PDA ROUNDTABLE

Speeding Innovation through Global Regulatory Convergence

25 MAR 2024

Welcome to the roundtable:

For today's discussion:

Assume anything is possible so prepare yourself to not limit your ideas based on what you know today or how the current global regulatory processes work.

We will be focusing on two areas:

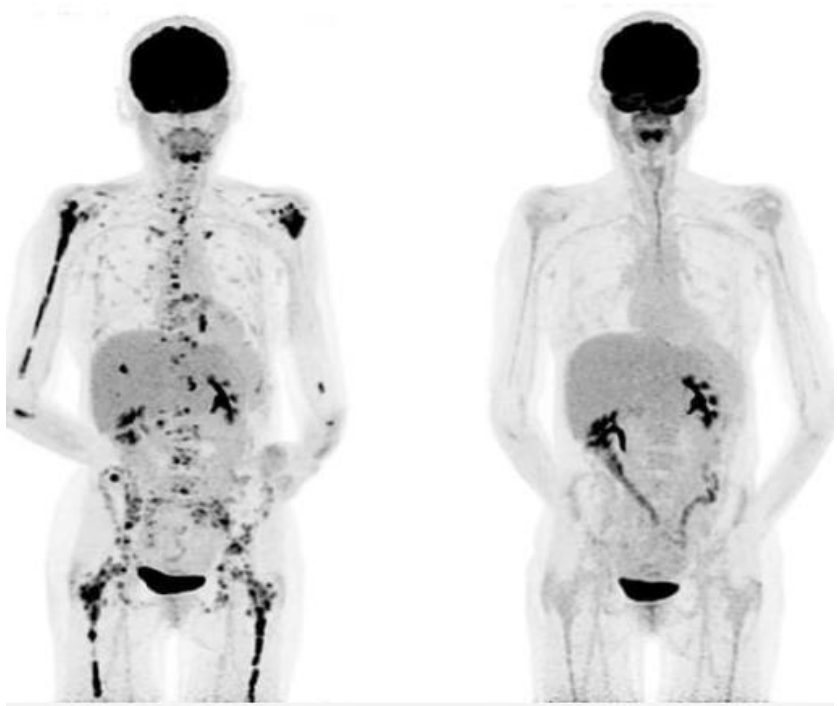
- The Global New Product submission, review, and approval process for *novel life saving products*
- The Global Post Approval Changes requiring a submission, review, and approval for changes to *implement manufacturing innovations that reduce drug shortages*

Example of what we mean by novel lifesaving drug products?

Products that treat conditions for which the patient has no other medical options, and their condition is terminal.

Not just transformational in how the diseases is treated but more importantly

Transformational for the patient!



Before (left) and after (right) PET scans of a patient with multiple myeloma treated with BCMA-targeted CAR T cells.
Credit: National Cancer Institute

Example of what we mean by novel lifesaving drug products?

Credit: National Institute of Health

Emily Whitehead – CAR T-Cell Pediatric Patient #1 at Age 6, 2012

CAR T-Cell therapy for reoccurring B-cell Acute Lymphoblastic Leukemia (ALL)

Prior to entering clinical trial, medical recommendation was hospice care

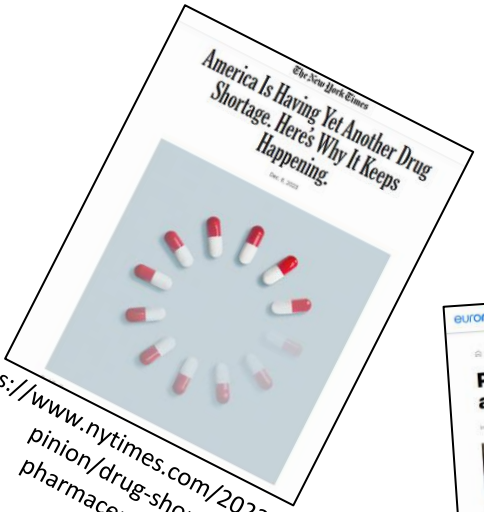
Approximately 3 weeks after receiving CAR T-Cell therapy, no cancer detected

Today she is celebrating her 13th year of being cancer free

Example of what we mean by manufacturing innovation to reduce drug shortages?

