>Drug Product Impurities</td>
<td>TBD</td>
</tr>
</tbody>
</table>
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
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]
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
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

Mix of data sources

Documents

eDMS
RIM-1
RIM-2
SAP
eSubs

Documents

Database

EMA
NL
DE
AT
US

* only some electronic sources
many manual/offline
Future State

Life-cycled data
- Proposed by industry
- Submitted by industry
- Approved by agency/industry
- Delete / archive (versioning)

Approval/Rejection Letter

Response Document

eDMS

EMA

NL

DE

AT

US

* only some electronic sources
many manual/offline
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*

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

**Examples from EMA - why do we need standardization?**

<table>
<thead>
<tr>
<th>Use Case</th>
<th>Benefit</th>
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| 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 |

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

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

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

- 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

Risk of Doing Nothing

10/11/18
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)**

<table>
<thead>
<tr>
<th>Component</th>
<th>Narrative</th>
<th>Tabular</th>
<th>Tabular + Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.6</td>
<td>S.3.1</td>
<td>S.1.1</td>
<td>S.5</td>
</tr>
<tr>
<td>S.2.2</td>
<td>S.2.4</td>
<td>S.1.2</td>
<td></td>
</tr>
<tr>
<td>S.2.5</td>
<td>S.2.6</td>
<td>S.1.3</td>
<td></td>
</tr>
<tr>
<td>S.3.2</td>
<td>S.7.1</td>
<td>S.2.1</td>
<td></td>
</tr>
<tr>
<td>S.4.2</td>
<td>S.7.2</td>
<td>S.5.1</td>
<td></td>
</tr>
<tr>
<td>S.4.3</td>
<td></td>
<td>S.5.2</td>
<td></td>
</tr>
<tr>
<td>S.4.5</td>
<td></td>
<td>S.5.3</td>
<td></td>
</tr>
<tr>
<td>S.7.1</td>
<td></td>
<td>S.5.4</td>
<td></td>
</tr>
<tr>
<td>S.7.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.7.3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Total 32S**

- As Received
- Component
- Narrative
- Tabular
- Tabular + Component

**M3 transformation section by section**

**32P (as received)**

<table>
<thead>
<tr>
<th>Component</th>
<th>Narrative</th>
<th>Tabular</th>
<th>Tabular + Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>P.7</td>
<td>P.2.2</td>
<td>P.1</td>
<td>P.5.4</td>
</tr>
<tr>
<td>P.4.5</td>
<td>P.4.6</td>
<td>P.4.1</td>
<td></td>
</tr>
<tr>
<td>P.5.2</td>
<td>P.5.3</td>
<td>P.5.1</td>
<td></td>
</tr>
<tr>
<td>P.5.5</td>
<td>P.5.6</td>
<td>P.6</td>
<td></td>
</tr>
<tr>
<td>P.5.9</td>
<td>P.8.1</td>
<td>P.8.2</td>
<td></td>
</tr>
<tr>
<td>P.8.3</td>
<td>P.8.4</td>
<td>P.9</td>
<td></td>
</tr>
<tr>
<td>P.2.0</td>
<td>P.2.1</td>
<td>P.2.2</td>
<td></td>
</tr>
<tr>
<td>P.2.2</td>
<td>P.2.3</td>
<td>P.2.4</td>
<td></td>
</tr>
<tr>
<td>P.2.5</td>
<td>P.2.6</td>
<td>P.3.3</td>
<td></td>
</tr>
<tr>
<td>P.4.5</td>
<td>P.4.6</td>
<td>P.4.7</td>
<td></td>
</tr>
<tr>
<td>P.5.2</td>
<td>P.5.3</td>
<td>P.5.4</td>
<td></td>
</tr>
<tr>
<td>P.5.5</td>
<td>P.5.6</td>
<td>P.5.7</td>
<td></td>
</tr>
</tbody>
</table>

