IPQ
INTERNATIONAL PHARMACEUTICAL QUALITY
Inside the Global Regulatory Dialogue

CURRENT INSIGHTS FROM LEADING REGULATORS

WHO and EMA Leaders Shed Light on WHO Listed Authorities (WLA) Initiative to Increase Global Regulatory Capabilities




During a WHO townhall session at the DIA Europe Conference, held in Brussels in mid-March, leaders from WHO and EMA explored the role that the new WHO Listed Authorities (WLA) initiative will play in WHO's global regulatory capacity strengthening efforts. Participants in the session included: • WHO Regulatory Convergence and Networks Team Lead Samvel Azatyan, who introduced and moderated the session • WHO Regulatory Systems Strengthening Team Lead Alireza Khadem Broojerdi – speaking about the objectives and progress of the WLA initiative • WHO Facilitated Product Introduction Regulation and Safety Unit Team Lead Marie Valentin, who continued the discussion of WLA as a pathway to regulatory efficiency and reliance, and • EMA International Affairs Head Martin Harvey Allchurch – discussing EMA/EU support for and engagement with the WHO regulatory strengthening, collaboration and reliance efforts.

UPDATES IN BRIEF: GLOBAL CMC/GMP DEVELOPMENTS

• WHO Alert on Falsified Propylene Glycol • Counterfeit Versions of Botox in Multiple US States • WHO Draft GMP Guidelines and National Registration Out for Comment • EMA GACP Guidelines for Starting Materials of Herbal Origin • GMP/GDP Inspectors Working Group 2023 Annual Report • Malaysia Seeking Feedback on Bioequivalence Inspection Guideline • US Congressional Hearing on FDA Oversight • Cofepris Enforcement and Regulatory Convergence Activities

FDA DRUG GMP WARNING LETTERS

Company	Facility Location	Product Type
Master Paints & Chemicals	Puerto Rico	Finished
Natco Pharma	India	Finished
C&T Dream Co	South Korea	Finished

FDA DRUG RECALLS

Among the four recalls posted in FDA's enforcement report during the week, one drew the most serious, Class I, rating. It involved the presence of particulate matter in one lot of methocarbamol injection.

INTERNATIONAL PHARMACEUTICAL QUALITY provides in-depth coverage of emerging drug, biologic and combination product CMC and GMP issues and developments with a mission of helping advance and harmonize the quality regulatory process globally. Headquartered in Washington, D.C., IPQ is read by regulatory agencies, manufacturers, suppliers, consultants, law firms, and universities around the world.

IPQ tracks the industry/regulator dialogue at key international forums along with the developments, initiatives, regulations, guidances and standards in the quality regulatory arena to create a uniquely valuable resource for the intelligence gathering and knowledge management needs of the pharmaceutical community.

IPQ's "actionable intelligence" is particularly valuable for thought leaders and decision makers who need to have a deeper understanding of the issues and their context to help shape regulatory policy and develop implementation strategies. Subscriber support allows IPQ, in turn, to make an important contribution to the efforts of key non-profit associations and public service organizations engaged in addressing the increasingly complex manufacturing and regulatory challenges for medicines in the global context.

IPQ is published online, and the substantial archive at IPQ.org is easily searchable through its keyword search indexes. Links to documents referenced and cross-links to related previous IPQ coverage in the area are included, allowing readers to quickly dig as deeply into an issue and its context as needed.

IPQ's ***"News Alerts"*** provide links to the first few paragraphs of the stories newly posted online. Subscribers and license holders can click through to the full stories.

The ***"Monthly Updates"*** provide the stories that went online during the month in a print-friendly PDF format, and are an easy way for subscribers to keep up with the critical developments impacting the quality regulatory process worldwide. Included are ***"Updates in Brief"*** on recent CMC/GMP developments of note with links to the referenced documents and to our related in-depth analysis. Also included is an annotated listing of FDA drug GMP warning letters and recalls as well as EU GMP non-compliance statements posted during the month.