Implementation of new equipment with advanced automated process control (AI/Digital Twin) that improves/increases product yield (Changes are made to the process)

- Continuous Manufacturing
- Bioreactors with AI and Machine learning (Automatically adjusting the process)
- Fully automated filling lines with AI and Machine learning (Automatically adjusting the process)
- Next generation of gloveless filling isolators capable of running long campaigns of multiple lots of the same product (continuous filling).



https://www.nytimes.com/2023/12/06/opinion/drug-shortages-pharmaceuticals.html

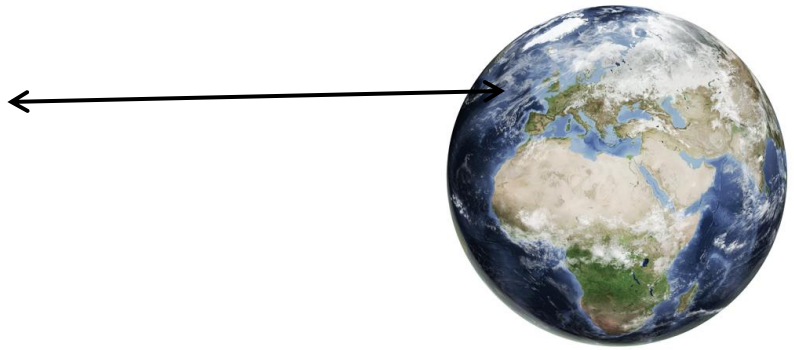
https://www.euronews.com/health/2023/07/13/prescription-for-disaster-europe-faces-alarming-medicine-shortages-crisis

https://www.cnn.com/2024/02/06/health/drug-shortages/index.html

Current Situation:

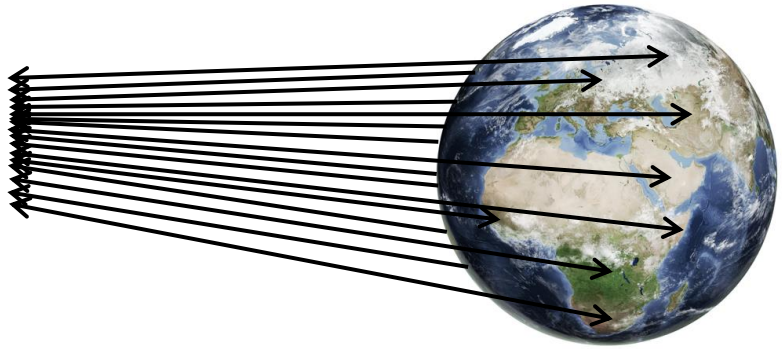
- For both New Product Submissions and Post Approval Change Submissions requiring approval, the current global process requires multiple, repetitive reviews from each regulatory authority (regional or local)
- Often additional information is requested or required from each regulatory authority
- Individual repetitive rounds of Q&A occur
- The process can be very long (many, many years for global approval)
- The current model stretches the limited resources of both Industry and Regulators creating delays and backlogs

New Product / PAC Submission



Simplified Perspective from a single *Regulatory Agency when Viewing a Submission from a Company*

New Product / PAC Submission



Simplified perspective from a single *Company when Viewing Submission to Regulatory Agencies Globally*

