# Improving Supply of Medicines* Through SCIENCE & RELIANCE

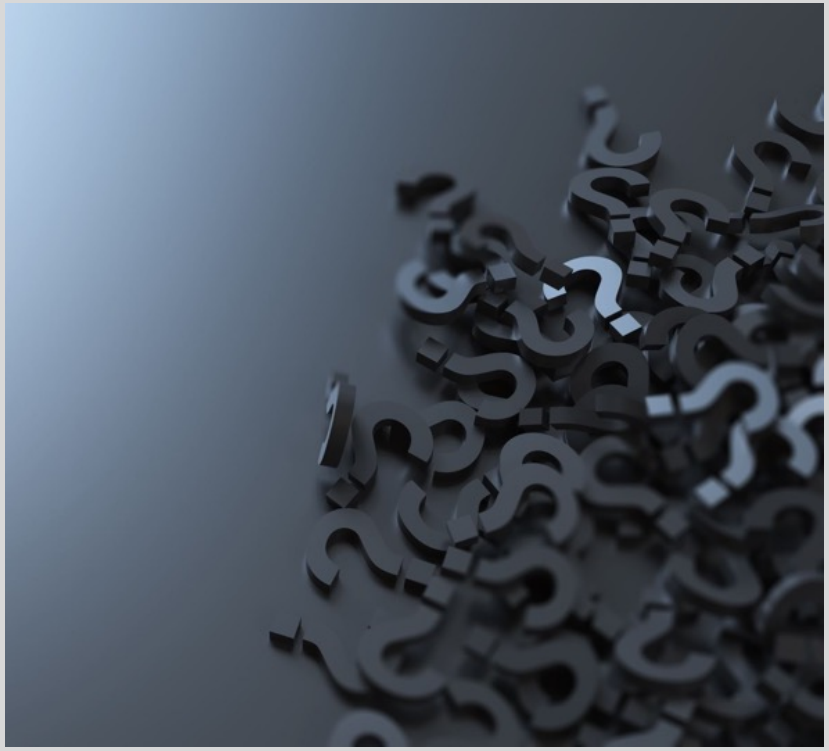

**One-Voice-Of-Quality on Post-Approval Changes Initiative**

Sponsored by the Chief Quality Officers of the top 25 pharmaceutical companies

What Are the Solutions ?


* Medicines: pharmaceutical drug products & vaccines

# What is the Problem ?



The global regulatory framework for managing Post Approval Changes (PACs) is ***not agile*, slows down continual improvement and innovation, is a threat to securing the supply chain, and can contribute to drug or vaccine shortages***