WHO and EMA Leaders Shed Light on WHO Listed Authorities (WLA) Initiative to Increase Global Regulatory Capabilities

The WHO-Listed Authorities (WLA) initiative is gaining momentum in its efforts to strengthen regulatory capabilities and further open global cooperation and reliance pathways.

Building on the current Stringent Regulatory Authorities (SRA) scheme, the WLA framework provides the opportunity for a wider range of authorities to demonstrate reliance leadership capabilities based on assessment against a Global Benchmarking Tool (GBT) and performance evaluation (PE).

A successful pilot phase in 2022-2023 led to the publishing of a WLA "Operational Guidance" and a "Performance Evaluation Manual" in November 2023, which define the three risk-based pathways to achieve WLA status: ● a "routine" pathway used for countries that have never been benchmarked by WHO ● a streamlined pathway for countries previously assessed by WHO or a partner organization, and ● a shorter "abridged" pathway for current SRAs. A related Q&A was released in early March.

The first three agencies to be recognized as WLAs are Korea's Ministry of Food and Drug Safety (MFDS), via the streamlined pathway, Singapore's Health Sciences Authority (HSA), via the routine pathway, and Swissmedic, via the abridged pathway. The next group of WLA applicants is under assessment, with the announcement of additions to the list expected by July.

During the DIA Europe Conference in Brussels in mid-March, WHO held a "townhall" session at which key WHO and EMA officials discussed the background and objectives of the WLA initiative, how it fits into "facilitated product introduction" and other WHO reliance programs, and the "trusted partner" relationship between EMA and WHO.

Participating in these discussions were: ● WHO Regulatory Convergence and Networks Team Lead Samvel Azatyan ● WHO Regulatory Systems Strengthening (RSS) Team Lead Alireza Khadem Broojerdi ● WHO Facilitated Product Introduction Regulation and Safety Unit Team Lead Marie Valentin, and ● EMA International Affairs Head Martin Harvey Allchurch.

The session also covered strengthening clinical trials to provide high-quality evidence and the role of regulators in global efforts to address antimicrobial resistance (AMR). Insights on these issues were shared by WHO Science Division Senior Advisor Vasee Moorthy and WHO AMR Division Governance and Strategic Initiative Unit Head Jean Pierre Nyemazi.

WLA Listing Combines Benchmarking and Performance Evaluation

WHO RSS Team lead Khadem began the session by explaining the need for strengthening global regulatory systems, remarking that "only about 30% of countries have a functional...very stable and integrated regulatory system."

Following a 2014 mandate from the World Health Assembly to address this issue, two "important strategic priorities" were developed – to build regulatory capacity across the 194 WHO member states and, at the same time, encourage reliance, networking, and work-sharing. "Aligned with this strategy," Khadem explained, the idea of the WHO Listed Authorities was conceived.

A 2021 policy document defined the specific WLA objectives as: ● providing a transparent and evidence-based pathway for regulatory authorities to be globally recognized ● promoting access and the supply of safe, effective, and quality medical products, and ● optimizing the use of limited resources by facilitating reliance.

Khadem outlined the key considerations involved in the WLA assessment process in relation to benchmarking and performance evaluation and the "maturity level" of an authority and described the three evaluation pathways. ***[Khadem's full remarks are appended below.]***

A "technical advisory group" reviews the evaluation reports and advises whether and how an applicant authority should be added to the list.

Noting that the next meeting of the TAG was planned for mid-April, Khadem expressed hope that a new group of authorities would join the list soon. He also shared that "a lot of applications" were being received, some coming from SRAs, and some from other countries.

