Standardization of Pharmaceutical Quality Chemical Manufacturing and Controls (PQ/CMC): What is it? Where are things now? How can you learn more?

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FDA Generic Drugs Forum 2023 – April 13, 2023

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- This presentation should not be considered guidance, nor a change in guidance, nor does it necessarily reflect FDA's positions.

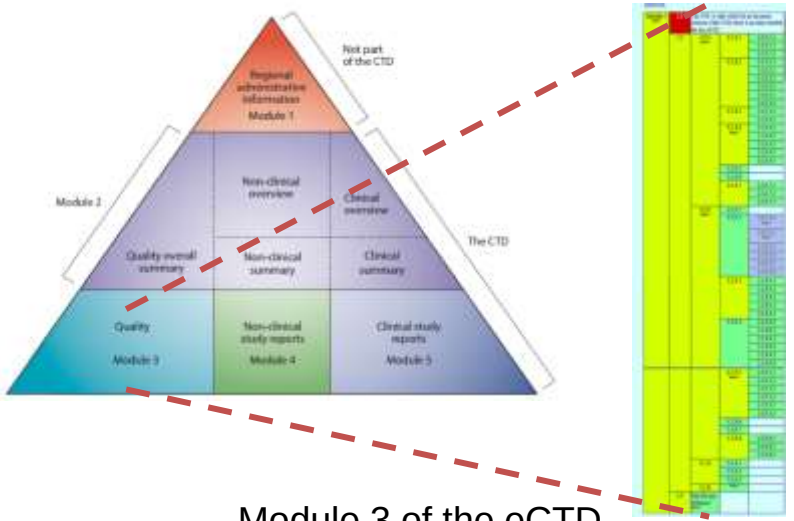
Learning Objectives

After this talk, you should be able to:

- ***Explain the problems PQ/CMC program intends to solve and how***
- ***Identify the Goals, Objectives, and Scope of PQ/CMC***
- ***Describe the process used to develop the PQ/CMC data standard***
- ***Understand stakeholder outreach taken by PQ/CMC***
- ***Discuss current and future work***
- ***Recognize where you can find out more***

Why is PQ/CMC needed?

Electronic Common Technical Document - eCTD



Module 3 of the eCTD

Module 3 Information arrives as “electronic paper”

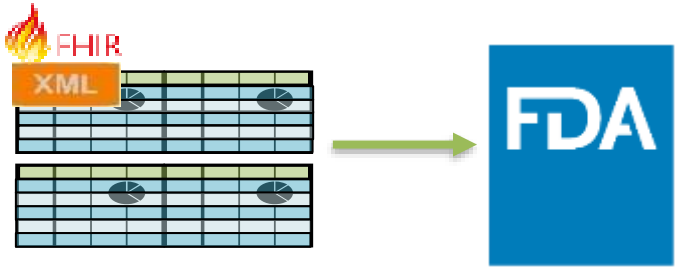
- Unstructured
- Non-standardized
- Manual work to create
- Manual transcription to analyze
- ***Time-consuming***

Information about Product Quality and Manufacturing and Controls (PQ/CMC)

What is the solution offered by PQ/CMC

Develop a data standard that supports PQ/CMC information that is:

- Consistent in format
- Uses consistent values
- Computable and ready for analysis



Sponsor Benefits:

- Clear format expectations
- Can pre-check content and quality before submission

FDA Benefit:

- Consistent format and values received
- Software-powered analysis, much faster review
- Can check for valid content and data quality on receipt

All Benefit:

- Sponsor submits information *one time*, FDA can use for *many purposes*

What are the core activities of the PQ/CMC Program?

Two overarching goals:

- Determine how to structure Module 3 information
- Work with HL7 to make this an **implementable data exchange standard**
  - Developed using HL7 FHIR (Fast Healthcare Interoperability Resources) Data Standard

What is the scope of the PQ/CMC Program?

- Module 3 (and 2.3) information that is amenable to structuring
- FDA Center coverage:
  - CDER (Drug); CBER (Biologics), CVM (Veterinary)
  - Application types: All; Dosage Forms: All

Phases of PQ/CMC standard development: Phase 1

Phase 1

- Specification
- Batch Information
- Batch Analysis
- Stability Study
- Stability Analysis
- Nomenclature of Drug Substance
- Composition of Drug Product
- Batch Formula
- Drug Substance – Control of Materials
- Drug Product – Control of Excipients
- Drug Substance Impurities
- Drug Product Impurities

Foundational concepts:

- Comprehensive definition of every drug product and every substance within a product
- Quality control tests and acceptance criteria for Products, Substances, Excipients and Raw materials
- Formulas for making batches of the drug product including multi-component products such as capsules
- Results of quality testing, stability, and analysis on batches of products and Active Pharmaceutical Ingredients (APIs)
- Details on packaging/containers

