Accumulus Synergy: FHIR Overview for the CMC data

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The Vision for Data Exchange

To achieve our mission, we will focus on delivering a cloud platform that aims to allow for exchange of structured data in alignment with changing regulatory needs.

The platform plans to allow customers the ability to:

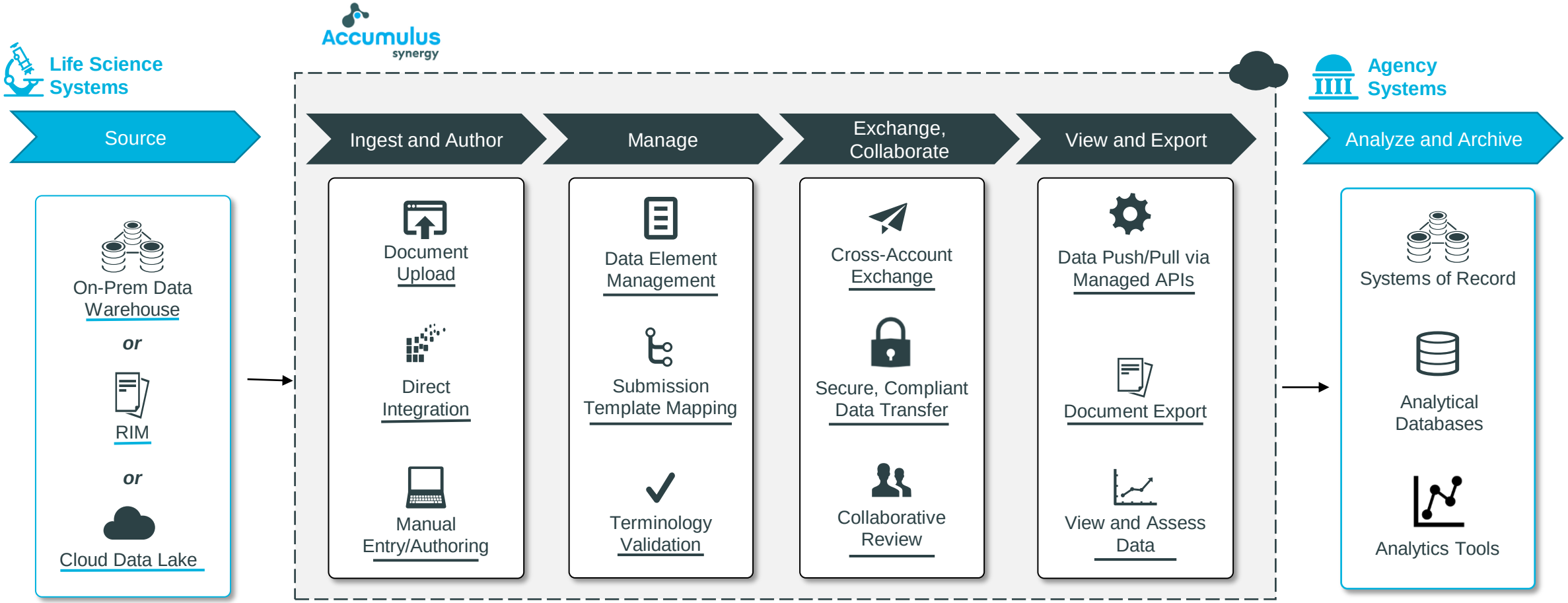
- **Store validated regulatory data in a common format**
- **Automatically map terminology across jurisdictions**
- **Construct templated filings from common data**
- **Exchange structured filings with global regulators**
- **Flexibly import/export data through key integrations**

Cross-Functional Application and Scalability

CMC | **Clinical** | **Pre-clinical** | **Safety**

Accumulus Synergy Platform Capabilities

Accumulus Synergy aims to provide a managed platform for life science organizations and regulators to securely exchange and collaborate on structured regulatory information



Leveraging the Accumulus Platform, DataX Application and Structured CMC Content Model Aims to Enable Future State Interoperability

Present State

Based on stability results available to date, a shelf life of XX months is proposed for drug product stored at the recommended storage condition of X°C to X°C (referred to as X°C). The secondary packaging effectively protects the drug product vial from light exposure.

