# Revolutionizing Regulatory Submissions Through Digital Innovation

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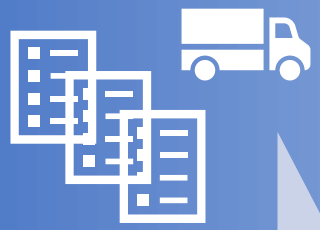
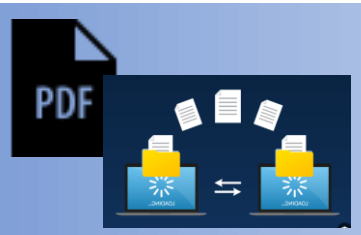
**EU CASSS CMC Strategy Forum**
**22 October 2025**

# Regulatory Submissions: Then, Now and Next



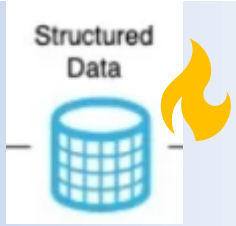
1990

Paper submissions




2000

E-paper submissions




2024

Standards & templates

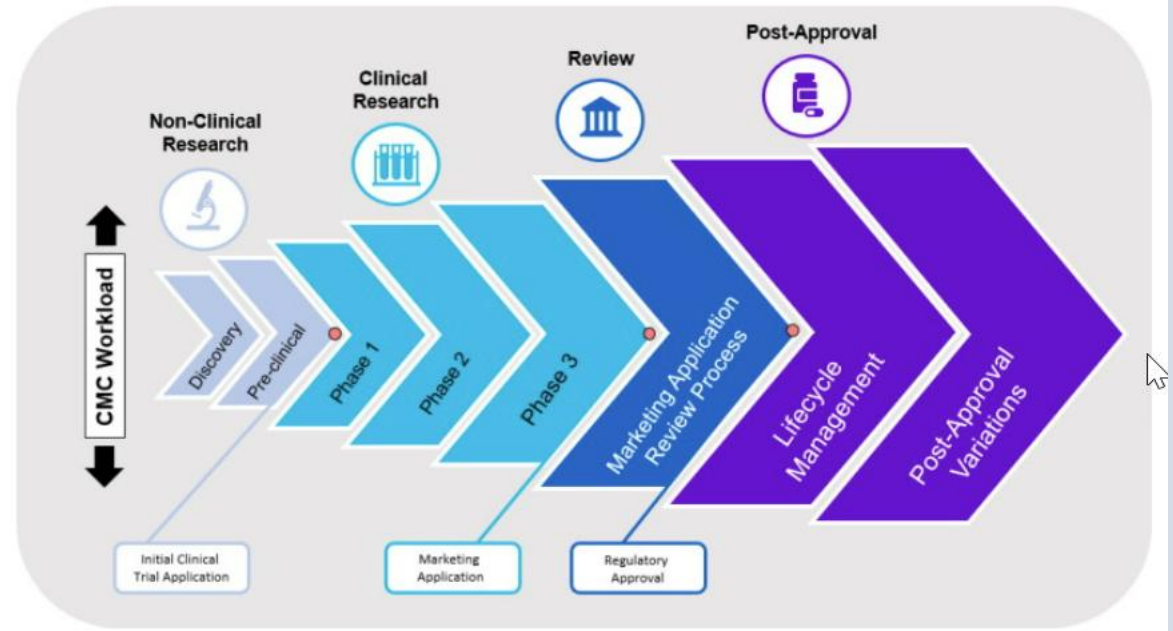

2026

automated submission preparation

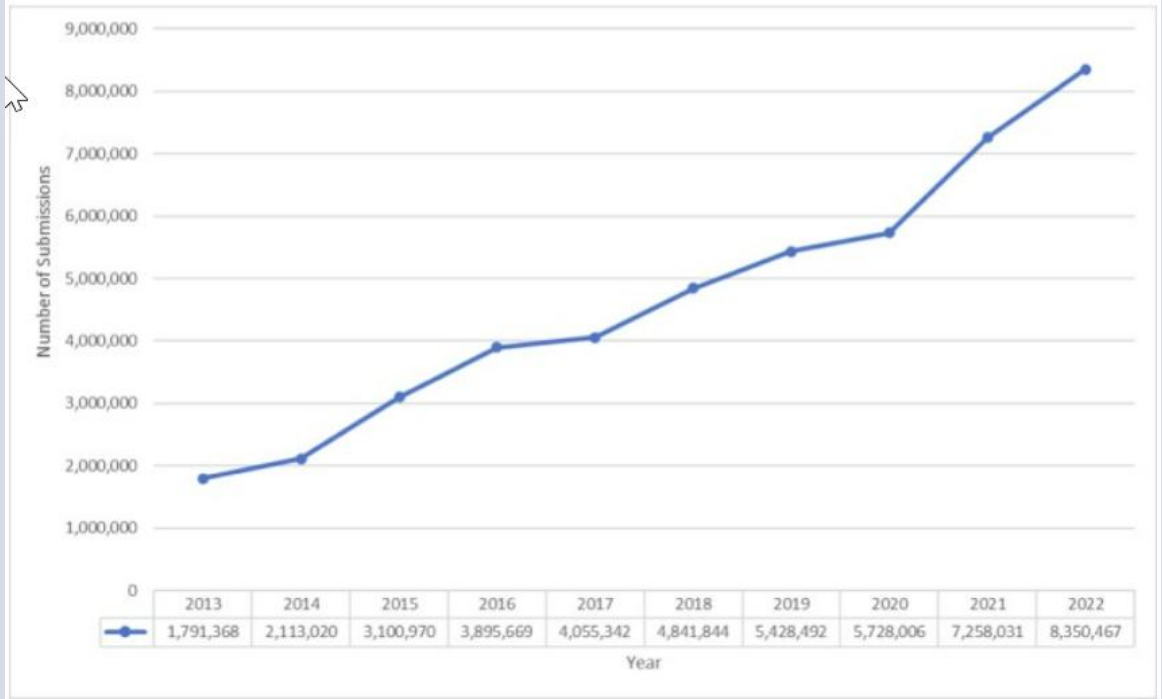
Cloud based data exchange

ONE CLICK SUBMISSION

# The Challenge: Submission Volumes Continue to Increase

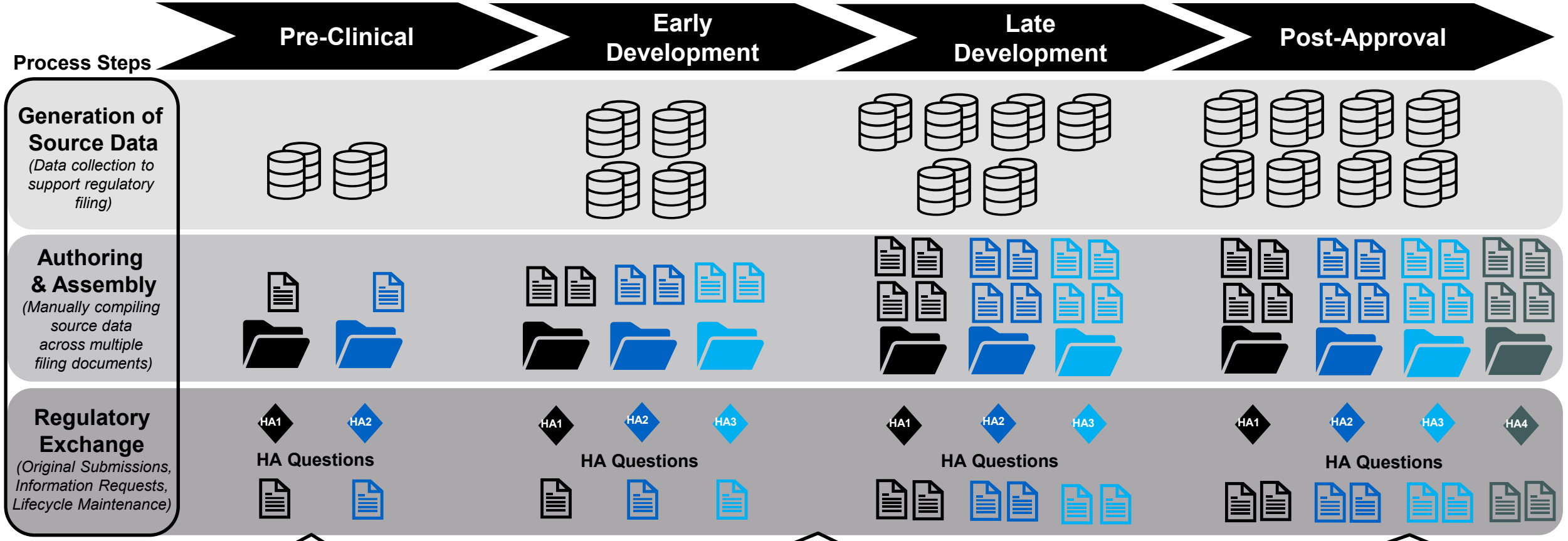



Workload through Phases of Medicinal Product Development Lifecycle




