Near-Concurrent Collaborative Reliance with Accumulus Technologies to Streamline Post-Approval Variations

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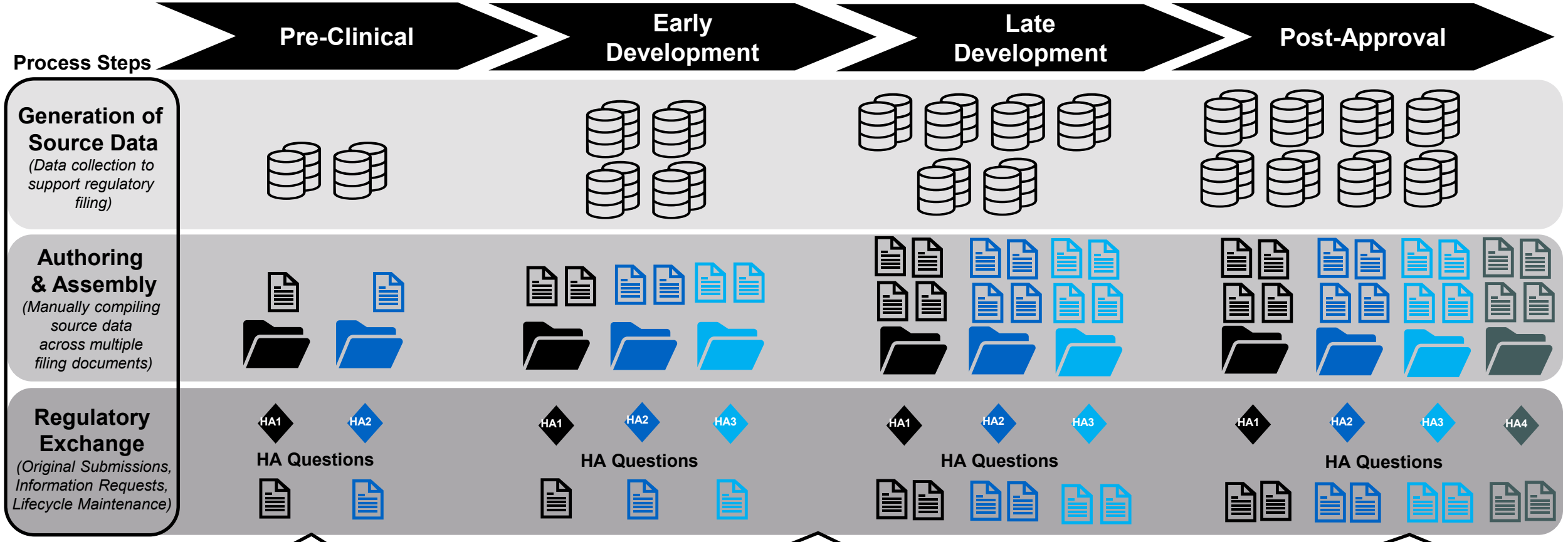
Current Manual Regulatory Authoring Process Is Successful But Cumbersome And Inefficient



1300+ hours to author and data verify 1 clinical trial application

Quantity of documents to submit and maintain increases as development progresses

Maximum workload is in post-approval: 242,000+ hours annually to submit and maintain regulatory information

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

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The High Cost of Delayed Global PAC Approvals

Inventory Holding Costs

- Need to maintain stock of the legacy product until all countries approve the change

Operational Complexity

- Multiple supply & manufacturing lines complicate production planning and distribution logistics

Regulatory Burden

- Require multiple submission for each country
- Results in multiple regulatory queries, inspections and documentation

Delayed Benefits

- Process improvements or cost-savings cannot be realized globally
- Delays in quality enhancement or efficiency gains reaching patients

Patients are the Driving Force for Digital Regulatory Transformation

Challenge

- How to streamline global patent access to high-quality medicines?
  - Increase Manufacturing capacity and efficiency
  - Streamline global regulatory submissions
  - Reduce or eliminate divergent, global, lifecycle dossiers
  - Move toward the future of digital transformation for regulatory submission and review