Regulatory Convergence and Digitalization

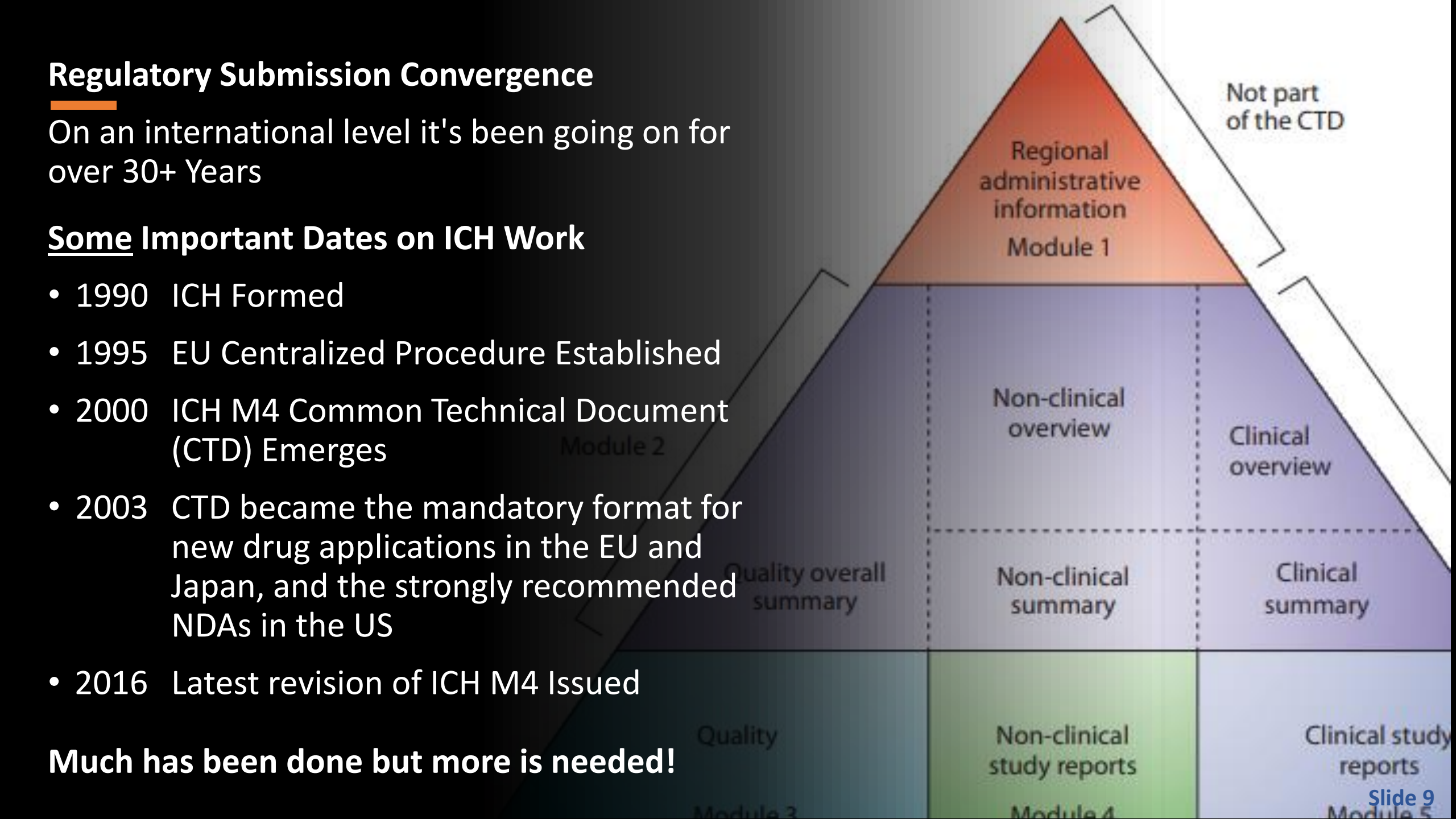
Regulatory Submission Convergence

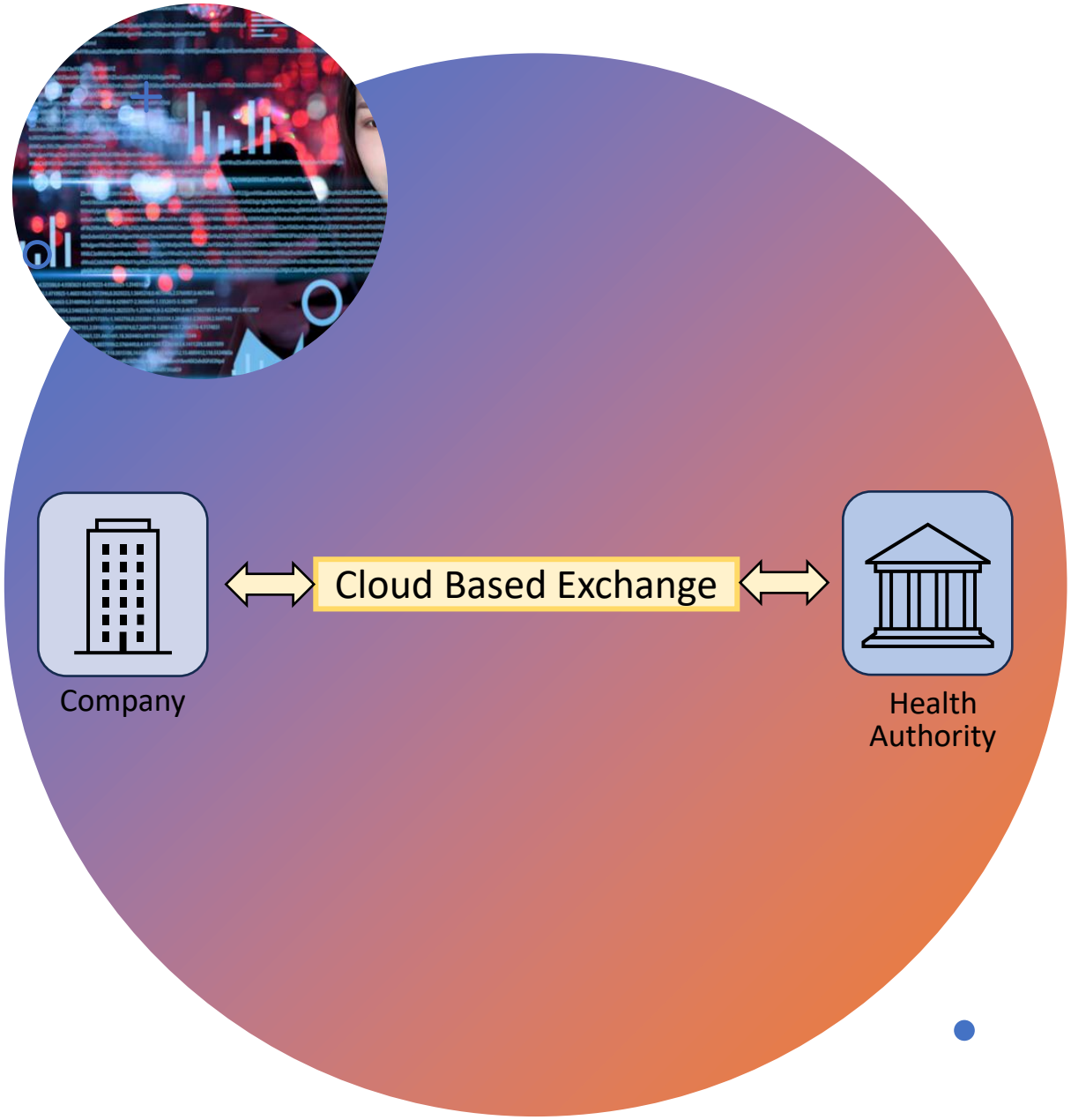
On an international level it's been going on for over 30+ Years

Some Important Dates on ICH Work

- 1990 ICH Formed
- 1995 EU Centralized Procedure Established
- 2000 ICH M4 Common Technical Document (CTD) Emerges
- 2003 CTD became the mandatory format for new drug applications in the EU and Japan, and the strongly recommended NDAs in the US
- 2016 Latest revision of ICH M4 Issued

Much has been done but more is needed!