1. Lot Information

Two presentations were manufactured for clinical development and will be used for commercial production: XXX mg (XX mL) and XXX mg (XX mL) single-use vials containing XX mg/mL AMG XXX. The 2 presentations are considered to be equivalent, differing only in fill volume and container size. The results from the XXX mg and XXX mg drug product presentations were combined to support product shelf life, and at least 1 lot from each presentation was assessed for all evaluations.

A summary of the drug product lots in the stability program is provided in Table 1. The drug product stability program consists of 14 lots stored at the recommended storage condition of X°C. The overall program includes supporting, primary, and production lots. Comparability has been demonstrated between clinical and commercial sites (3.2.P.2.3, Product Comparability). All lots in the stability program were used to establish the proposed shelf life.

Transition State

Core Data Element	Sub-Element 1	Definition (Source)	PQ/CMC?	Data Type
Drug Product Identification				
Product Names & Identifiers				
Product Name		Name as authorised by a Medicines Regulatory Agency Note 1 to entry: This may be either an invented name, not liable to be confused with the common name, or a common or a scientific name accompanied by a trade mark or any other applicable descriptor (ISO IDMP 11615)	N	Text
	Product proprietary name	The exclusive name of a drug substance or drug product owned by a company under trademark law regardless of registration status with the Patent and Trademark Office (PQ/CMC & FDA SOPP 8426)	Y	Text
		A name unprotected by trademark rights that is entirely in the public domain. It may be used without restriction by the public at large, both lay and professional (PQ/CMC 2021)	Y	Text
Strength StrengthNumericNumerator, StrengthNumericDenominator		The content of an active ingredient expressed quantitatively per dosage unit, per unit of volume, or per unit of weight, according to the pharmaceutical dosage form. This should be the strength as listed on the label (PQ/CMC, adapted from NCI EVS C53294) — The quantity of the substance contained in a Manufactured Item or Pharmaceutical Product. The strength (quantitative composition) shall be provided based on a	Y	Numeric

Accumulus Synergy Planned Future State

Create New Stability Study – Drug Product *(P.8.1, P.8.3)*

Drug Product Information Add Row

Product Proprietary Name	Product Non-Proprietary Name	Strength	Strength UOM
	AMG XXX	XXX	MG

"Data sourced from "Product" Content Block; linked to S.1.1, P.1" Edit

Batch/Lot Information Add Row

Batch/Lot Number	Batch Size	Batch Size UOM	Batch Utilization	Manufacturing Site	Manufacturing Date
	500	KG	Stability	ATO	05/04/2022