COVID-19 has amplified this state and the issue continues to grow

We need closer to real-time implementation of PACs

* It usually takes a minimum of 3-5 years for worldwide approval of a single PAC

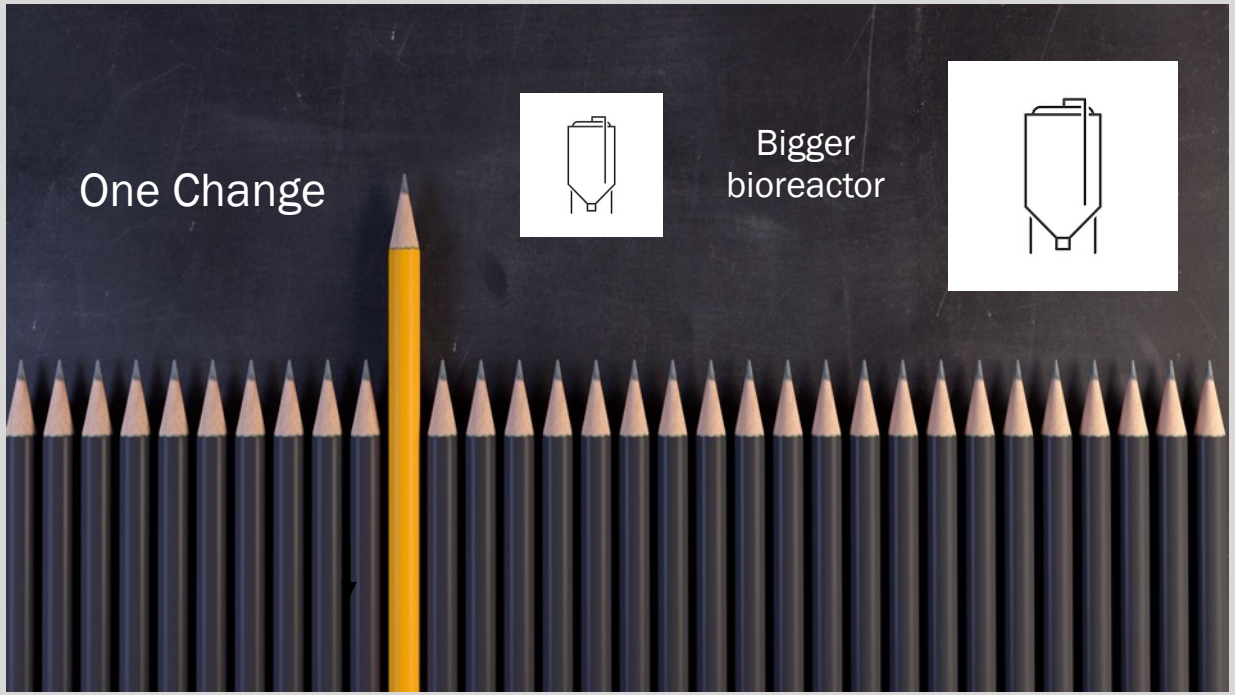
Note: Ensuring the security of the supply chain and reducing drug shortages is a wicked problem (*i.e.* highly resistant to solutions and highly complex) which has many contributing factors. Diseases are global; preventing and treating them requires global solutions developed by all relevant stakeholders together in a dialog. Solving for one stakeholder only will not solve the overall global problem

# PACs are a Natural and Essential Part of a Pharmaceutical Product's Commercial Lifecycle


- Upgrading (aging) manufacturing and testing facilities and equipment
- Maintaining cGMP compliance and a state of control
- Implementing evolving regulatory requirements and new technologies
- Emerging new knowledge about products and processes
- Supplier changes
- Continuous improvement

Bringing a vaccine or drug product to market is not the finish line.
The objective for manufacturers is an ***uninterrupted supply*** throughout the product's commercial lifecycle