FDA Total ESG Submissions 2013 - 2023

# The Challenge: Current Manual Regulatory Authoring Process Is Successful But Cumbersome And Inefficient

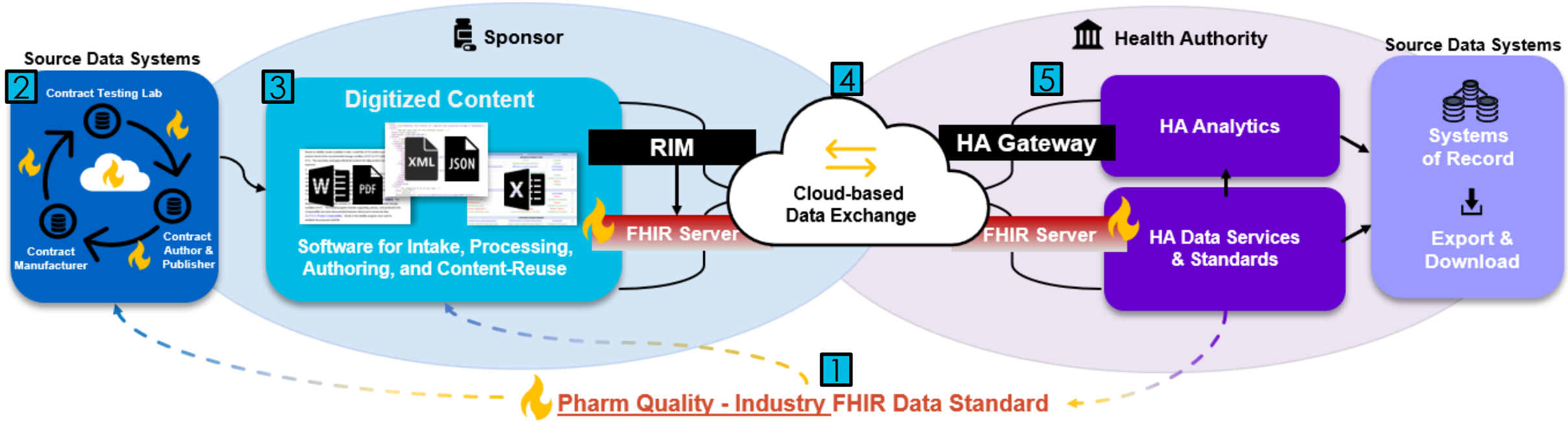



**5000+ different events (authoring, review, verification) needed to assemble full package (~300 documents)**



AMGEN®

# The What: Future State Vision for Regulatory Exchange Published in 2023




1. Health authority and industry FHIR standards are used to standardize data at the source
2. Sponsor Source data systems are connected through structured, standardized data
3. Digital content management systems render data in the required format
4. A cloud-based data exchange system connects the sponsor and regulator environments
5. Regulators receive structured, standardized data that can be used in analytics software

