GILEAD
Creating Possible

Post Approval Change Management

Collaboration, Creativity and Commitment in a Complex Global Environment

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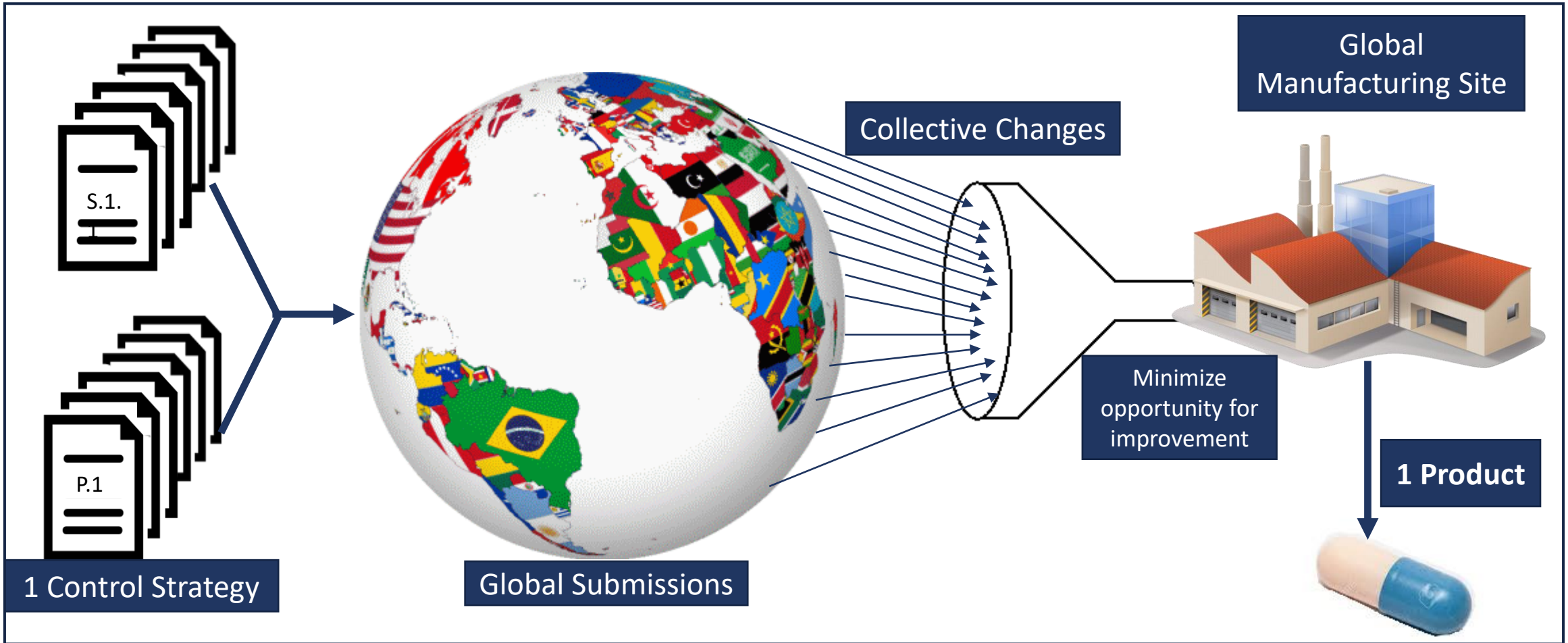
Linking to the Patient

- Continuing supply
- Timely/prompt supply
- Reduced regulatory burden (both regulators and industry)
- Building global efficiency

A Global Control Strategy/One Global Product



Shared Goal: Create incentives for rapid, continuous quality improvements and adequate supply to patients

The Starting Point

- ICH has dramatically improved global harmonization of regulatory expectations.
- ICH Q guidelines have provided direction for global regulatory convergence based on science & risk-based approaches.
- Interpretation & implementation have been inconsistent, especially for ICH Q – 8, 9, 10, 11 and 12.
- Lifecycle harmonization remains a significant regulatory management concern for multi-national companies & regulatory authorities.
- Ongoing efforts focus on expanding insights regarding risk and “the story.”