Digitalization

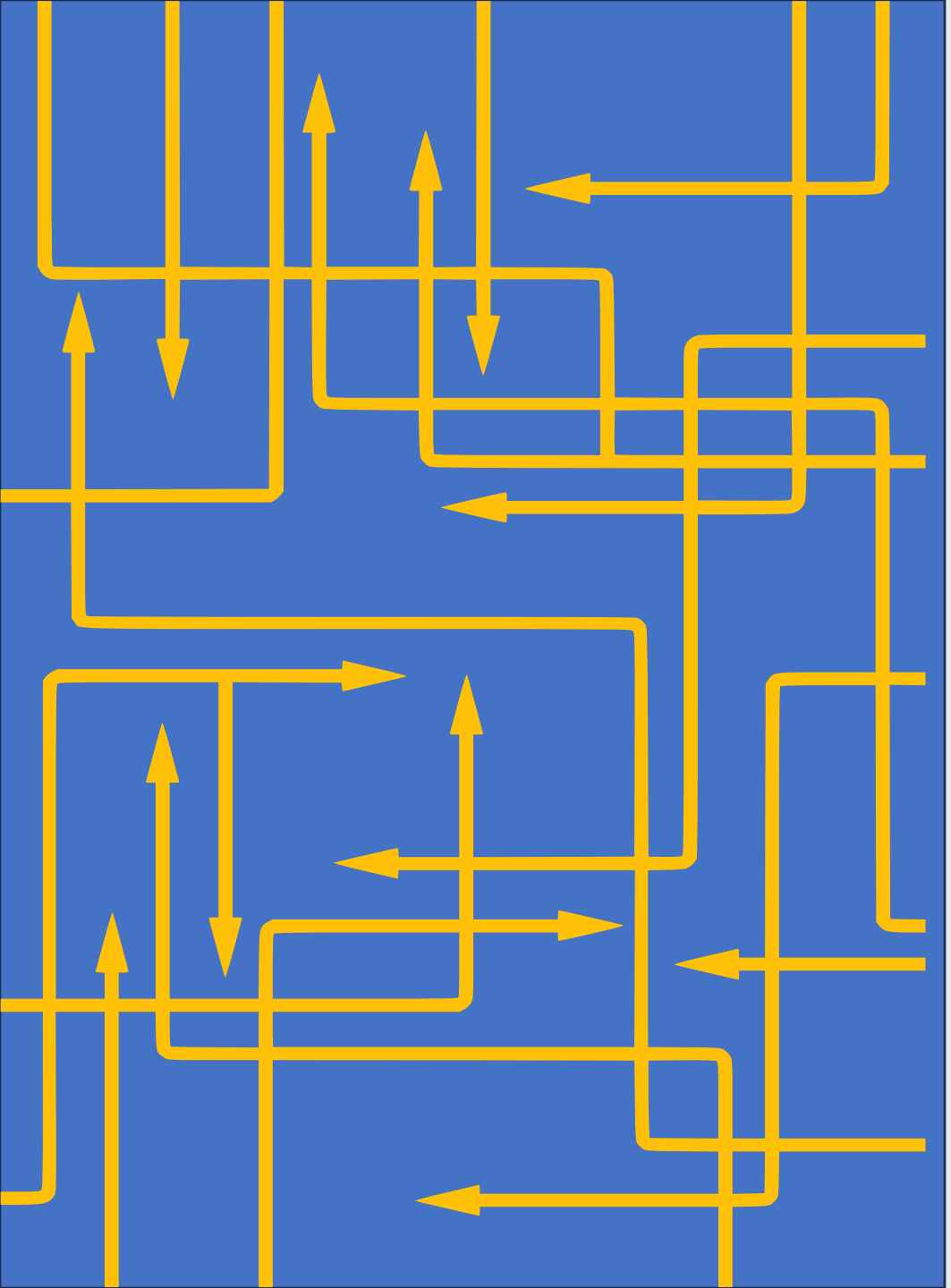
Starting to see digital cloud-based exchanges

- Designed to provide near real-time exchange of information/data between companies and regulators
- Repository of information and evaluations
- Increases standardization of data exchange throughout the product lifecycle
- Increases efficiencies and speed of access to information
- Ensures the security of the information
- Enabler of regulatory convergence

Example: Accumulus Synergy

Global nonprofit organization dedicated to developing such an exchange

https://www.accumulus.org/



Keeping that mindset that anything is possible. No limitations.

From an Industry Standpoint

If you had the power to establish a global convergent regulatory process for new product applications and/or post approval changes, what would it look like?