In closing, Khadem reiterated the benefits of the WLA framework, commenting that, in the wake of the conference's opening plenary on partnerships for sustainability, he could add a new one to the list in the future – the environmental benefits of reliance and work-sharing due to reduced duplication of testing and documentation. ***[See IPQ's Weekly Supplement for the week ending April 5, 2024.]***

WLA Framework Provides a Pathway to Regulatory Efficiency and Reliance

Following Khadem to the podium, WHO's Valentin focused on the efficiencies that can be achieved through reliance and work sharing. She highlighted how the WLA framework will contribute to the established WHO reliance pathways such as the Collaborative Registration Procedure, Global Health Procedures, and Regional Joint Assessments. ***[Valentin's full remarks are appended below.]***

Pointing out that duplication of work "is not the best way to use the resources of the regulators and the industry," she emphasized the imperative for a risk-based approach so that resources are used "where they are most needed" – concentrating on products that have not been evaluated by any regulators and utilizing the "output of others" for medical products that have been prequalified or approved by stringent regulatory authorities.

Valentin explained the rationale for the transition from SRAs to WLAs – a move that offers the opportunity for "up and coming regulators" to be recognized for their efficiency and performance and to serve as a reference authority for reliance in a "transparent and evidence-based system."

Reliance can be used in many regulatory functions, she noted. The WLA initiative enables a modular approach for functions including inspection, batch release, registration, and post-authorization activities. It also acts as a "capacity building exercise" when regulators are exposed to assessment and inspection reports from other authorities.

She highlighted the recently published WLA Q&A, which addresses "a lot of questions" received to date – such as period of validity, transitional WLAs, determination of scope, and how the WLA will be used in the context of prequalification – and invited delegates to submit any others for consideration in the next update of the Q&A. ***[A link to the WLA webpage, which includes the Q&A, is provided below.]***

Synergies Between EMA Activities and WHO Highlighted

Later in the WHO session, EMA's Harvey had the opportunity to reflect on synergies between "what WHO is trying to do at a global leadership level and what we at EMA are trying to do in terms of responding and contributing to what WHO is doing."

He spoke about the "trusted partner" relationship between EMA and WHO, the EU-Medicines for all (EU-M4all) initiative, and EMA's involvement in the collaborative and facilitated pathways discussed by Valentin – pointing out that EMA has a "reliance model of 30 regulators of incredible diversity in size, competence and skill sets" in the European regulatory network.

Acknowledging the "huge amount of responsibility" and work done by the WHO Regulation and Prequalification team, he highlighted the "extraordinary cooperation" with EMA during COVID-19 on Emergency Use Listing for vaccines and therapeutics, and the Opening Procedures at EMA to Non-EU Authorities (OPEN) pathway ***(see Part I of IPQ November 14, 2022).***

Another example of where EMA engages with WHO is on Certificates of Pharmaceutical Product (eCPP), the "unsung heroes of reliance." Harvey commented that around 1,300 certificates were issued by EMA last year and that there were only five countries for which EMA had not issued CPPs since they were introduced – speaking to their value "in promoting and supporting reliance."

Training is also an "incredibly important" area where EMA – and the wider EU regulatory network – can support WHO by bringing in "hands-on experts" to contribute to training other regulators.

At the request of the session moderator, WHO's Azatyan, Harvey also responded to questions submitted before the Q&A session began around why an SRA would "actually step up and do all that work to become a WLA?" He explained that a major reason was credibility. EMA may want to collaborate and partner with other regulators around the world, but "if we haven't done the work and gone through the process of becoming a WHO-listed authority, we are not credible as a partner for other regulators."

Support for WLA Initiative Explored in Q&A

Following their presentations, session speakers answered questions from the audience on a range of topics including: ● facilitating acceptance of WLAs as reference authorities ● updates on authorities undergoing evaluation with the global benchmarking tool ● encouraging countries with more developed regulatory systems to use reliance, and ● incentives for a Stringent Regulatory Authority to apply for WLA status.

The WHO team clarified that the motivation for the WLA initiative originated from the member states, and that current WHO guidelines referring to SRAs will be updated to replace them with WLAs to help facilitate acceptance of the new framework.

The transitional period will end by March 2027, but Khadem shared that "according to our expectations, perhaps before the end of this year or by the middle of next year, we will have all the previously recognized SRAs on the list." He suggested that one of the reasons for this is the authorities' "mandate and contribution to public health and global health."