Phases of PQ/CMC standard development: Phase 2

Phase 2

Manufacturing Process, Products:
- Solid Orals
- Liquids
- Blood Products
- Vaccines
- Cell/Gene Therapy
- Sterile Product
- Combinations Products
- Transdermal
- Implants

Drug Substance Manufacturing Process, Substances:
- Small molecules
- Biologics

Annual Lot Distribution Report

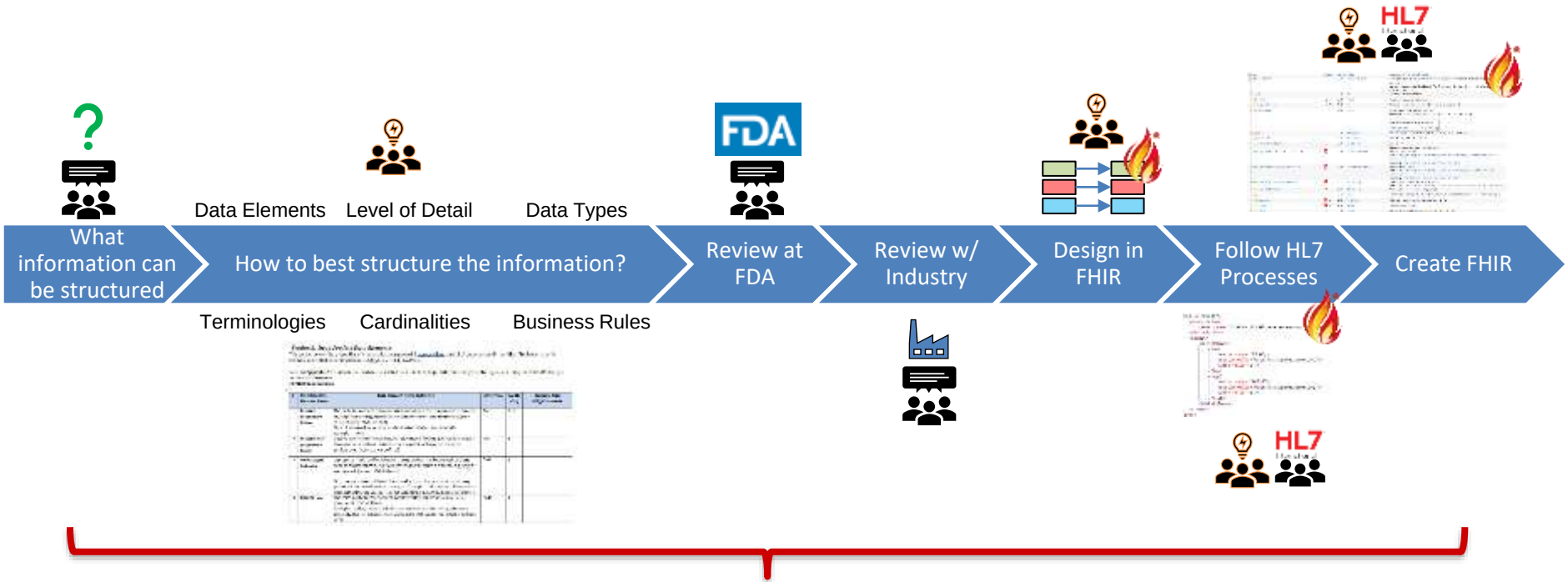
CMC Changes in Annual Report

Description of manufacturing processes for drug substances and drug products.

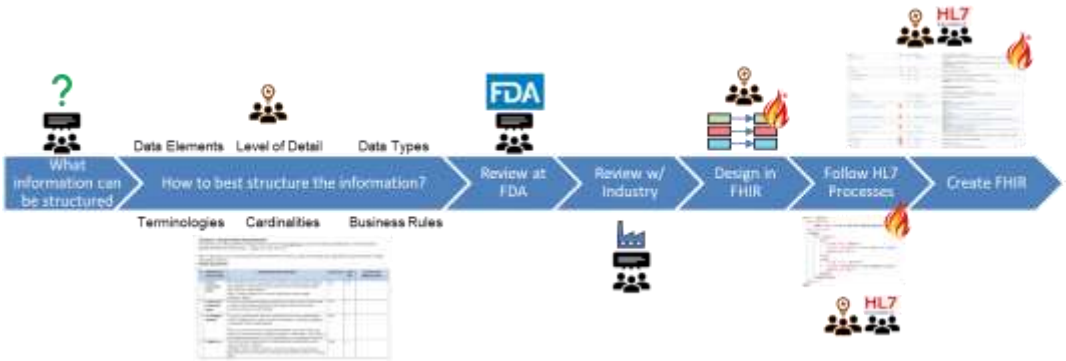
How a manufacturer:

- puts everything together to create the products
- Every step, every mechanism, machine, process, etc.
- What steps takes place at which facility, of which there are many for one product

Creating a data standard takes time but doing it right is worth the work



Culmination of work results in the Implementation Guide



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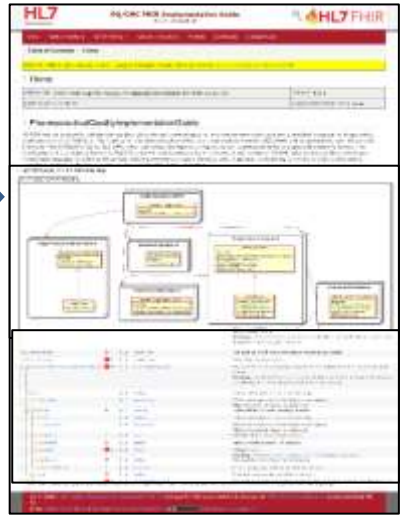
Hundreds of data elements and dozens of terminologies

PQ/CMC FHIR Implementation Guide



Why use HL7 FHIR?

- Consensus-based standard for public use
- Maximum flexibility to represent data needs exactly
- Much built-in support for PQ/CMC Pharmaceutical Definitions and concepts
  - Propelled at HL7 by FDA PQ/CMC team, EMA, and HealthCanada participants
- Harmonizes with other FHIR development in the same space: i.e., EMA SPOR work on IDMP

Public / Industry outreach is critical to getting this right

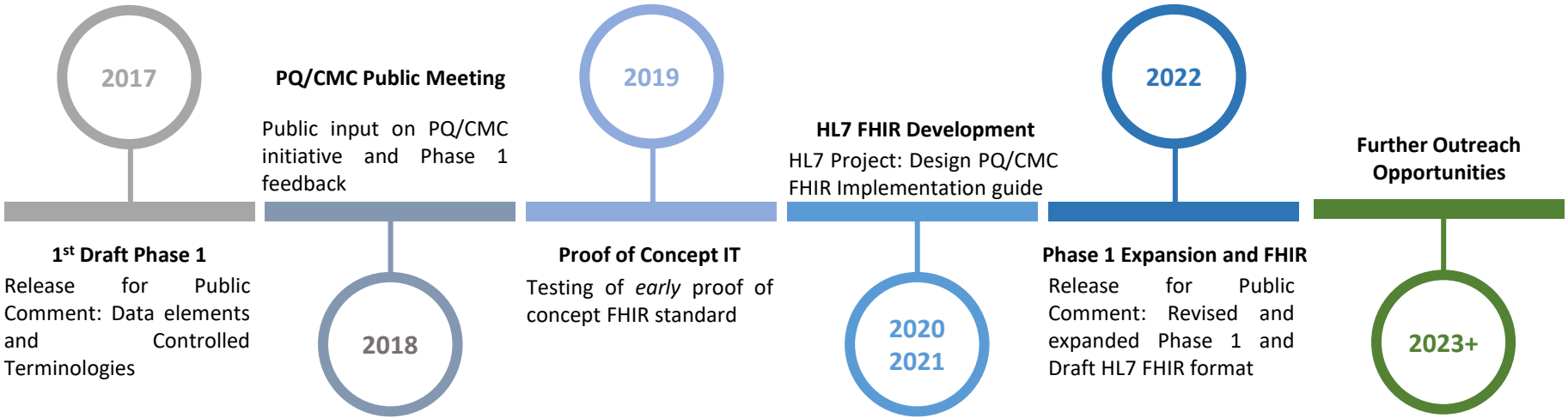
Updates where relevant

Public comments

Draft data structures → Review at FDA → Review w/ Industry

Federal Register Notices asking for Comment

Public / Industry outreach is ongoing



Where are we now?

- Phase 1 structuring complete
- Phase 2 structuring underway
- Early Draft HL7 Implementation Guide with Phase 1 information is in development
  - Current draft IG ***informational only*** as part of HL7 PQ/CMC project
    - Note: ***not*** final - nor binding - ***in any way*** (again, informational only)
  - Revisions and additions expected as Phase 2 structuring, after public comment, gets represented as FHIR

Where are we heading?

- Completion of Phase 2 structuring
- Decisions on “staging” (what parts of PQ/CMC to implement and when)
- We anticipate future rounds of Industry-participation pilot testing
- Continue outreach efforts and capture public comments to ensure pertinent stakeholder input are reflected in the PQCMC standard

How can you learn more?

- PQ/CMC Project Page at FDA.gov
- Continued releases of more structured parts of PQ /CMC for public comment
- PQ/CMC FHIR project page at HL7
  - Biomedical Research and Regulatory (BR&R) workgroup
- Contact us: PQ-CMC@fda.hhs.gov

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Thank You!