Opportunity

- Leverage rapidly advancing technology as in other highly regulated industries
  - Move toward the future of digital transformation for regulatory submission and review
  - Enable, facilitate, and support innovation for collaborative review among national regulatory authorities
- Evaluate the results of global pilots based on impact for patients
  - Converge on the approaches that increase global patient access to medicines
  - Consider how to align regulatory laws and policies in the new era for the maximum benefit of patients

Proposal

- Communicate pilot approaches / strategies that serve patients best (based on results)
  - Align on regulatory pathways / platforms
  - Reliance plus the Accumulus cloud-based platform has yielded outsized results for many patients

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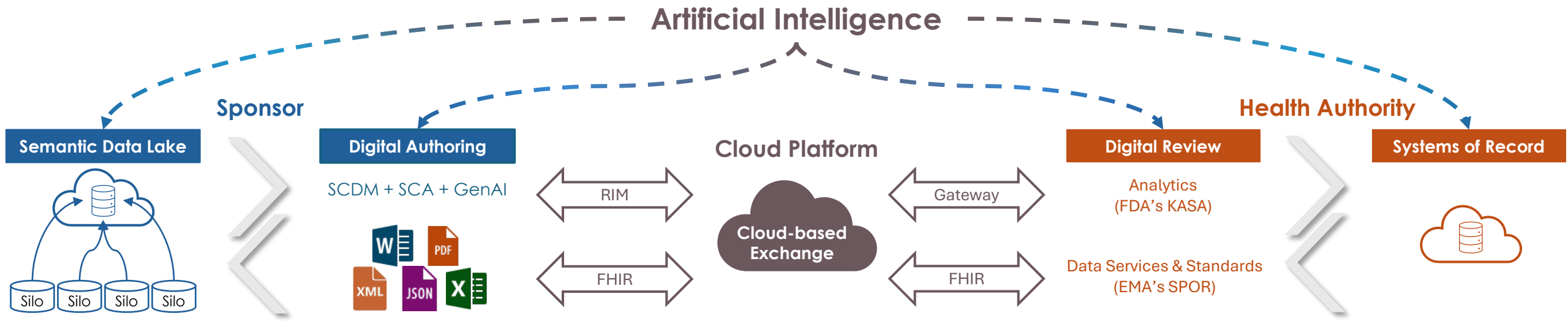
Practical Application of Regulatory Exchange



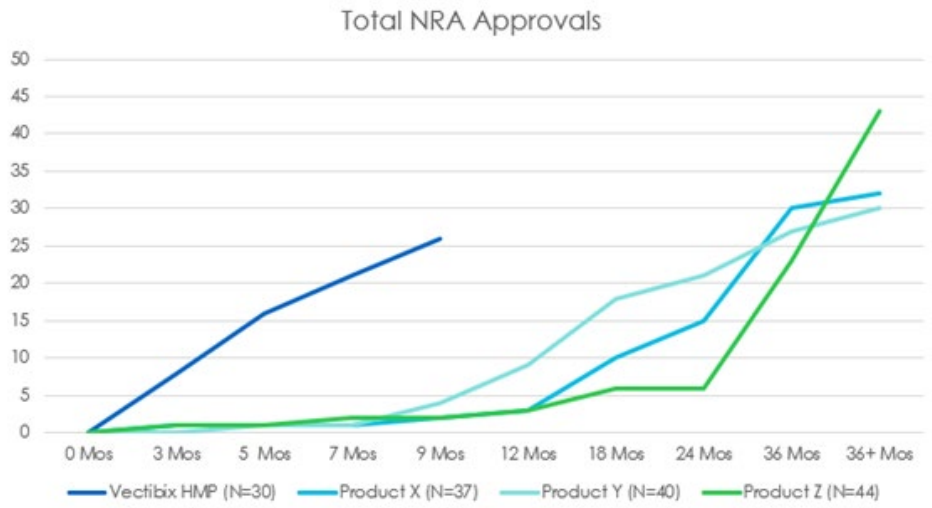
Foundational End-to-End Data Standards (PQ-CMC, ISO IDMP, HL7 FHIR Pharm Quality - Industry)