Regarding updates on authorities undergoing evaluation, Khadem explained that the member states requested that the information not be made public until successfully completed. However, a "Coalition of Interested Parties" is supporting the authorities through the process, and they are made aware of the status with the consent of the authorities involved.

EMA's Harvey shared that the EU Medicines Network is applying for WLA status as part of its responsibility to contribute to public health delivery and that each individual agency will become "recognized as a WLA in their own right."

Referring to reliance as a "21st-century regulatory tool," he suggested that a "different narrative" needs to be established to encourage reliance as part of being a mature regulator. "Reliance actually is a strength and should be seen as a strong way of regulating in the 21st century – knowing the complexity of tools, the complexity of drug development, and the complexity of new medicines, and the resource constraints we are all under."

In his closing remarks, Azatyan concurred with Harvey, noting that a central theme at the current session and at a pre-conference workshop on reliance had been that "the patient is at the center of all of this work, and we should not forget about it."

"And it is true that not any single regulator – even the most resourced one, the strongest one – can do everything alone. And they don't need to do it alone. This was, in my opinion, the perfect conclusion of this discussion today: that only by joining forces with all involved stakeholders – regulators, industry, patient organizations, academia, researchers, all of us – can we achieve our goal of improved access to the most important life-saving medical products for all."

[Editor's Note: See IPQ's Weekly Supplements for the weeks ending February 23, 2024, and March 1, 2024, for insights from WHO, FDA, EMA, PMDA, and ANVISA on "transforming global regulatory CMC practices in an age of regulatory innovation" and the international collaboration initiatives to manage the evolving landscape.]

WHO 2021 Technical Report Provides Reliance Roadmap

Part of WHO's mission to enable patient access to quality medical products is to develop, establish, and promote international standards, which it does through an Expert Committee on Specifications for Pharmaceutical Products (ECSPP).

ECSPP meetings have been held annually since 1947, and the committee's work has expanded significantly over the years – especially since the COVID-19 pandemic. A comprehensive summary of ECSPP meeting discussions and outcomes is published in WHO's Technical Report Series (TRS). Adopted guidelines are provided as annexes to the reports, which are available on the WHO website, dating back to 1965.

At the October 2020 ECSPP meeting, WHO's Azatyan and Valentin, representing the Regulatory Convergence and Networks Team, presented a proposal for "good reliance practices" (GRelP). This proposal, along with companion guidance on "good regulatory practice" (GRP), aims to "provide a more efficient approach to regulatory oversight, thereby promoting access to quality-assured, effective, safe medical products."

The GRelP and GRP guidelines were adopted and appear in Annexes 10 and 11, respectively, of TRS 1033, published in 2021. The report describes the background, development, and stakeholder and public consultation carried out on the guidelines. ***[Links to the WHO Technical Report 1033 and ECSPP webpage are provided below.]***

The 30-page Good Reliance Practices guideline offers a detailed roadmap addressing key concepts such as: ● reliance versus recognition ● unilateral versus mutual reliance or recognition ● lifecycle approach ● risk-based approach, and ● regional reliance mechanisms.

Also outlined are the "principles of good reliance practices," such as "universality," sovereignty of decision-making, transparency, respect of national and regional legal bases, consistency, and competence. Other sections include potential barriers and enablers for reliance and practical examples.

THE DEFINITION OF RELIANCE IN WHO'S GRelP GUIDELINE

The act whereby the regulatory authority in one jurisdiction takes into account and gives significant weight to assessments performed by another regulatory authority or trusted institution, or to any other authoritative information, in reaching its own decision. The relying authority remains independent, responsible and accountable for the decisions taken, even when it relies on the decisions, assessments and information of others.

April RPQ Newsletter Provides Updates on Coalition of Interested Parties

During the WHO Townhall panel discussion, WHO's Khadem referred to the "Coalition of Interested Parties" (CIP) group supporting the RSS work. The CIP was established in 2021 to provide a framework for collaboration between WHO and a network of organizations contributing to the RSS initiatives.