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

**Tabular views**

<table>
<thead>
<tr>
<th><strong>32P1 English</strong></th>
<th><strong>32P1 Dutch</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product name:</strong></td>
<td><strong>ProduQt</strong></td>
</tr>
<tr>
<td><strong>Manufactured dose form:</strong></td>
<td><strong>film-coated tablet</strong></td>
</tr>
<tr>
<td><strong>Strength:</strong></td>
<td><strong>50 mg</strong></td>
</tr>
<tr>
<td><strong>Active substance:</strong></td>
<td><strong>Qdrug</strong></td>
</tr>
<tr>
<td><strong>ID number:</strong></td>
<td><strong>Number-123</strong></td>
</tr>
<tr>
<td><strong>Colour:</strong></td>
<td><strong>blue</strong></td>
</tr>
<tr>
<td><strong>Shape:</strong></td>
<td><strong>oval</strong></td>
</tr>
<tr>
<td><strong>Primary container type:</strong></td>
<td><strong>alu/pvc blister</strong></td>
</tr>
<tr>
<td><strong>Quantity in primary container:</strong></td>
<td><strong>10</strong></td>
</tr>
<tr>
<td><strong>Seconardary container type:</strong></td>
<td><strong>carton box</strong></td>
</tr>
<tr>
<td><strong>Quantity in seconardary container:</strong></td>
<td><strong>one or more</strong></td>
</tr>
</tbody>
</table>

**Translations**

| **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**

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**

<table>
<thead>
<tr>
<th>32P1 concentrate for solution for injection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product name:</strong> ProQuit</td>
</tr>
<tr>
<td><strong>Manufactured dose form:</strong> concentrate for solution for injection</td>
</tr>
<tr>
<td><strong>Concentration:</strong> 5 mg/mL</td>
</tr>
<tr>
<td><strong>Administrable dose form:</strong> solution for injection</td>
</tr>
<tr>
<td><strong>Strength/Concentration:</strong> 500 mcg/mL</td>
</tr>
<tr>
<td><strong>Active substance:</strong> Qdrug</td>
</tr>
<tr>
<td><strong>Colour:</strong> colourless (clear)</td>
</tr>
<tr>
<td><strong>ID number:</strong> Number-456</td>
</tr>
<tr>
<td><strong>Primary container type:</strong> glass vial</td>
</tr>
<tr>
<td><strong>Quantity in primary container:</strong> 3 mL</td>
</tr>
<tr>
<td><strong>Minimum extractable volume:</strong> 2 mL</td>
</tr>
<tr>
<td><strong>Secondary container type:</strong> carton box</td>
</tr>
<tr>
<td><strong>Quantity in secondary cont.:</strong> 1</td>
</tr>
</tbody>
</table>

Roche/eCTDconsultancy  
CMC from document to data
## Implementation Risks and Barriers

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

<table>
<thead>
<tr>
<th>Opportunities</th>
<th>Challenges / Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CDER / CBER Data Standards Action Plan</td>
<td>• Overarching strategic plan and roadmap</td>
</tr>
<tr>
<td>• Streamlining submission of structured product information</td>
<td>• Duplication of effort for sponsors and Agency</td>
</tr>
<tr>
<td>• Quality across product lifecycle</td>
<td>• Impact to current submission practices</td>
</tr>
<tr>
<td>• Improved communication and information sharing within FDA</td>
<td>• Fixed definitions and data elements</td>
</tr>
<tr>
<td>• Consistent definitions and integrated data structure</td>
<td>• FHIR</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Opportunities</th>
<th>Challenges / Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Structured collection of data</td>
<td>• Alignment / Connection with PQ/CMC and other data standardization initiatives</td>
</tr>
<tr>
<td>• Product lifecycle</td>
<td>• Information flow between eCTD and KASA</td>
</tr>
<tr>
<td>• Facilitates risk assessment</td>
<td>• Timeline for expansion to NDAs and BLAs</td>
</tr>
<tr>
<td>• Streamlining of text-based narratives</td>
<td>• Alignment of data standards with other ICH regions</td>
</tr>
<tr>
<td>Opportunities</td>
<td>Challenges / Questions</td>
</tr>
<tr>
<td>------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>• Value of eCTD standard</td>
<td>• Region-specific content placement and terminologies</td>
</tr>
<tr>
<td>• CDER / CBER Data Standards Program Action Plan</td>
<td>• Supported versions of eCTD should support all requested data elements and terminologies</td>
</tr>
<tr>
<td>• Mutual Reliance on ICH Partners</td>
<td>• Impact on ICH Q12</td>
</tr>
<tr>
<td>• Alignment of submission vs inspectional data elements</td>
<td>• Alignment with Established Conditions</td>
</tr>
<tr>
<td></td>
<td>• Potential expansion of NDA data requirements vs ICH</td>
</tr>
</tbody>
</table>
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
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
• 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
• FDA should clarify how sponsors/license holders can address existing CTDs that do not necessarily reflect FDA’s current proposal
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
• 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
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
• 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
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
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