# Global Regulatory Complexity, an Example




**1** SUBMISSION WITH 6 PACs → **7** PRODUCTS IMPACTED → LICENSED IN **138** COUNTRIES

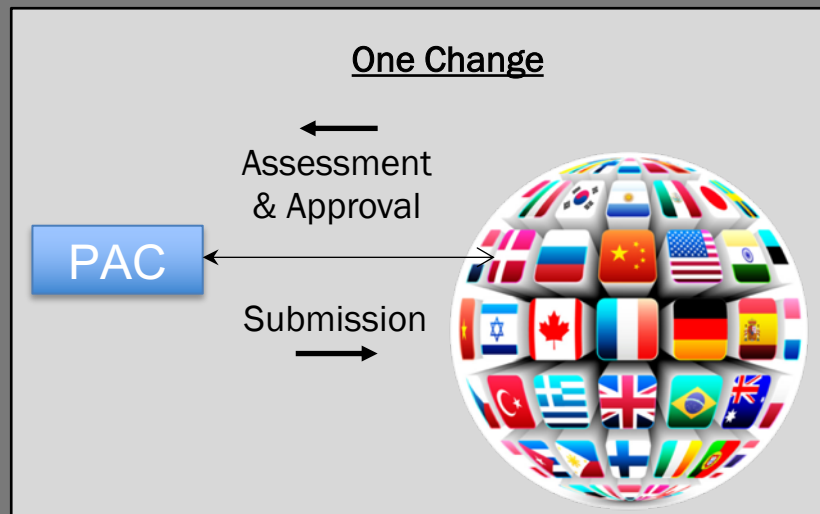
Country reporting category

- **39** NO REPORTING
- **37** MINOR CHANGE
- **62** MAJOR CHANGE

→ **22** (of the 62) COUNTRIES HAD **177** QUESTIONS OF WHICH **19** WERE DIFFERENT

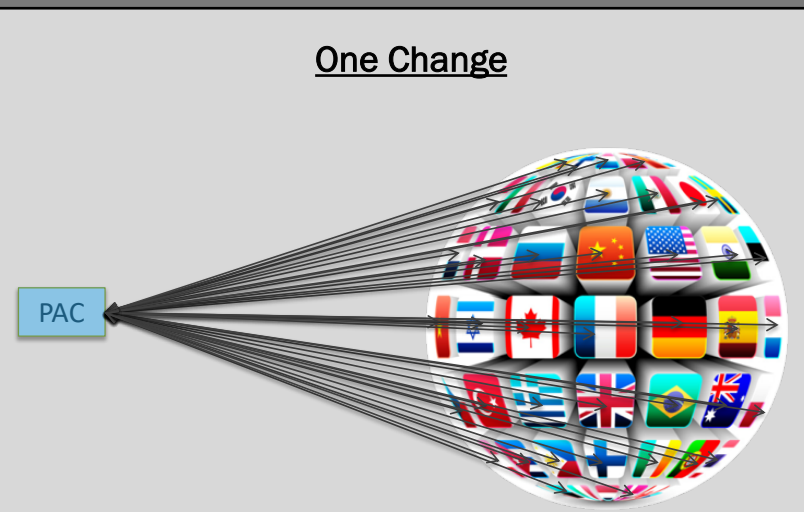
# ONE PAC seen from Two Different Angles