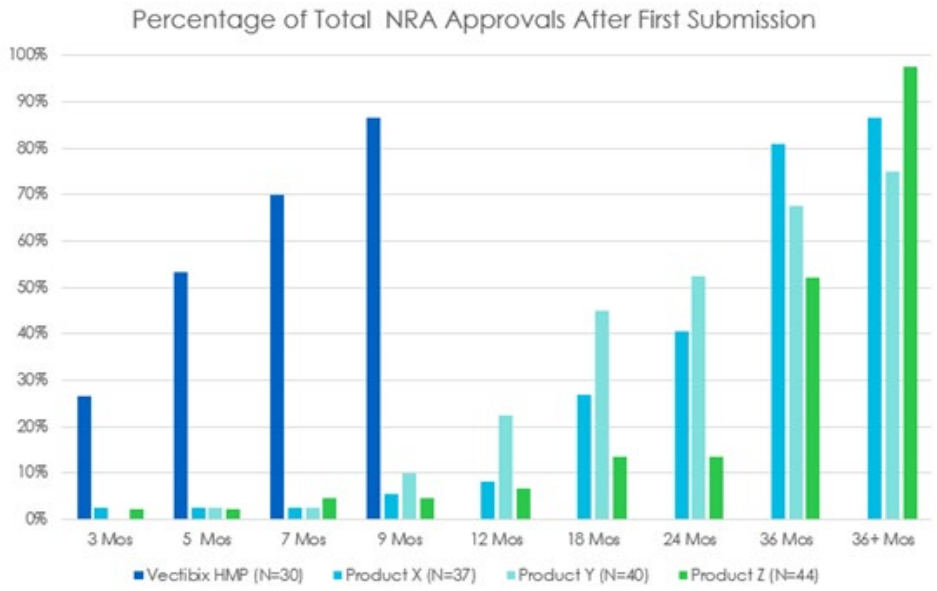
Benefits of Digitalization

- 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

VECTIBIX HMP PILOT RESULTS: CONFIRM ACCELERATION OF GLOBAL REGULATORY APPROVALS THROUGH PAC RELIANCE AND ACCUMULUS COLLABORATION





92%
COUNTRY APPROVALS TO DATE

800 - 2700 %
FASTER APPROVAL RATE

84%
COUNTRY ENGAGEMENT

73%
NRA PARTICIPATION

- **24 approvals of 27 NRA submissions since Feb 2025 (File Validation date)**
- **50 approvals out of 53 countries since Feb 2025 (File Validation date)**
- **800% to 2700% faster approval rate versus similar variations using the traditional approach -** accelerating patient access
- **Singapore Health Authority issued approval only 2 months after receiving access to Accumulus -** enhancing efficiency
- **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**.

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Accumulus Technologies: a Cloud-Based Platform for Sharing Information

- Accumulus is a cloud-based Software as a Service (SaaS) platform to share information across sponsors and agencies with a simple internet connection.
  - **Allows users (sponsors, health authorities, and contract development & manufacturing organizations) to share regulatory information and collaborate on review**
  - Information is currently shared in the form of published regulatory documents ready for submission
  - **Each user has access to secure workspaces and controls when and if information is "released" for sharing with other users**

- Advantages: facilitate collaboration and allow for…
  - **Instantaneous and simultaneous access to shared information among all designated users**
  - Work sharing supported by notifications and comments on documents between users
  - **Visibility for all users to shared health authority questions and Amgen's responses (i.e. health authorities can review each other's questions)**

- Value
  - **Accelerate patient access to medicines by streamlining Global CMC variation submission and review across the industry**
  - Leverage available technology for maximum impact through digital transformation
  - Advocate for collaborative review to the extent that this approach accelerates patient access

Accumulus Technologies is the only operational cloud platform for live, collaborative, regulatory review by multiple health authorities simultaneously

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Reliance for Post Approval Changes (PAC) / Variations

PAC Reliance or Regulatory Reliance:

- **A regulatory pathway in which multiple health authorities agree to rely on a Reference HA assessment**
  - The reference health authority is designated for the evaluation of a post approval variation submission
  - Typically implemented for CMC post approval changes or variations (dubbed PAC Reliance)
  - 2013 - the term regulatory reliance was circulated by the International Coalition of Medicines Regulatory Authorities (ICMRA)
  - 1969 - the concept was first described by WHO in "Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce"

- Mechanism and Advantages
  - All participating health authorities receive the same dossier at the same time as the reference authority
  - A designated reference health authority shares its final assessment of a PAC / variation
  - Participating (reliant) health authorities may use that review to support a potentially faster assessment / aligned approvals
  - **Collaborative reliance with near-concurrent review rather than sequential traditional reliance**

- Value
  - Streamline the review and assessment and align review timelines among multiple health authorities
  - **Reduce the window of time between completion of first and last country assessments**
  - **Accelerate patient access to medicines**

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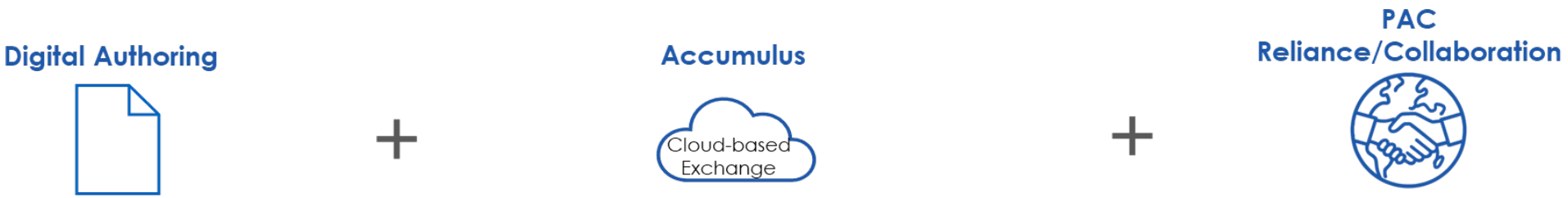
Why Implement Reliance and Accumulus Together?

- **Accumulus and Reliance together move the industry closer to the full vision of One Global Dossier**
  - Simplifies the review process, enabling shared regulator opinions and increased transparency
  - Facilitates real-time updates and enhanced collaborative capabilities
  - **Reduces repetitive information requests and mitigates the introduction of region-specific content**

- Veeva RIM integration with Accumulus Technologies will create a seamless, single workflow
  - **Health authority questions uploaded to Accumulus will automatically populate RIM**

- Value
  - Combined benefits of both reliance and Accumulus
  - **CMC pilots to date have received fewer health authority questions, reducing regulatory burden**
  - **Accelerate patient access to medicines**



COUNTRIES/REGIONS PARTICIPATING IN AMGEN RELIANCE/ACCUMULUS PILOTS

Argentina	Malaysia	Taiwan
Australia*°	Mexico	Thailand
Bosnia & Herzegovina	Montenegro	Turkiye
Brazil	New Zealand	Ukraine
Canada°	Oman	United Arab Emirates
Chile	Panama	United Kingdom*
Colombia	Peru	
Egypt	Philippines	
Europe*°	Qatar	
Guatemala	Saudi Arabia	
Israel	Serbia	
Jordan	Singapore	
Kuwait	South Africa	

***Reference Health Authority**

°Participated in Reliance without using Accumulus

Last Updated: 7/14/26

Amgen is Striving Forward with Pilots for Post-Approval Changes

Pilot	Change	Notes
2	Drug Substance Single Use Centrifuge	One final assessment (approval) achieved within 3 weeks of validation
3	Clinical Indication Expansion	Amgen's first clinical variation leveraging reliance (10 NRAs participating)
4	Drug Substance High Mass Process	Amgen's first reliance / Accumulus pilot to include a partner
5	Drug Product Technology Transfer	Targeting a fourth health authority to serve as reference authority