"Data sourced from "Batch/Lot Information" Content Block; linked to P.5.4" Edit

Container Closure System

Primary Packaging Component Add Row

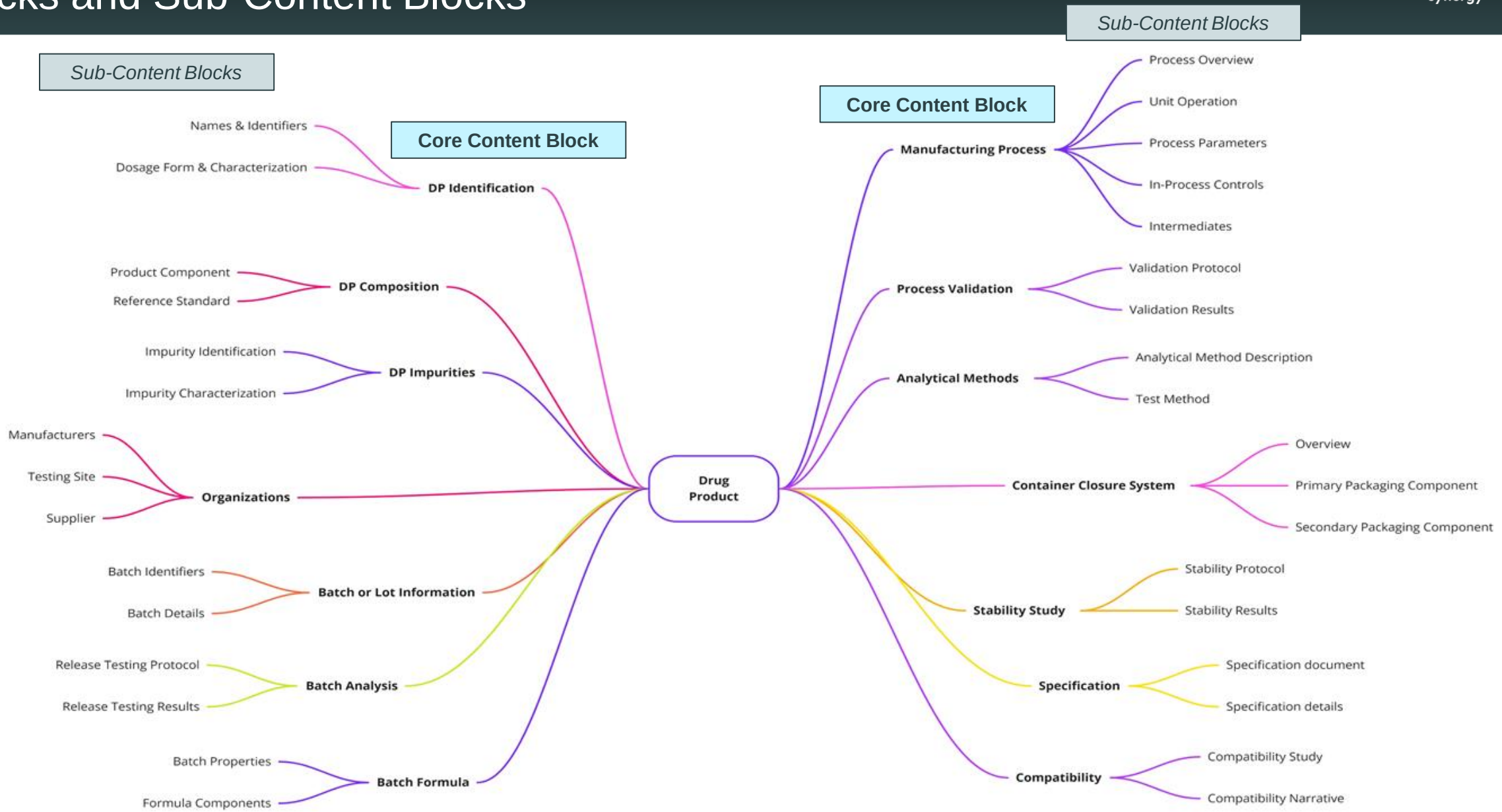
Container Closure System Description	Container Type	Container Size	Container Size UOM	Container Fill	Container Fill Unit	Closure Type
Amber, opaque, single-use glass vial	Vial	5	mL	2	mL	Child-resistant, metal