## REGULATORY AGENCY'S VIEW



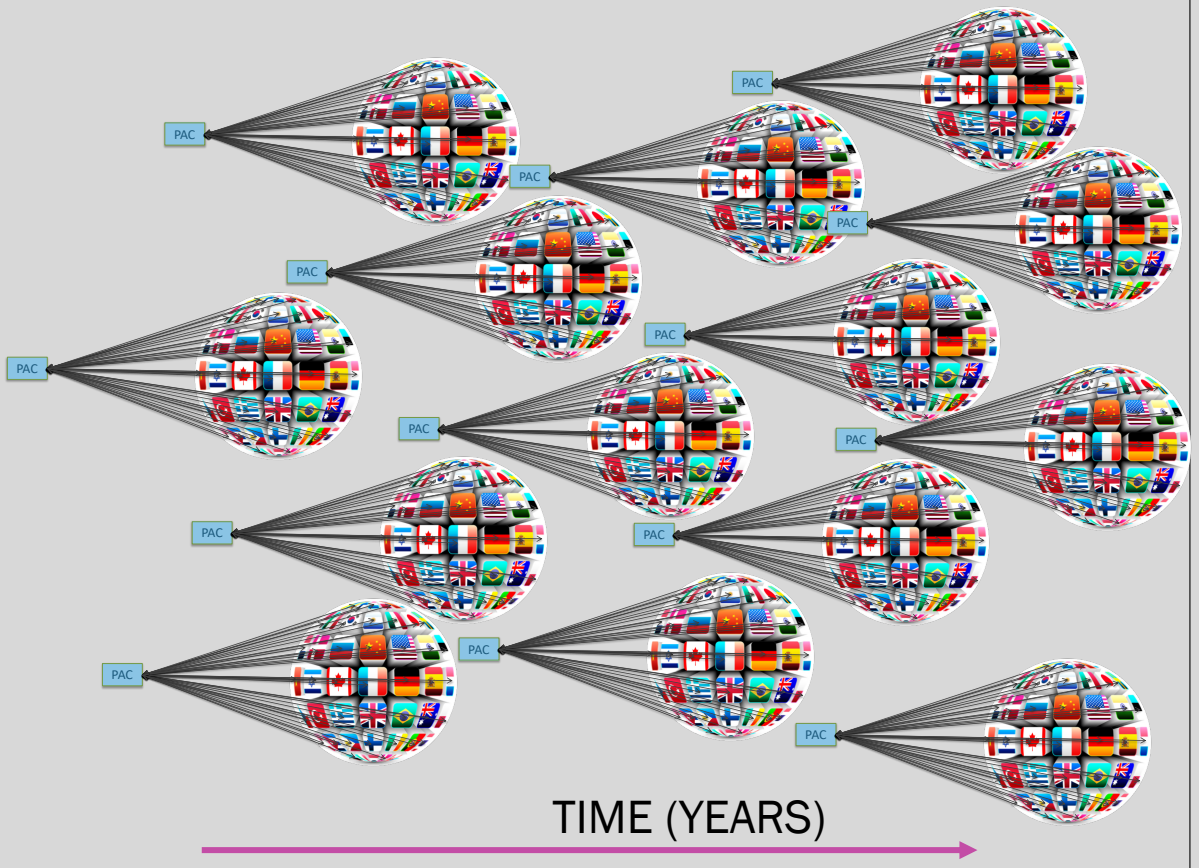

*ONE* submission, *ONE* assessment

## COMPANY'S VIEW

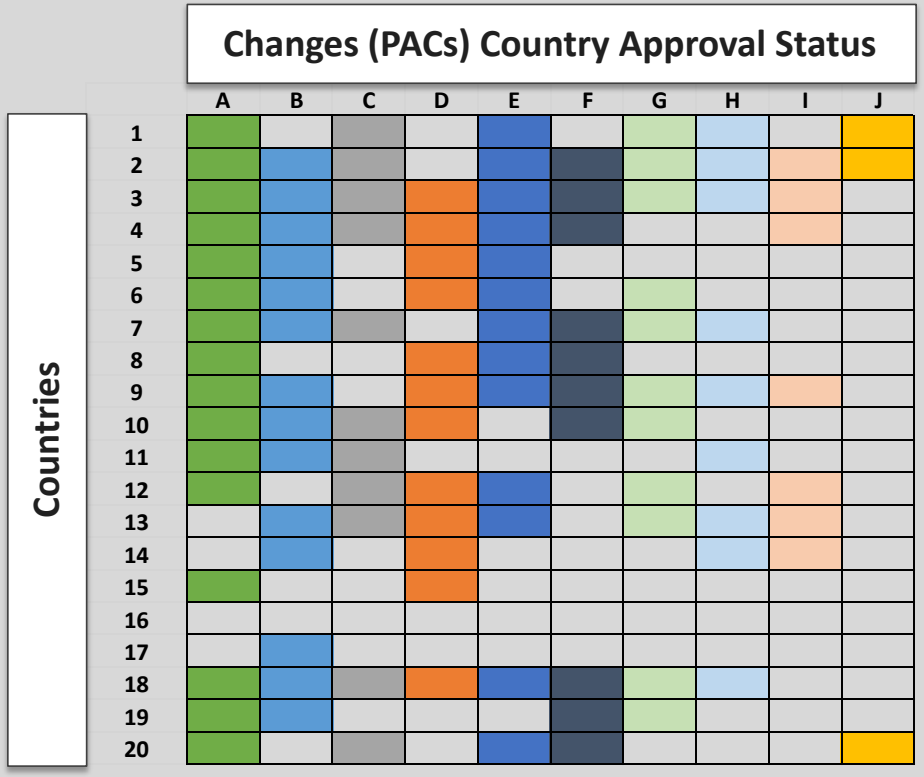



*MANY* submissions, *MANY* assessments

# Reality - Not One but Many PACs

# Ensuring Global Supply is Challenging When Managing an Inventory of Multiple Product Versions at the Same Time




Current global regulatory framework does not incentivize companies to implement new knowledge

Companies must manage an inventory of multiple versions of the same product depending on country approval status of individual PACs

***Deviations from expected country approval timelines, sudden changes in demand, or a need for urgent changes can lead to drug shortages***

Even Regulatory Agencies approving PACs with agility can be impacted with drug shortages due to the overall global regulatory complexity. The complexity continues to grow bigger; optimizing supply in isolation one country at a time is not a viable solution