Two Strawmen to get the conversation going

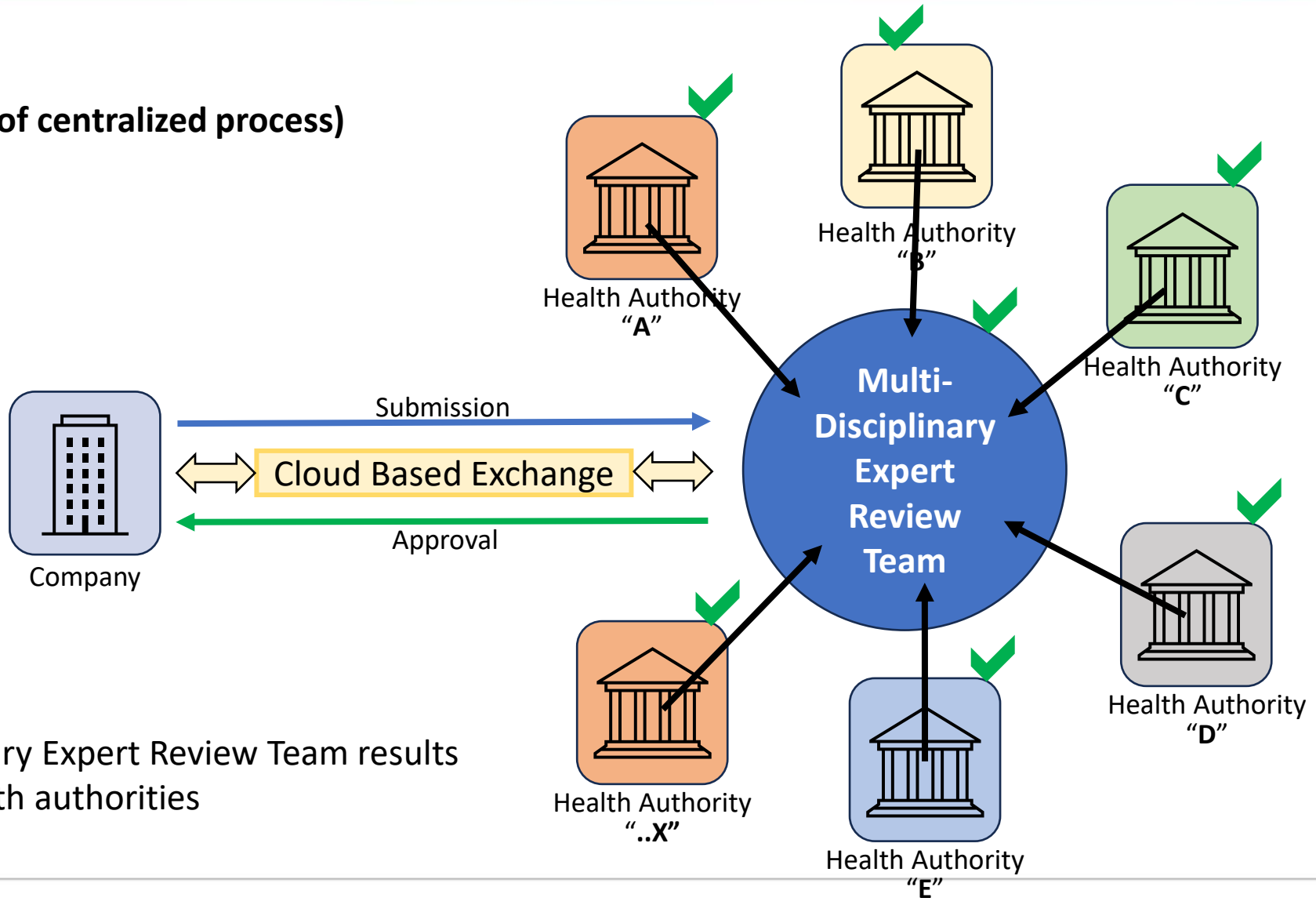
Strawman 1:

(Built loosely off EU model of centralized process)

Submission from Company to Multi-Disciplinary Expert Review Team for Review

Cloud Based Exchange (ongoing sharing of information/data)

Approval by Health Authorities through the Multi-Disciplinary Expert Review Team Approval



Approval by Multi-Disciplinary Expert Review Team results in rapid approval by all health authorities