Secondary Packaging Component Add Row

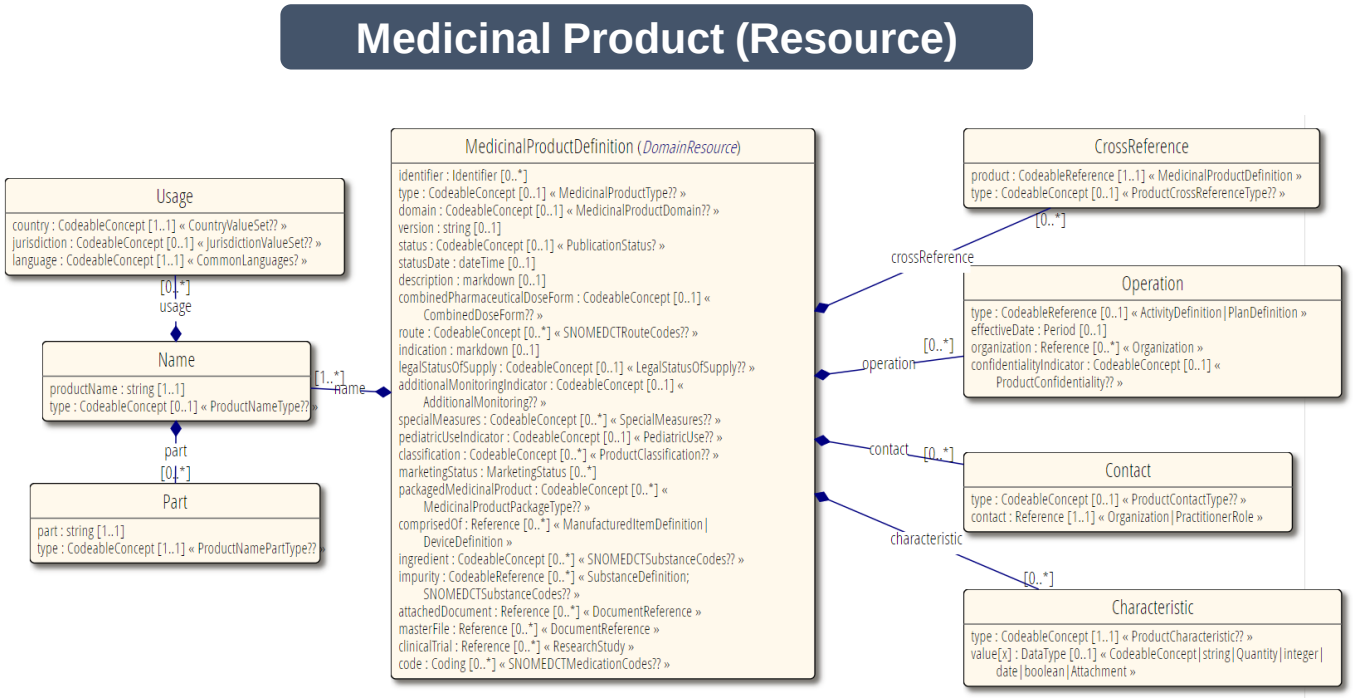
Container Closure System Description	Container Type	Container Size	Container Size UOM	Container Fill	Container Fill Unit	Closure Type
Aluminum canister, protects from light	Canister	10	mL	5	mL	Roll-on, metal

Accumulus Synergy's Module 3 Content Model aims to establish a data model and information architecture to support the transition from the present state to the future state.

The CMC Content Model Organizes CMC Information Into Core Content Blocks and Sub-Content Blocks



FHIR as an Enabler for Structured Data



http://hl7.org/fhir/index.html

- **FHIR – Fast Healthcare Interoperability Resources**
- Healthcare data exchange standard with accompanying application program interface (API)
- Accepted formats include XML, JSON, HTTP, REST, UML
- Capability to manage structured and semi-structured data, as well as file attachments
- Compatible with external controlled terminology lists for codable elements
- Standardized templates with customization options

FHIR is increasingly being adopted to support Regulatory Affairs activities to enhance data interoperability, searchability, accessibility, and standardization

FHIR-Based Structured Data Transformation

Current State

3.2.P.7 Container Closure System

The drug product tablets are packed in white, high density polyethylene (HDPE) plastic bottles, or in blister packs with aluminum lidding.

Each bottle is capped with a white, child-resistant closure containing a pulp liner and aluminum foil induction seal

Tablets are also packaged as unit-dose in a base film consisting of rigid blister film laminated to a barrier film. A configuration scheme of the tablets is presented in Table 1.