From Anderson, Algorri, Abernathy 2023



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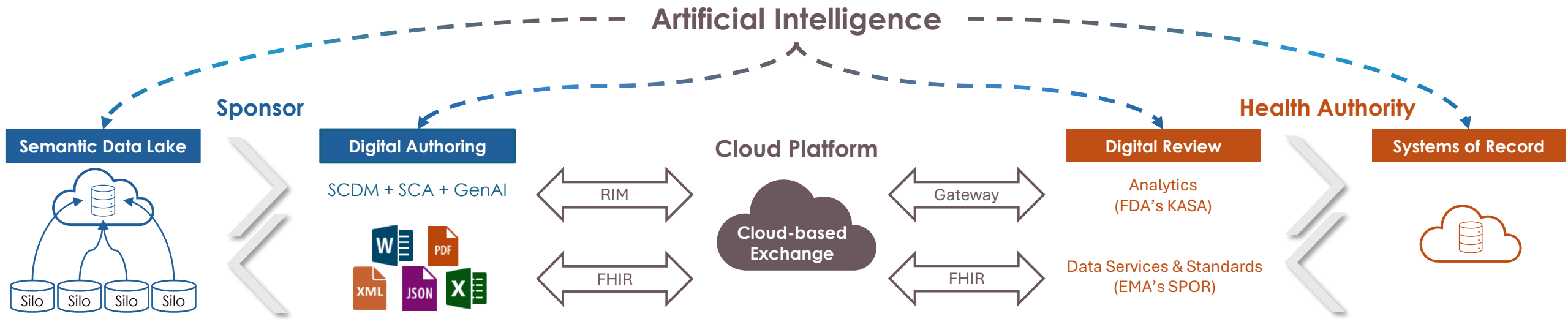
# The What: Practical Application of Regulatory Exchange



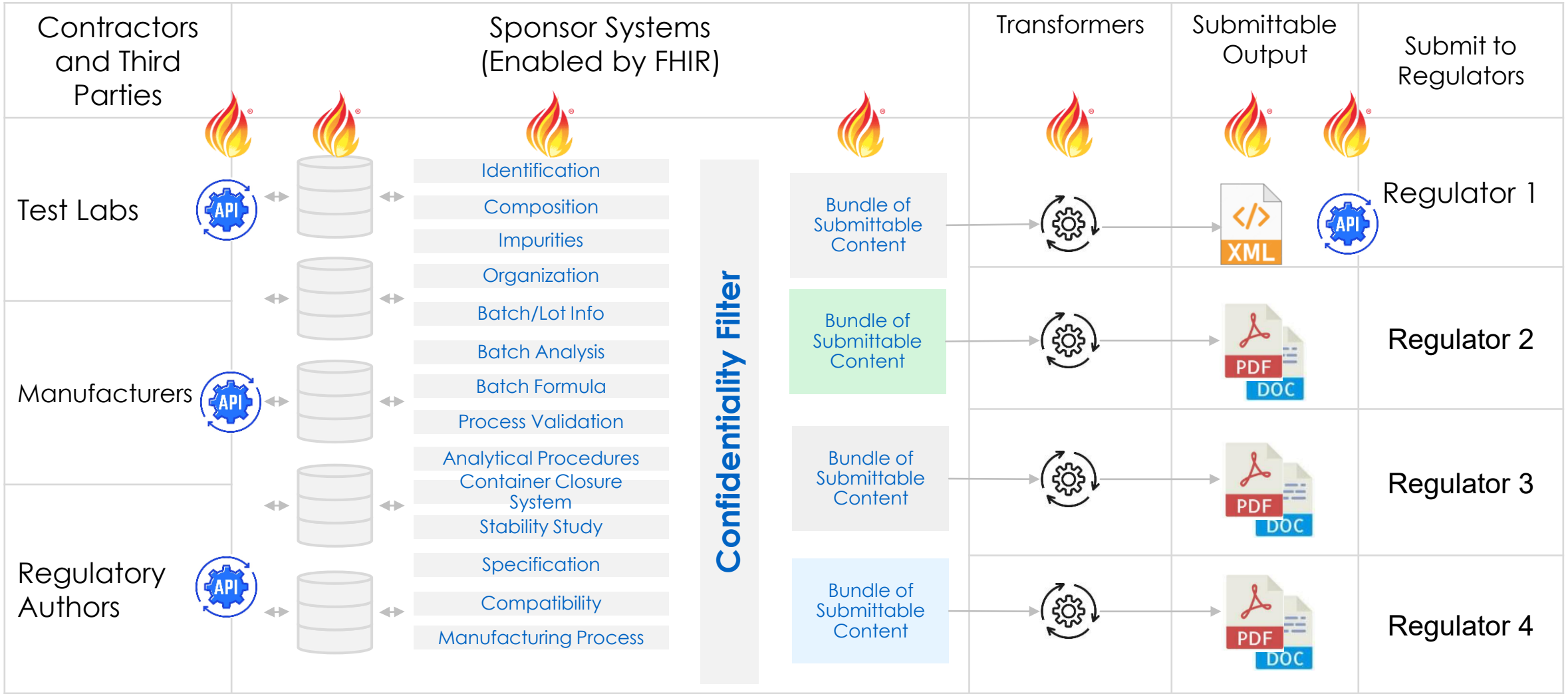

**Foundational End-to-End Data Standards (PQ-CMC, ISO IDMP, HL7 FHIR Pharm Quality - Industry)**

## Benefits of Digitalization

- Time Efficiency & Optimization
- Manual Error Reduction
- Increased Manufacturing Capacity
- Reduced Medicinal Waste
- Real-time Collaboration
- Accelerated Approvals
- Global Patient Access

Figure from "The Future of Regulatory Filings: Digitalization," Ahluwalia et al., 2025, doi: 10.1186/s41120-025-00113-7

# The How: FHIR Data Pipeline – Pharmaceutical Quality (Industry)



# The How: Connecting Data Using FAIR Principles

Figure 1. Existing Challenges Associated with Data Value Realization

CHALLENGE #1

Data Accessibility

Poor visibility and re-use of existing data assets to the broader enterprise limits value and spawns redundancies

CHALLENGE #2

Technical Interoperability

Heterogeneous functional integration layers and data representation complicate cross-functional data aggregation

Key Challenges in Adopting FAIR Principles

CHALLENGE #3

Semantic Interoperability

Lack of common, codified, and stewarded semantics across and even within functions hampers effective analytics