# The Global Regulatory Framework Problem Has Been Known for a Long Time

2002

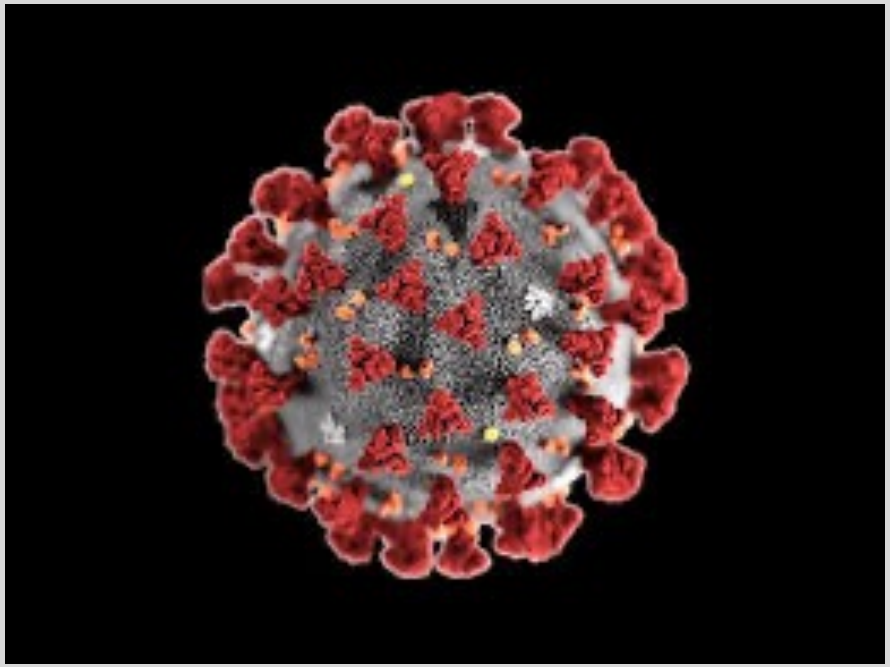
FDA Vision

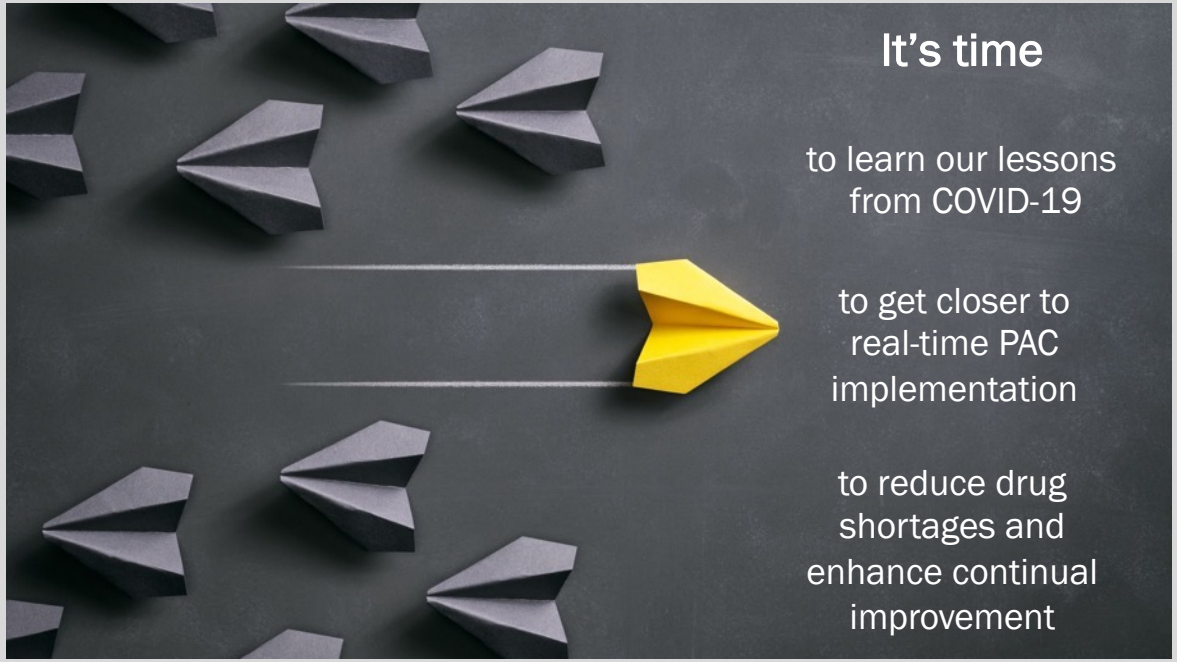
*"A maximally efficient, agile, flexible Pharmaceutical manufacturing sector that reliably produces high quality drugs without extensive regulatory oversight."*