Table 1: Configuration Scheme

Strength	Package Type	Supplier	Count
45 mg	white, high density polyethylene (HDPE) plastic bottles with child-resistant closure containing a pulp liner and alumnium foil induction seal	Container Co. of America (all components)	28 tablets
	Unit-dose blister strips consisting of a rigid blister film laminated to a barrier film; the package contains 2 blister strips of fourteen tablets	Foil – Reynolds Wrap USA Film - Plastics of America	28 tablets
350 mg	white, high density polyethylene (HDPE) plastic bottles with child-resistant closure containing a pulp liner and alumnium foil induction seal	Container Co. of America (all components)	28 tablets
	Unit-dose blister strips consisting of a rigid blister film laminated to a barrier film; the package contains 2 blister strips of fourteen tablets	Foil – Reynolds Wrap USA Film - Plastics of America	28 tablets

Proposed Future State

Package : *Section 10 - Container Closure System*
Description: Any textual comments that describe the sum of container closure system (CCS) components that together contain and protect the dosage form or drug substance.

Packaging
Type: Box
Material: Cardboard
Shelf Life: 2 a

DRAFT

Manufacturer
Organization : *Section 4.1 - Manufacturer*
Identifier: 3008816891
Name: A+ Secure Packaging, LLC
Address: 339 Mason Rd, La Vergne, Tennessee, 37086, USA

Property
Type: Functional
Value: false

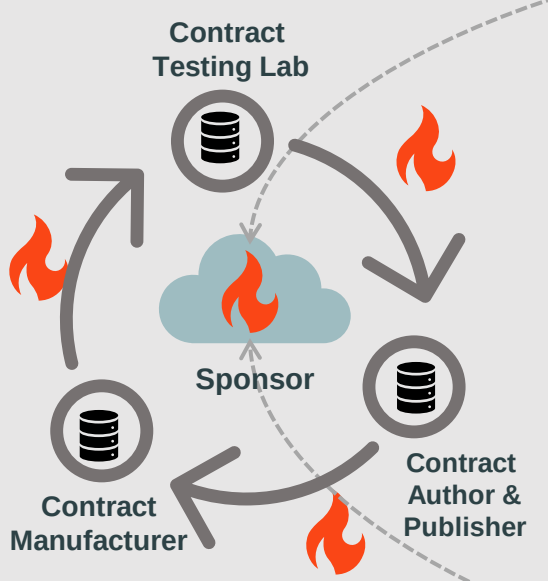
Property
Type: Quality Standard
Value: USP

Packaging (part)
Type: Tape
Material: Plastic

Manufacturer
Organization : *Section 4.1 - Manufacturer*
Identifier: 3008816891
Name: A+ Secure Packaging, LLC
Address: 339 Mason Rd, La Vergne, Tennessee, 37086, USA

Future Vision – Application of CMC Standards

Life Sciences Organization Workflow



DX-PQ Standard

Workflow Function:
Aims to foster intra- and inter-connectivity between internal sponsor systems and vendor systems; Constructs FHIR messages based upon existing/emerging international standards