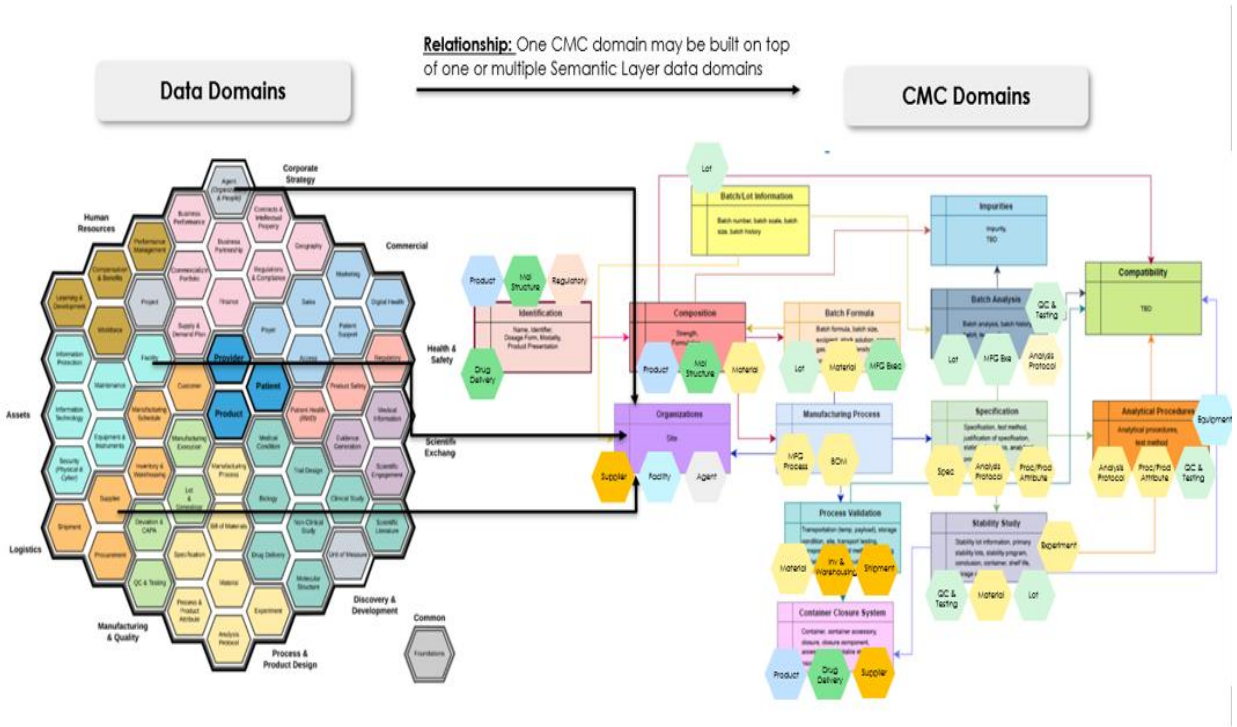
CHALLENGE #4

Culture of Sharing

Data is functionally siloed; sharing and re-use is not incentivized or broadly governed; ideation on data we have vs. data we need

Findable Accessible Interoperable Reusable

Figure 2. Source System Semantic Layer to PQI Domain Mapping




Figures from "Competing to Win: Lessons Learned from Fantasy Sports Data as Applied to the Biopharmaceutical Industry", Abernathy and Algorri, 2025. Under Review

# The How: Structured/Standardized Data and Content Facilitates Automation

## STATIC

**Table 1. Formulation Buffer Batch Formula**

| Formula Ingredient | Reference to Standard | Target Concentration | Target Amount per XX kg Batch Size <Smallest batch> | Target Amount per XXX kg Batch Size <Largest batch> |
|---|---|---|---|---|
| | | | | |

* USP = United States Pharmacopeia; NF = United States National Formulary

**2. X% Polysorbate 20/80 Solution**

Polysorbate 20/80 is added during drug product formulation as a X% stock solution. The formulation ingredients and amounts for the X% polysorbate 20/80 solution are shown in the table below. The batch size for the polysorbate 20/80 solution is fixed at 1.0 kg.

### Unstructured Content

- Difficult to keep updated
- Time consuming to format
- Limited scalability & reusability

## AUTOMATION-READY

**Table 1. Formulation Buffer Batch Formula**

| Formula Ingredient | Reference to Standard | Target Concentration | Target Amount per Batch size [Buffer].minimum Batch size [Buffer].range Units Batch Size | Target Amount per Batch size [Buffer].maximum Batch size [Buffer].range Units Batch Size |
|---|---|---|---|---|
| Excipient1.name | Excipient1.grade abbreviation | Strength [Excipient1] Strength.unit | Excipient1 quantity per batch [Buffer].minimum Quantity.unit | Excipient1 quantity per batch [Buffer].minimum Quantity unit. |

**2. Strength [Stock Solution Excipient] Stock Solution Strength [unit] Stock Solution Excipient.name Solution**

Stock Solution Excipient.name is added during drug product formulation as a Strength [Stock Solution Excipient] Stock Solution Strength [unit] stock solution. The formulation ingredients and amounts for the Strength [Stock Solution Excipient] Stock Solution Strength [unit] Stock Solution Excipient.name solution are shown in the table below. The batch size for the Stock Solution Excipient.name solution is fixed at batch size [Stock Solution] Stock Solution batch size [Stock Solution].units.

### Structured Content

- Independent from submission
- Human & machine readable
- Individual building block

## ASSEMBLED

Illustrative

**Table 1. Formulation Buffer Batch Formula**

| Formula Ingredient | Reference to Standard | Target Concentration | Amount per 50 kg Batch | Excipient batch quantity per <Enter Batch size [Buffer].maximum > |
|---|---|---|---|---|
| Proline (USP, PhEur, JP) | | 220 mM | 1260 g | |
| Acetic acid, glacial (USP, PhEur, JP) | | 20 mM | 59.8 g | |
| Sodium hydroxide, 10M solution (NF, PhEur, JP) a | | qs | qs to target pH b | |
| Water for injection (USP, PhEur, JP) | | qs | qs to target weight | |

JP = Japanese Pharmacopeia; NF = United States National Formulary; PhEur = European Pharmacoepeia; qs = quantum suffict; USP = United States Pharmacopeia

**2. 0.01 mg/mL Polysorbate 80 Solution**

Polysorbate 80 is added during drug product formulation as a 0.01 mg/mL stock solution. The formulation ingredients and amounts for the 0.01 mg/mL Polysorbate 80 solution are shown in the table below. The batch size for the Polysorbate 80 solution is fixed at 1.5 kg.