Different health authorities have agreed to serve as the reference authority for Amgen pilots
Several additional pilots are planned for the near future

Cloud-Based Regulatory Collaboration to Enable Other Innovations

Dossier convergence facilitates reliance and also supports innovative, aligned, global pharmaceutical development

Efficient Lifecycle Assessments

Decreased assessment time is the most often described, general benefit of cloud-based regulatory collaboration. Consider how innovation in one aspect unlocks other innovations across the industry

Q14/Q2(R2)

The impact of standardized analytical method development and validation can be compounded by cloud-based collaborative review and alignment on scientific evidence

ICH Q6

Globally defined and aligned specifications are characteristic of a global dossier which fosters reliance review pathways and accelerated by cloud-based review

Advanced Analytical Methods

The generation of more complex data from technically advanced analytical methods is well-suited for cloud-based collaborative review

Industry 4.0 / Pharma 4.0

More abundant, detailed, digital manufacturing data from modern manufacturing facilities are complemented by efficient data sharing and simultaneous health authoring monitoring and review

Emerging Technology

The value of the Emerging Technology Program (US FDA), the Innovation Task Force (EMA), and other similar national initiatives could be extended and enhanced via collaborative review

Streamline collaboration, reduce regulatory fragmentation, increase global harmonization, & leverage innovation for patients

Challenges to Cloud-Based Regulatory Collaboration: Real & Perceived

Several challenges have been raised by industry stakeholders, but together we can overcome these for patients

1. One Global Dossier

Quality

Alignment of global specifications poses a challenge. Considering modern QMS and global supply chains why not align specifications to internal manufacturing limits?

2. Institutional Change

Sponsors & Health Authorities

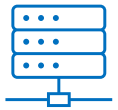
Effective change management is critical for both sponsors and NRAs. Some challenges are real while others derive from our human tendencies.

3. Country Adoption

Digital Infrastructure

Concerns that some countries may not be able to meet new technology demands; What have other industries shown us? (telecom, finance, etc.)

4. Technology Risks



Data Security

Genuine concerns exist around data security, privacy, & accountability. What have other industries shown us? (telecom, finance, etc.)

5. Laws & Regulation

Regulatory Policy

Laws and policies are intended and established to protect patients. Where might these be outdated with today's rapidly advancing technology?