Accumulus synergy

Facilitates and drives cloud-based information exchange

PQ/CMC*
**HL7-supported Project*

Other related initiatives:
ISO IDMP/ SPOR
ICH SPQS

Health Authority Workflow

Systems of Record

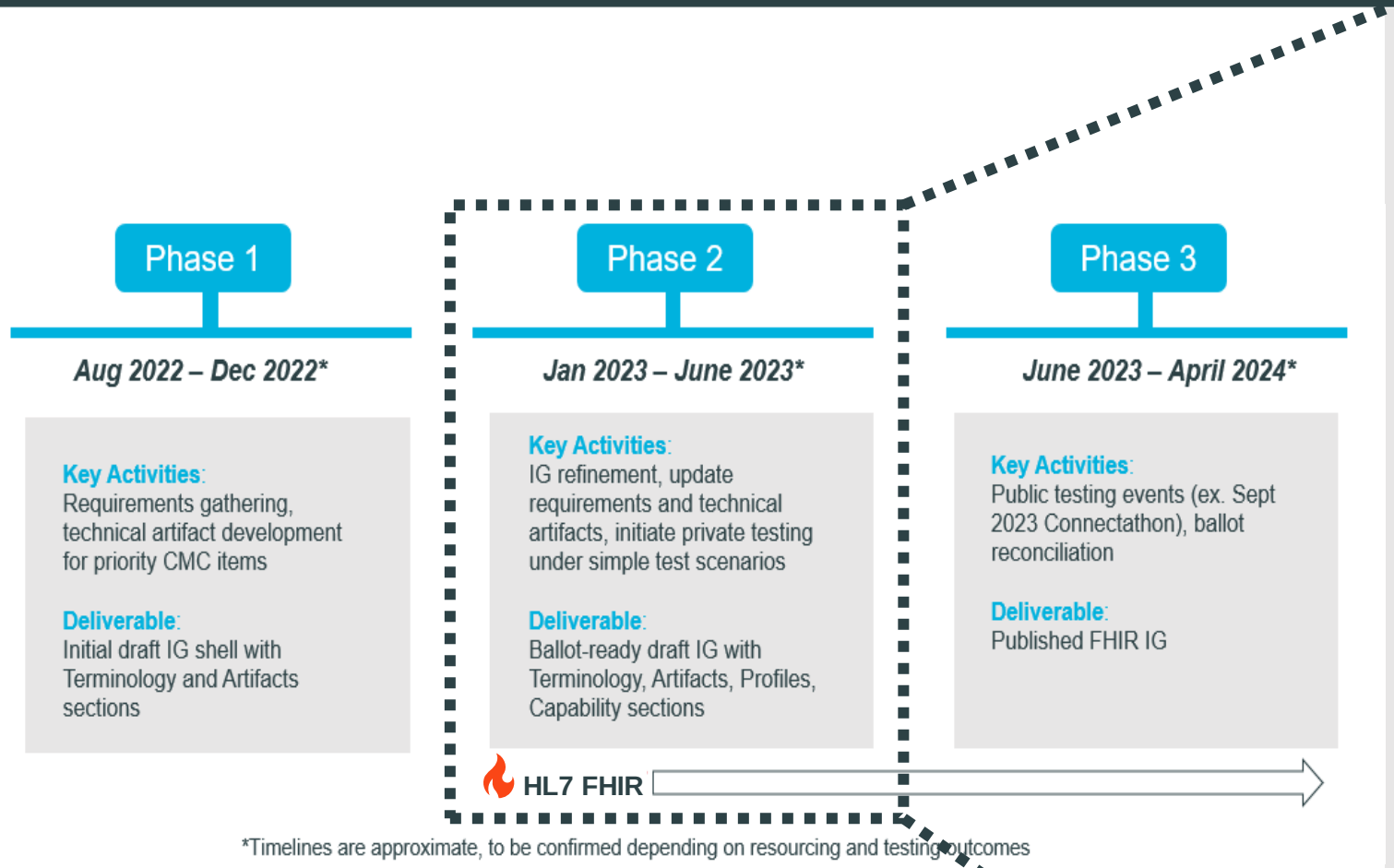
Analytical Databases

Export & Download

Workflow Function:
Aims to enable exchange of standardized regulatory information between sponsor and health authority

ILLUSTRATIVE

Project Timeline and Activities



Anticipated Testing Schedule

- **April 2023 – Private Testing Event 1**
  - **Scope**: Stability, Specification, Batch Analyses, DS/DP Identifiers
- **July 2023 – Private Testing Event 2**
  - **Scope**: Manufacturing Process, Analytical Procedures, Process Validation, Container Closure System
- **Sept. 2023 – Public Testing Event: HL7 FHIR Connectathon**
  - **Scope**: Full IG

- Linked here is an early draft version of the Pharmaceutical Quality Data Exchange IG

Potential for Collaboration Between Accumulus and Allotrope Foundation

- **DX-PQ Data Standard Development**
  - Ensure DX-PQ alignment with Allotrope Data Format and Data Models
  - DX-PQ standard is open for public contribution
- **DX-PQ Controlled Vocabulary Lists**
  - Examine content areas of overlap and leverage any relevant Allotrope products (Ontologies, Taxonomies) where applicable

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