### Structured Content Authoring

- Automated authoring
- Reuse across documents
- Reduce DV requirements

# The How: Automation Facilitates Digitalization and Flexible Outputs

**Current Filing Templates** → **Convert and Transform** → **Automation-Ready Templates**

## Only unstructured Word/PDF documents are used

Stability studies are conducted at the recommended storage condition to support the shelf life and were performed per ICH Harmonized Tripartite Guide, *Stability Testing of Biotechnological/Biological Products* (Q5C) and *Stability Testing of New Drug Substances and Products* (Q1A). Stability studies at elevated temperatures are also conducted to assess the effect of these conditions on product quality. In addition, experimental drug product studies including ICH and clinical photostability, temperature cycling, and transportation were performed.

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 2°C to 8°C (referred to as 5°C). Storage for a single period of up to X months is proposed for the drug product stored at a maximum of XX°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: 100 mg (10 mL) and 500 mg (50 mL) single-use vials containing 10 mg/mL <<INN>>. The 2 presentations are considered to be equivalent, differing only in fill volume and container size. The results from the 100 mg and 500 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 5°C. The overall program includes supporting, primary, and production lots. Comparability has been demonstrated between clinical (Amgen Thousand Oaks [ATO])

## Automation-ready Templates are Compatible with Structured Data Formats

Amgen commits to continue the ongoing stability studies described in 3.2.S.7.1 (Stability Summary and Conclusions) until completion.

For future production of drug substance, a minimum of {{Stability lots [DS, post-approval].quantity}} lot(s) of {{Name.nonproprietary}} drug substance will be added to the postapproval- stability program annually, stored at the recommended condition of {{Storage condition [DS, recommended].temp}}°C ({{storage condition [DS, recommended].temp range max}}- {{storage condition [DS, recommended].temp range min}}°C), and tested according to the protocol provided in Table 1. If drug substance is not manufactured during a given year, a stability study is not required for that year.

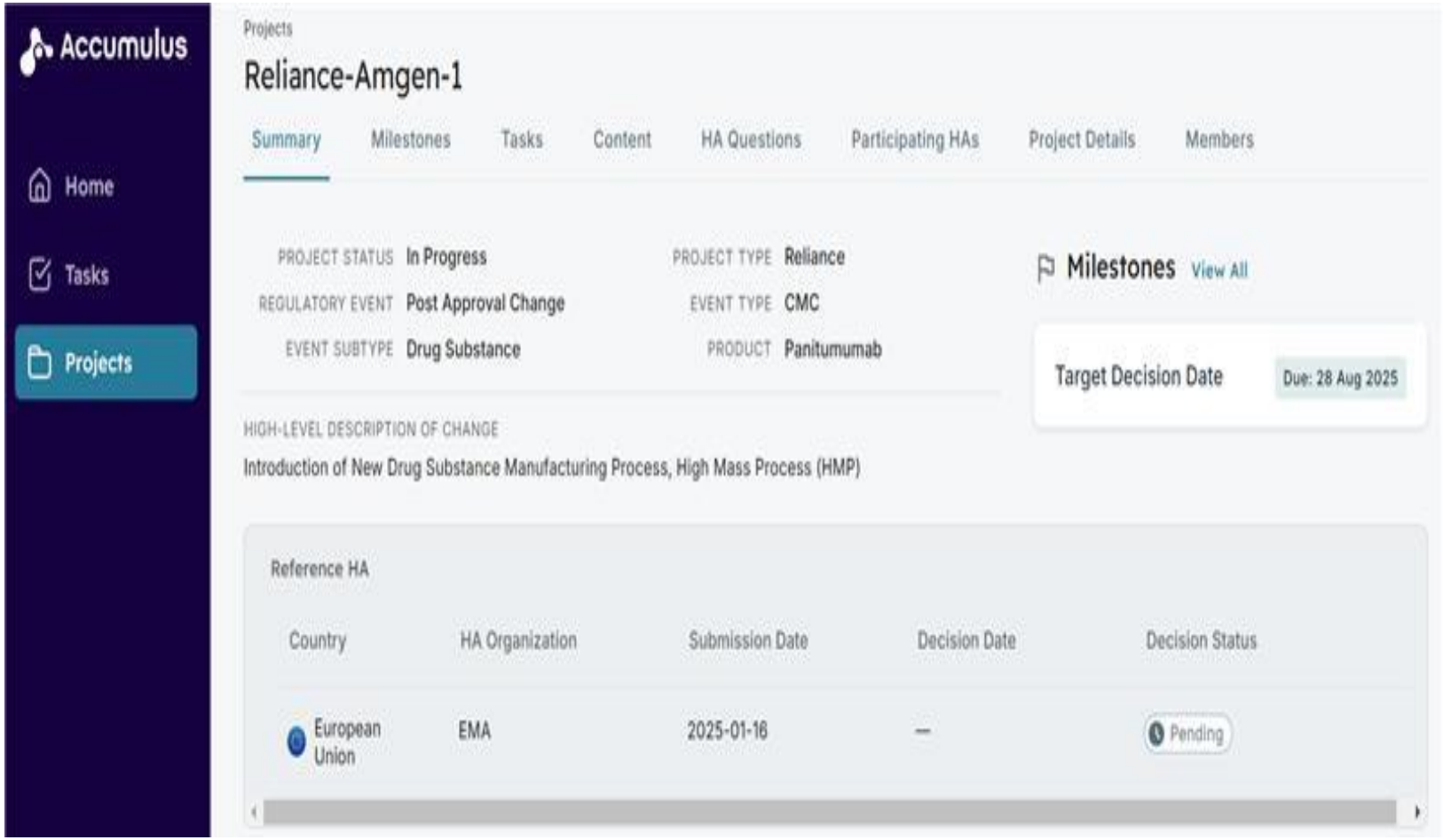
| | A | B | C | D | E | F | G | H | I |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Table 1. Post-approval Test Schedule for Product.Name Drug Substance Stored at the Recommended Storage Condition (°C) | | | | | | | | |
| 2 | | | | | | | | | |
| 3 | Time Point (months) | | | | | | | | |
| 4 | | | | | | | | | |
| 5 | | | | | | | | | |
| 6 | | | | | | | | | |