2005

*"Delays in the implementation of innovation and continual improvement for existing products may occur due to different expectations in the three regions"*

# COVID-19 Has Demonstrated that the Global Regulatory Framework for PACs Is Not Agile Enough to Manage a Pandemic






National/regional emergency procedures implemented across the globe to avoid COVID-19 related shortages. Commonality: ***Regulatory Agencies relying more on each other and on companies***

TIME (~~YEARS~~ DAYS)

# During the Pandemic Regulatory Agencies have Used Various 'Emergency' or 'Exceptional' Ways to Improve PAC Agility

Regulatory Agencies have "down-graded" reporting level for some COVID-19 related PACs. Some Agencies have also relied more on the company's own PAC assessments. Common characteristics include*

- Formal application of Quality Risk Management (ICH Q9)
- Documentation of the company's PAC assessment in the PQS (ICH Q10)
- Emphasize accountability of the Quality role (GMP)

*An example of this is the Exceptional Change Management Process (ECMP) in EU
Note: Some Regulatory Agencies have also emphasized application of robust product and process understanding in line with ICH Q12 Guideline

# What are the Solutions ?


Solution #1: Reduce Regulatory Agency PAC ***approval timelines***

Solution #2: Enhance regulatory ***reliance*** for PACs amongst Regulatory Agencies

Solution #3: Manage more PACs in the PQS only* using a ***science*** and risk-based approach for companies using the latest product and process knowledge and demonstrating an effective PQS for managing PACs

*Managing more PACs in the PQS only (rather than as prior approval variations/filings) using a SCIENCE and risk-based approach is the focus for the 1VQ on PAC Initiative work. The solution builds on ICH Q9, Q10, & Q12

# Solution # 1: Reduce Regulatory Agency PAC Assessment **TIMELINES** & Make Them More Predictable

Encourage Regulatory Agencies to adopt and adhere to WHO guidance timelines for assessment of major prior approval PACs in no more than 6 month

*Example: Reducing worldwide PAC approval from an average 3 years to 6 months would be a ~80 % reduction in open PACs awaiting Regulatory Agency prior approval at any given time*

# Solution # 2: Enhance **RELIANCE** on Individual PAC Assessments Between Regulatory Agencies

Encourage National Regulatory Agencies to rely more on other Regulatory Agencies (WLAs) for assessment of individual PACs following WHO guidance based on the 5 principles: *Sovereignty, Transparency, Consistency, Legal basis, Competency*

The 1VQ on PAC Initiative is interested in dialog with Regulatory Agencies on harmonization of PAC processes

# Solution # 3: Manage More PACs in the PQS only* using a **SCIENCE** and Risk-Based Approach When a Company Demonstrates Effective PQS and Product and Process Understanding**

The Chief Quality Officers (CQOs) of the top 25 pharma companies have published how a company can demonstrate an effective PQS for managing PACs