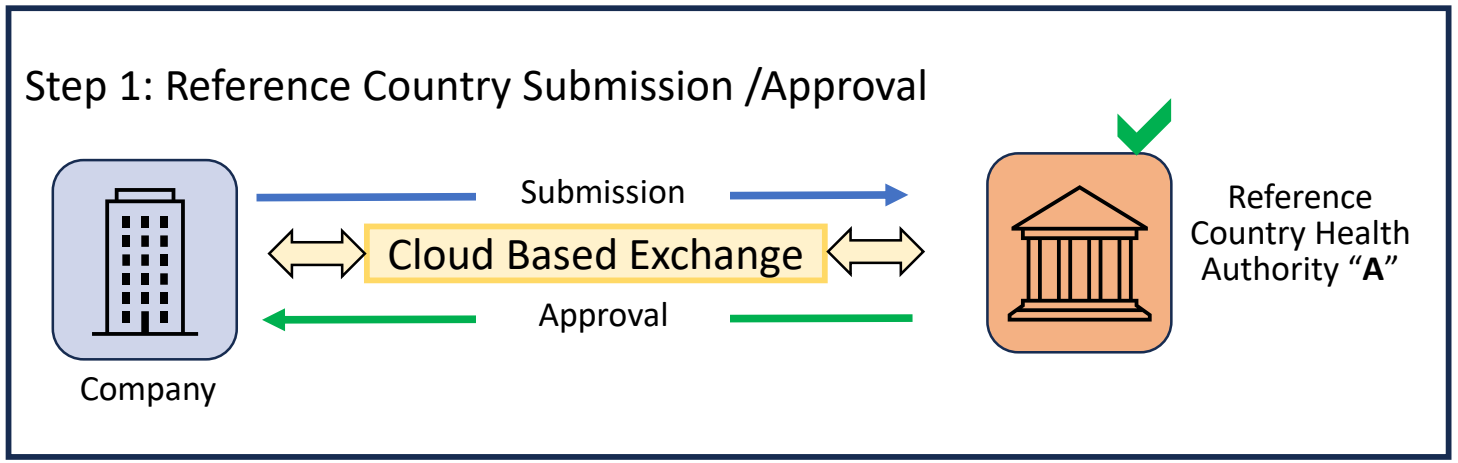
Strawman 2:

(Built loosely off old EU model of reference country process)

Submission from Company to Reference Country Health Authority

Cloud Based Exchange (ongoing sharing of information/data)

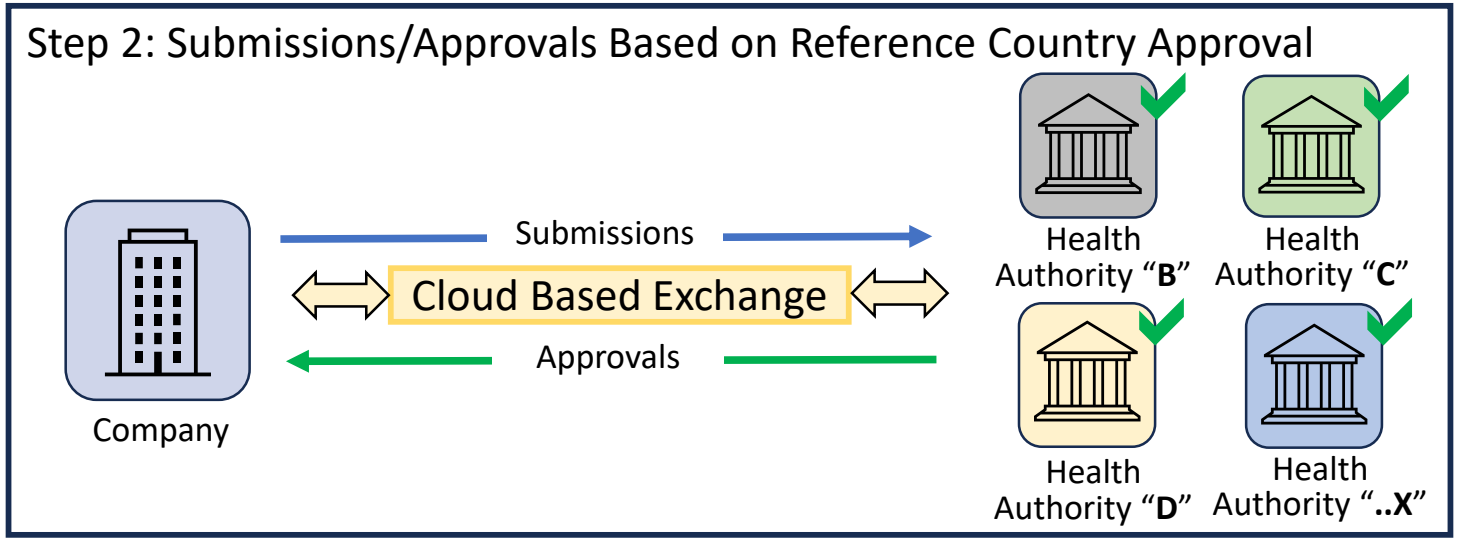
Approval by Reference Country Health Authority as First Step



Submissions from Company to Countries for expedited review.

Reference country's approval and all Q&A and assessments provided

Follow-on Approvals based on limited review and reference country approval



Approval by Reference Country results in expedited review and approval by each of the other Health Authorities

What would your global convergent regulatory process look like?