| STABILITY LOT INFORMATION | | |
|---|---|---|
| *Summary Info* | | |
| Stability lot [DS/DP].Description = | Description of stability lot information;Drug product used in stability testing was taken from several sources: | Text (Default |
| Batch size [DS/DP].range = | Value - Value (range) | Numeric - Numeric |
| Batch size [DS/DP].range units = | Kilograms, grams, pounds, etc. | Codeable |
| Primary stability lots.quantity = | Number of primary lots | Numeric |
| Supporting stability lots.quantity = | Number of supporting lots | Numeric |
| Commercial stability samples.Description = | Brief description of commercial stability samples, if present | Text (Variable) |
| validation stability lots.quantity = | Number of validation lots | Numeric |
| *Detailed Data Table* | | |
| Batch Number [DS/DP, packaged/internal/external/bulk/filled ] = | DP batch number for packaged product, bulk materia | Text (Variable) |
| Batch [DS/DP, copack].date = | dd/mm/yyyy | Date |
| Strength = | [Quantity] | Numeric |
| Strength.unit = | milligrams, grams, etc. | Codeable |
| Site [DS/DP].name = | Manufacturer name and acronym | Text (Variable) |
| Batch size [DS/DP].units = | [Quantity] | Numeric |
| Batch Size [DS/DP, filled units] = | Kilograms, grams, pounds, etc. | Codeable |
| Stability Program [DS/DP] = | Long-term, forced degradation, etc. | Codeable |
| Batch.utilization = | Clinical, Nonclinical, Primary, Validation, Supporting | Codeable |
| Latest Stability Time Point = | [Time] | Numeric |
| Latest Stability Time Point. units = | Days, Months, Years, Other (Free Text) | Codeable |
| Batch.process variant = | CP 1.1, CP 1.2, etc. | Text (Variable) |


```
<action>
  <title value="Stability Test Protocol for Long-term and Accelerated
  <action>
    <!-- TODO add codes here for the different levels? -->
    <title value="Long-Term"/>
    <description value="30°C/65% RH"/>
    <action>
      <!-- 0 months -->
      <title value="Initial"/>
      <timingTiming>
        <repeat>
          <boundsRange>
            <low>
              <value value="0"/>
              <unit value="months"/>
              <system value="http://unitsofmeasure.org"/>
              <code value="mo"/>
            </low>
            <high>
              <value value="0"/>
              <unit value="months"/>
              <system value="http://unitsofmeasure.org"/>
              <code value="mo"/>
            </high>
          </boundsRange>
          <frequency value="1"/>
        </repeat>
      </timingTiming>
      <action>
        <!-- the categories to do at this step -->
        <title value="XY"/>
        <!-- Long term -->
        <definitionCanonical value="ActivityDefinition/activityLongTerm30XY-Initial"/>
```


- **Auto-generation of text and tables**
- **Reuse of data components across templates**
- **Virtual replication of filing content to support regional filings**

# The How: Leading the Way in Cloud-Based Exchange
# Amgen's Vectibix High Mass Process (HMP) Pilot




**84%**
COUNTRY ENGAGEMENT

**73%**
NRA PARTICIPATION

- **53 of 63 Vectibix licensed countries participating in PAC Reliance -** enhancing efficiency, collaboration, and accelerating patient access
- **27 out of 37 National Regulatory Authorities participating in PAC Reliance**
- **Of those 27 NRAs, 25 are are using Accumulus** to access the Vectibix PAC dossier, the EMA Assessment Report, and other regulator questions and Amgen responses **in real time**.

* Platform Demonstration to Follow Presentation Time Permitting

# The Why: PAC Reliance/Collaboration Accelerates Patient Access To Medicines - *(Cloud-based Exchange Makes It Even Faster)*

**The High Cost of Delayed Global PAC Approvals**

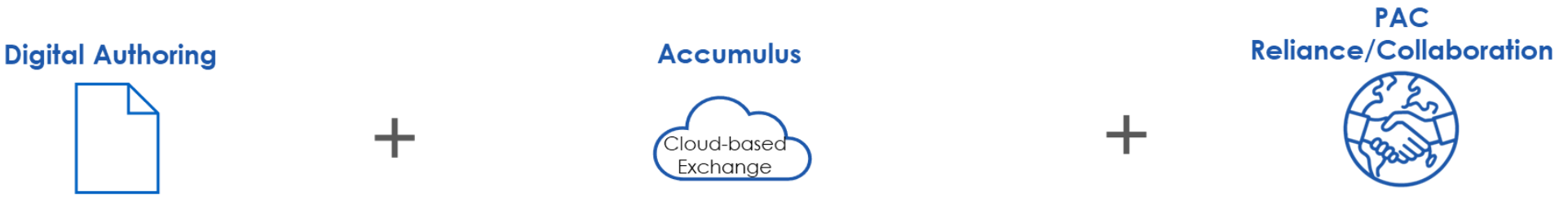
| Inventory Holding Costs | Operational Complexity | Regulatory Burden | Delayed Benefits |
|---|---|---|---|
| Need to maintain stock of the legacy product until all countries approve the change<br><br>Increases storage and working capital requirements | Multiple supply and mfg lines complicate production planning and distribution logistics | Requires multiple submissions for each country<br><br>Results in multiple regulatory queries, inspections, and documentation | Process improvements or cost-savings cannot be realized globally<br><br>Delays in quality enhancements or efficiency gains reaching patients |

## "Traditional' Reliance

A Health Authority (the reference authority) shares its assessment of a PAC, and other authorities (*reliant Health Authorities*) use that review to support faster, aligned approvals.

## Parallel 'Real-time' Reliance/Collaboration

A single dossier is submitted simultaneously to multiple health authorities who conduct **concurrent reviews** in parallel with the Reference Authority. - ex., Amgen's Vectibix PAC Reliance Accumulus pilot



# The Why: Benefits Realization

## Enablers

### Digital Authoring

SCDM + SCA + GenAI


+

### Accumulus

Cloud-based Exchange

+

### PAC Reliance

## Process Improvements & Efficiencies

### Time Efficiency & Optimization

- **Accumulus** usage is **75% more efficient** than conventional pathways, provides a dynamic, secure cloud-based technology, and a user-friendly interface
- **Single global submission** eliminates regional variations
- **Reduced number of RFIs**
- **Eliminated repeat questions**

### Manual Error Reduction

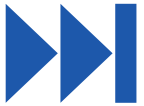
- Digital tools **improve filing compliance**
- **Reduction in variation** of registered details
- **Improves internal compliance** to registered regulatory details