The solution is in line with ICH Q9, Q10, and Q12 principles

The CQOs are

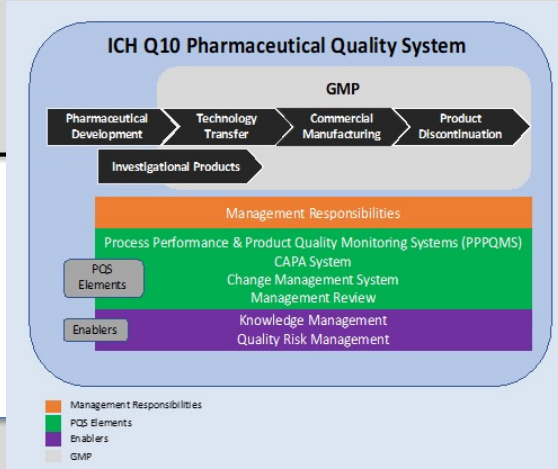
- Speaking with ONE VOICE (1VQ on PAC)
- Accountable for their company's PQS and its effectiveness
- Responsible for release of safe, efficacious, quality medicines to the market***

PDA Journal of Pharmaceutical Science and Technology July 2020, 74 (4) 456-467

The PQS provides the essential foundational framework for science and risk-based PAC decision-making

* Rather than through Regulatory Agency prior approval
** Realizing ICH Q10 Annex 1
*** Except for EU where the Qualified Person is responsible for batch disposition