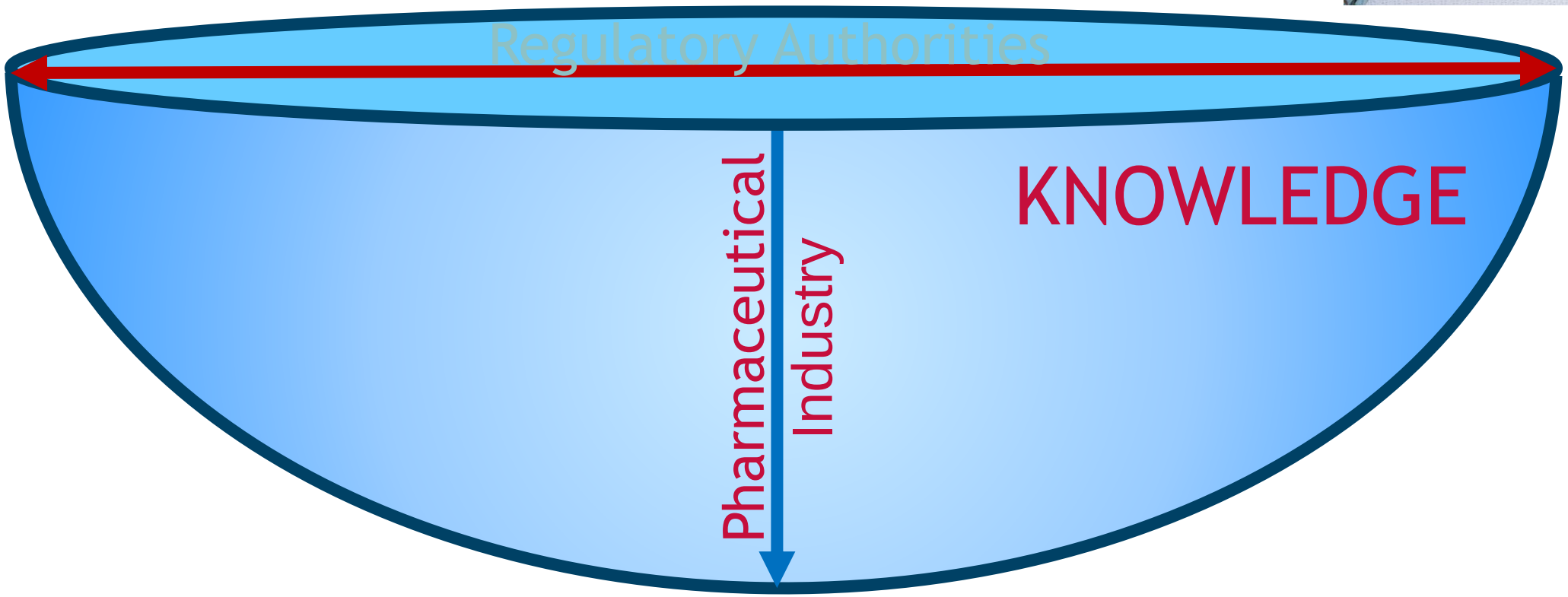
The Art of the Story

Industry
Regulators

Telling the story
Evaluating the story

Based on shared understanding

Leveraging Experience on Behalf of Patients



Regulatory Authorities possess a breadth of knowledge.
Pharmaceutical Industry possesses a depth of knowledge.

Current Landscape – Selected Ongoing Efforts

Q2(R2)/Q14 Analytical Procedure Development and Revision of Q2

Q3E Impurity Assessment and Control of Extractables and Leachables for Pharmaceuticals and Biologics

Q5A(R2) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin

Q9(R1) Quality Risk Management

Q12 Considerations for Pharmaceutical Product Lifecycle Management

Q13 Continuous Manufacturing

M4Q(R2) Revision of M4Q(R1) CTD on Quality Guidance

Also ICMRA Pilot!

International Coalition of Medicines Regulatory Authorities (ICMRA)

ICMRA is a voluntary, executive-level entity of worldwide Medicines Regulatory Authorities (MRA) complimenting ICH in supporting global and domestic collaboration by regulators and industry, thus facilitating global harmonization

ICMRA Pilot Programs

Collaborative Assessment: Use a collaborative assessment framework to identify and exploit areas of alignment between different regulatory agencies in terms of quality assessment for post approval CMC changes including PACMPs

Post Approval Change Management Protocol

Collaborative Hybrid Inspection (CHIP): Allow evaluation of a facility where multiple regulatory agencies have an interest in the facility and products to be covered by the on-site inspectorate via a hybrid inspection approach

Addition of new drug product manufacturing site for a sterile product

Advantages of ICMRA Collaborative Assessments and CHIP

- Collaborative partnership with participating and observing agencies
- Allow MRA's to take a single aligned regulatory action and thus potentially accelerate the availability of critical medicines in multiple markets, benefiting patients globally
- One single engagement with multiple MRA's, thus saving the manufacturing facility time, effort, and resources
- Potential cross regional convergence in assessment practices of CMC changes by MRA's.

Post Approval Change Management Moving Forward

- Implementing PACMPs globally (Q12 implementation globally)
- Using reliance (inspections) to support global PACMPs
- Cross product or cross site PACMPs
- Global dialog opportunities
- Building postapproval predictability = ensuring patient supply
- Facilitating knowledge sharing
- Expanding learnings from ICMRA pilot

Thank You