### Real-time Collaboration

- Simplifies **document management** and exchange
- Promotes submission and approval of a **single global dossier**
- Facilitates **cross-agency communication and collaboration**
- Provides for more **efficient information exchange**

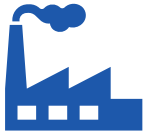
## Regulatory & Global Impact

### Accelerated Submissions and Approvals



- **Reduction from >4 years to <1 year** in global life-cycle management approval, in most instances **<6 months**

### Increased Manufacturing Capacity



- **$10 to $100 Million** benefit per Major Post Approval Change in available manufacturing capacity

### Reduced Medicinal Waste

- Reduced inventory scrap due to accelerated approvals and **transition to optimized product** SKU

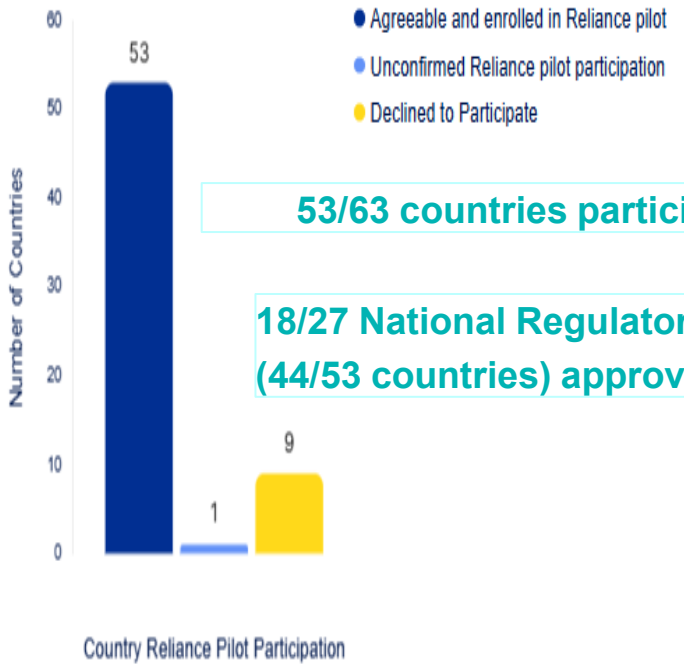
### Global Patient Access

- Accelerated **access to optimized product**
- **Facilitates changes** that would perhaps not be made due to long review and approval lag times

# The Results: Amgen Case Study: Leading the Way in Post-approval Change (PAC) Collaboration and Cloud-Based Filings

| Target | Target Countries |
|---|---|
| **63 countries** where Vectibix is licensed | Algeria, Argentina, Australia, Bahrain, Bosnia and Herzegovina, Brazil, Canada, Chile, Colombia, Costa Rica, Ecuador, Egypt, Guatemala, Israel, Jordan, Kuwait, Lebanon, Malaysia, Mexico, Montenegro, Morocco, Oman, Panama, Peru, Philippines, Qatar, Saudia Arabia, Serbia, Singapore, South Africa, Taiwan, Thailand, Turkey, UAE, UK, Ukraine and EU (27 countries: Austria, Belgium, Bulgaria, Croatia, Republic of Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain and Sweden.) |