# Solution # 3, cont'd: Manage More PACs in the PQS only. 1VQ on PAC Have Defined Effective PQS at **System Level**



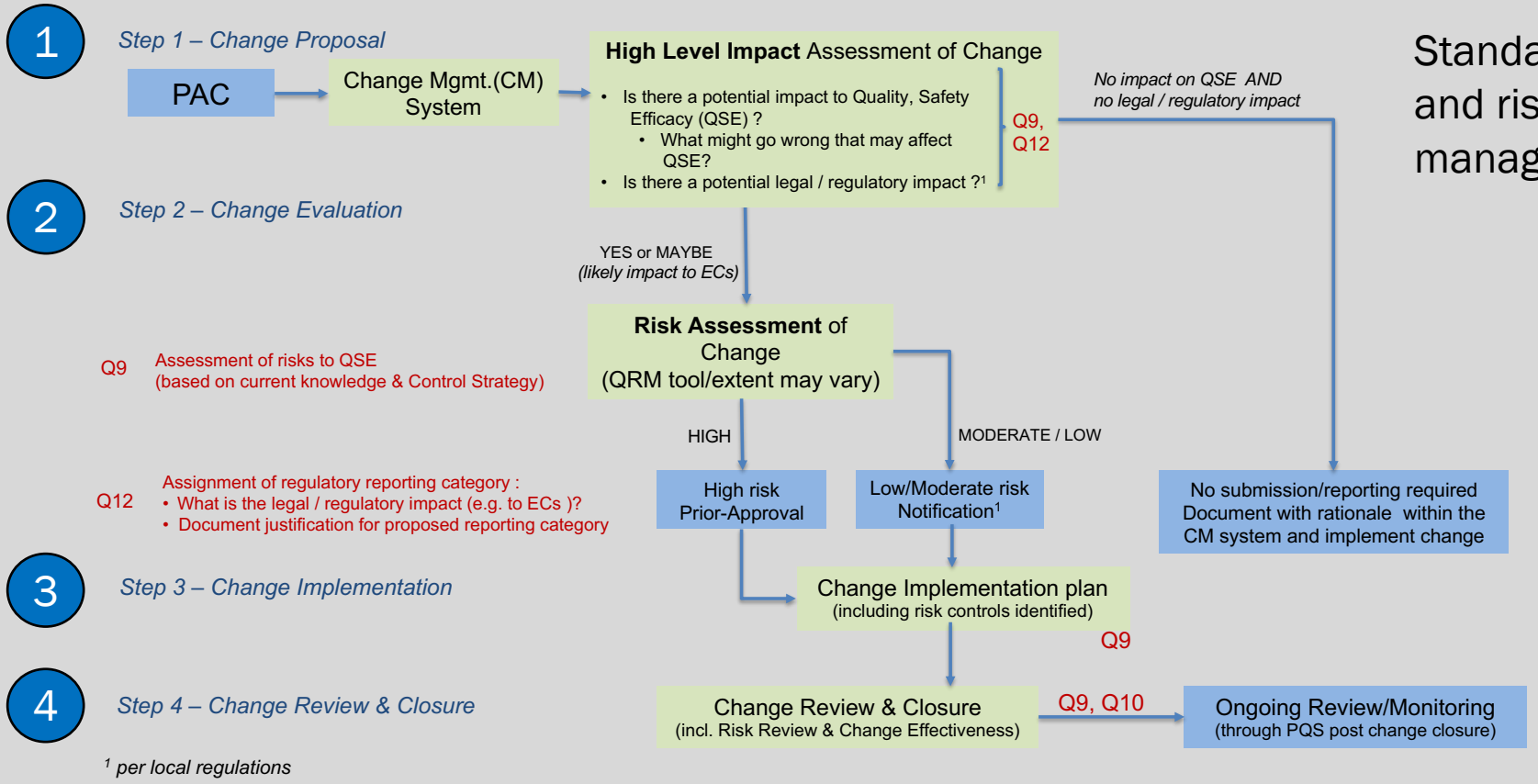

| ICH Q10 GUIDELINE | CQOs 1VQ on PAC PUBLICATION | EVALUATION |
|---|---|---|
| Pharmaceutical Quality System | Industry One-Voice-Of-Quality (1VQ) Solutions: Effective Management of Post-Approval Changes in the Pharmaceutical Quality System (PQS) through Enhanced Science and Risk-Based Approaches<br>*PDA J Pharm Sci and Tech 2020, 74, 456-467* | **Checklists or Guides** |
| **Enablers** | | |
| Knowledge Management (KM) | Effective PQS for managing PACs, **KM details** | |
| Quality Risk Management (QRM) | Effective PQS for managing PACs, **QRM details** | |
| **PQS Elements** | | |
| Process Performance and Product Quality Monitoring (PPPQM) | Effective PQS for managing PACs, **PPPQM details** | PPPQM: not published yet |
| Corrective Action and Preventive Action (CAPA) | Effective PQS for managing PACs, **CAPA details** | CAPA: not published yet |
| Change Management (CM) | Effective PQS for managing PACs, **CM details** | CM: published by PIC/S |
| Management Review (MR) | Effective PQS for managing PACs, **MR details** | MR: published by 1VQ on PAC |

Include the two enablers KM and QRM into evaluation checklists or guides for each of the four PQS elements

1VQ on PAC solution

Note: This solution requires that pharmaceutical companies fully implement and demonstrate that they have an effective PQS for managing PACs

# Solution # 3, cont'd: Manage More PACs in the PQS only. 1VQ on PAC Have Defined Effective PQS at **Individual PAC Level** As Well




Standard and practical science and risk-based approach to PAC management

Practical examples developed for
- Excipient supplier name change
- Shelf-life extension for pharmaceutical products
- Changes to analytical equipment deemed equivalent

More examples being developed & published

**1VQ on PAC solution**

# How Do We Get There ?

***First,*** acknowledge that the global regulatory framework for managing PACs is not agile and can't keep up with the pace of PAC change needed

**Initiate dialog** between stakeholders to develop a simpler global PAC framework based on

- Patient-centric global collaboration
- Practical, transparent, science & risk-based approach
- Harmonization towards standardization of PAC processes and data requirements
- Respecting Regulatory Agency sovereignty in decision making

Support initiatives aimed to **reduce** PAC assessment **timelines** in general

Encourage and support **regulatory reliance activities** to leverage Regulatory Agency resources, expertise and reduce global PAC timelines using the WHO Good Reliance Practice framework

Implement the 1VQ on PAC Science & risk-based Solution to **manage more PACs in the PQS only.** Ambition: >50 % reduction in prior approval PACs

# Where Can I Find More Information?

Website:
https://prst.ie/1vq/

**One-Voice-Of-Quality on**
**Post-Approval Changes Initiative**
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of the top 25 pharmaceutical companies

Concept Paper:
PDA Journal of Pharmaceutical Science and Technology 2019, 73 517-521

Solution Paper:
PDA Journal of Pharmaceutical Science and Technology 2020, 74 (4) 456-467