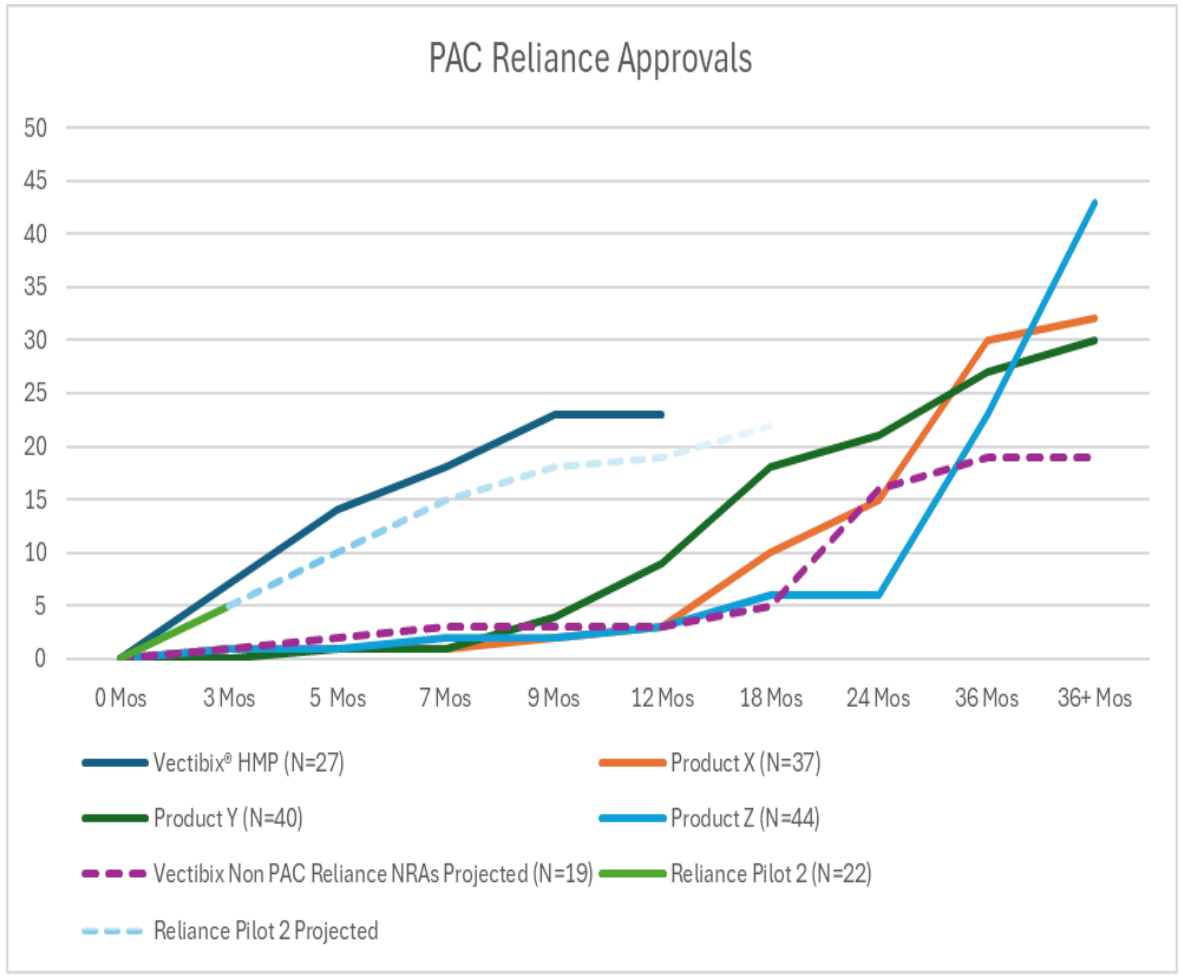
If we can change our mind-set, innovation can increase quality, enable speed, and accelerate patient access

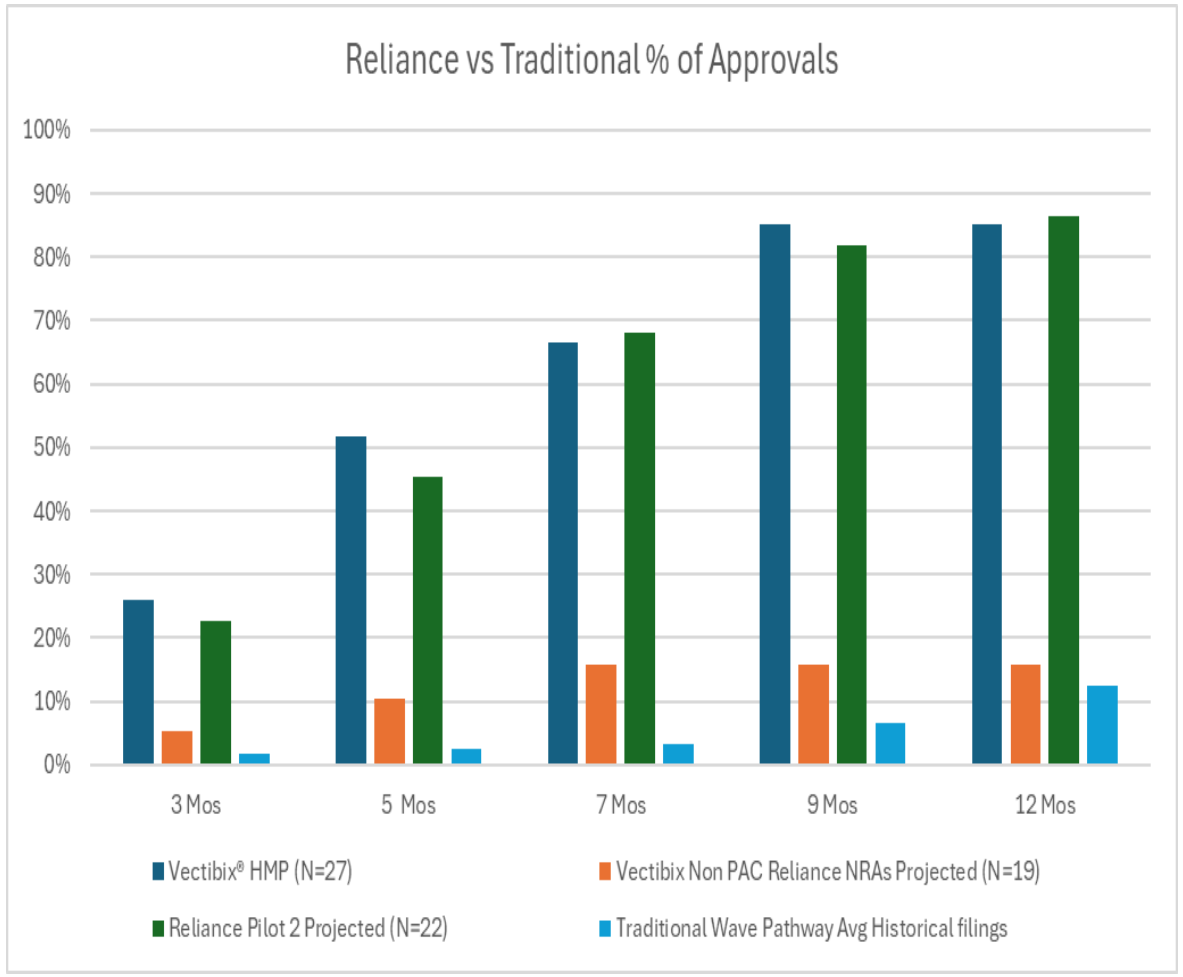
Global Data Indicate Reliance Pilots Significantly Accelerate Assessment