## Country Reliance Pilot Participation

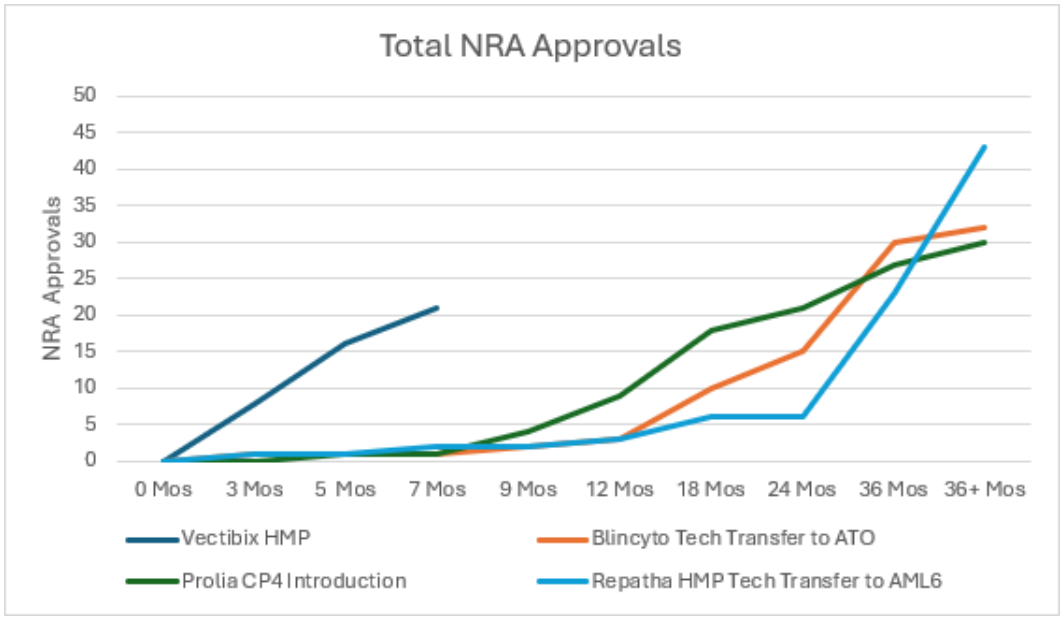


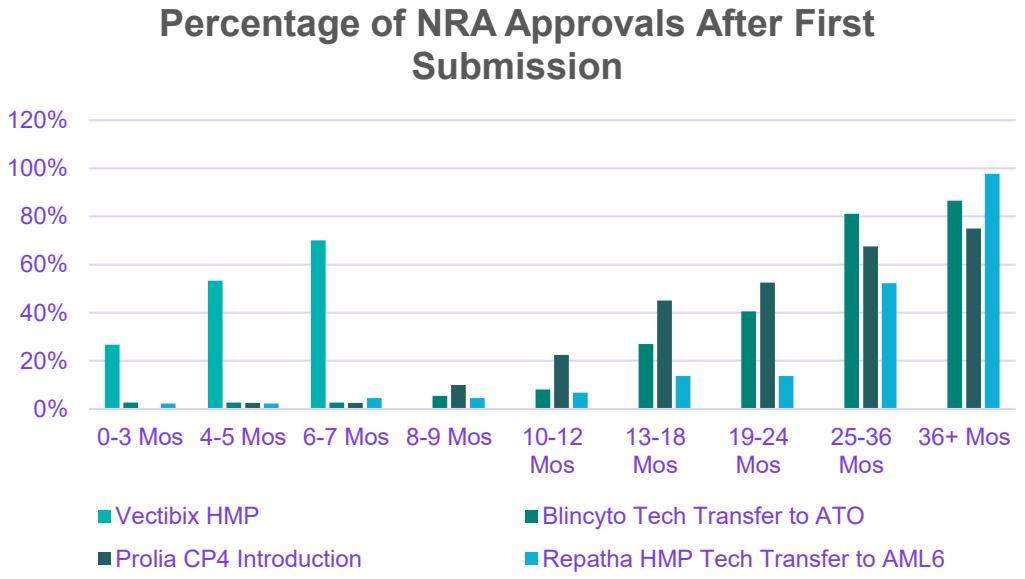

**53/63 countries participating (84%)**

**18/27 National Regulatory Authorities (NRA) (44/53 countries) approved in < 7 months**

## Country Reliance Pilot Participation Detail

| | |
|---|---|
| Number of Countries Participating in Reliance Pilot | 53 |
| Countries Agreeable and enrolled in Reliance Pilot | Argentina, Australia, Brazil, Canada, Chile, Colombia, Egypt, Austria, Belgium, Bulgaria, Croatia, Republic of Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Guatemala, Israel, Jordan, Malaysia, Mexico, Montenegro, Oman, Panama, Peru, Philippines, Saudi Arabia, Serbia, Singapore, South Africa, Taiwan, Thailand, Turkey, UK, Ukraine |
| Countries Unconfirmed Reliance Pilot participation | Algeria |
| Countries Declined to Participate in Reliance Pilot | Bahrain, Bosnia and Herzegovina, Costa Rica, Ecuador, Kuwait, Lebanon, Morocco, Qatar, UAE |



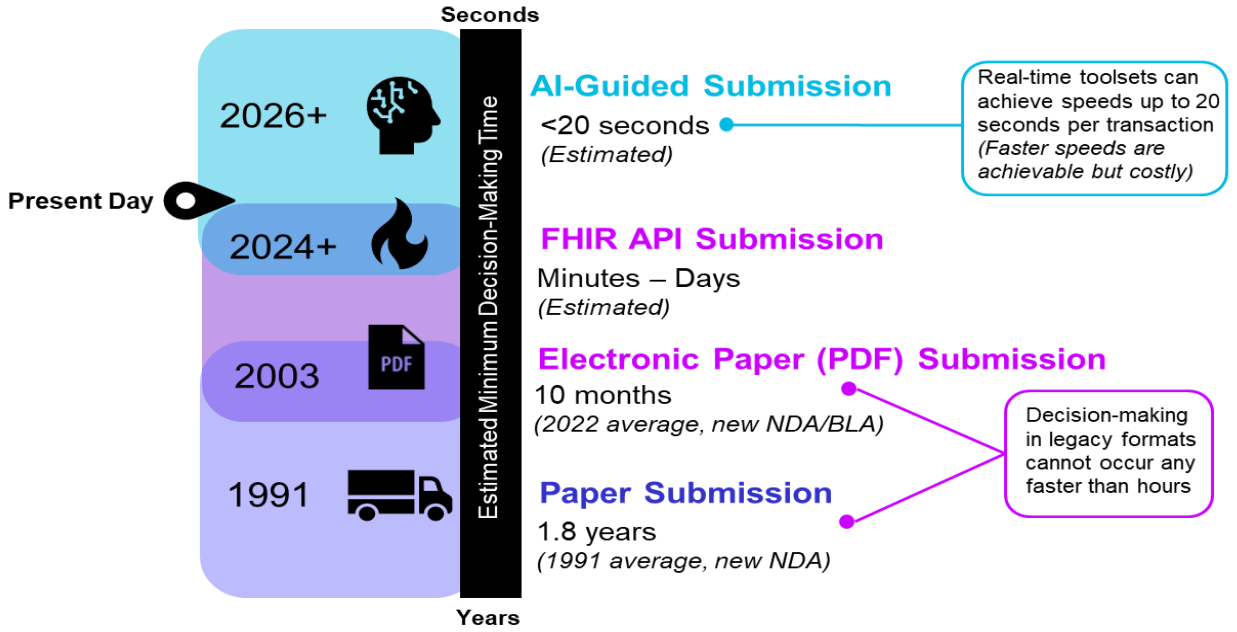



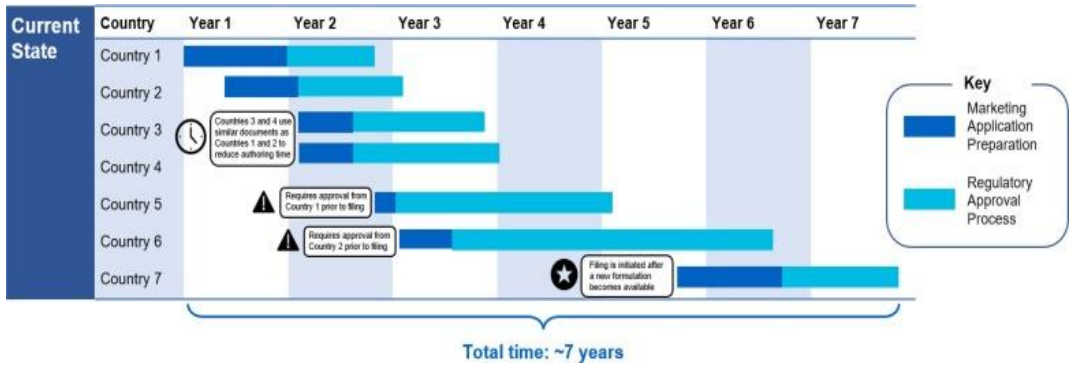
# The Art of the Possible in the Regulatory Ecosystem is Here

1. Accelerate document generation timelines (i.e., hours rather than weeks/months)

2. Enable real-time data exchange (i.e., seconds/subseconds)

3. Replace staggered submission wave model with simultaneous global submission model






From Anderson, Algorri, Abernathy 2023