Benchmark Pilots	Approved Submissions	Reliance (Median Days to Approval)	Conventional (Median Days to Approval)
Amgen	**34**	**148**	**937**
EFPIA PAC Reliance	**118**	**189***	**730***
Includes approvals across multiple pilots measured from the first global submission		*Number of days to reach 80% approval of the countries in scope for each pilot	

- Amgen experience aligns with external global data for reliance pilots
- Combining reliance with a cloud-base collaborative review enhances efficiency
- Amgen observed ~ 50% fewer health authority questions for the Vectibix HMP pilot submission
- The number of participating sponsors and health authorities continues to increase

Compelling Data Supporting a Shift to Cloud-based Exchange and Reliance/Collaboration





Digital Transformation Benefits

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

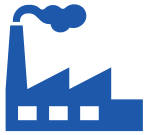
- Simplifies **document management** and exchange
- Promotes submission and approval of a **single global dossier**
- Facilitates **cross-agency communication and collaboration**
- Provides for more **efficient information exchange**

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

Acknowledgements

- Michael Abernathy
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- Nina Cauchon
- Sebreena Sandhu
- Monica Batra
- Vectibix Team…
- & Many Others

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The Art of the Possible in the Regulatory Ecosystem is Here

"Cloud-based regulatory platforms are a game changer! We have experienced notable efficiency of having an internet platform that allows National Regulatory Authorities to collaborate on our submissions."

— **Mark Taisey**
Senior Vice President, Global Regulatory Affairs Strategy, Amgen

"This marks a significant milestone for in our reliance project, celebrating our first-ever use of the Accumulus system to review uploaded documentation and observe other authorities' responses and approvals. Even more exciting, we have obtained this approval two months ahead of the estimated timeline, with approval received in approximately a 4-month period."

"The NRA referred to the information available on the platform, which helped address similar queries they initially had, thereby expediting the overall review process and approval."

"We have just been informed by our distributor that the variation has been approved on 29th Aug 2025. Obtaining the approval within such a short time is great news since the usual approval timeline of major variations is 15-18 months."

From Anderson, Algorri, Abernathy 2023