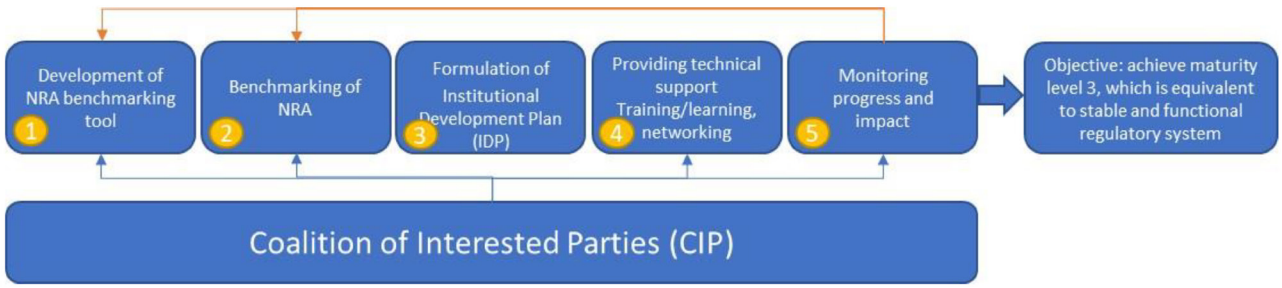
A CIP "global steering group" has laid out a five-year strategic plan for January 2023 – December 2027, with a mission statement to "promote collaboration and alignment of partnership efforts to support regulatory system strengthening at national, regional and global level, through an agreed platform for robust coordination, transparency, communication, and stakeholder engagement."

The April 2024 edition of the WHO Regulation and Prequalification newsletter reports that the CIP convened in mid-April for a second "support plan development meeting" and that four new members, including the United States Agency for International Development (USAID), joined the current membership of 29 organizations. ***[Links to the CIP strategic plan and WHO RPQ newsletter are provided below.]***

Among current members are: ● the African Union Development Agency (AUDA-NEPAD) ● the Bill & Melinda Gates Foundation (BMGF) ● the Centre for Innovation in Regulatory Science (CIRS) ● the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) ● Swissmedic ● USP ● Germany's Federal Institute for Drugs and Medical Devices (BfArM) ● Australia's Therapeutic Goods Administration (TGA) ● the Coalition for Epidemic Preparedness Innovation (CEPI) ● the European Directorate for the Quality of Medicines & Healthcare (EDQM) ● the Wellcome Trust, and ● EMA.

ROLE OF THE CIP IN REGULATORY SYSTEMS STRENGTHENING

Below is a graphic and list of objectives of the WHO five-step regulatory capacity-building model, taken from the Coalition of Interested Parties (CIP) "Terms of Reference," showing the stages in which the CIP network is engaged. Minor formatting changes have been made by IPQ. A link to the CIP Terms of Reference is provided below.



The **objectives** of the Network include:

- the more effective use of resources directed at strengthening regulatory systems, consistent with good regulatory practices
- enhancing the capacity, consistency and sustainability of regulatory support interventions
- promoting the sharing and adoption of best practices between participants in the Network, and
- reducing burden on regulatory authorities caused by uncoordinated, duplicative and potentially incongruous support activities.

MHRA Leader Stresses Importance of Agency Partnering

On January 1, 2024, the UK's Medicines and Healthcare products Regulatory Agency (MHRA) adopted new recognition routes with international partners intended to leverage "the expertise and decision-making of trusted regulatory partners" in facilitating "safe access to new medicines."

The International Recognition Procedure (IRP), detailed in a guidance released in August 2023, builds on existing partnerships developed through the Access Consortium and Project Orbis and aims to free up resources for the agency to focus on its Innovative Licensing and Access Pathway (ILAP). ***[See IPQ January 12, 2022, Part II. A link to the IRP guidance is provided below.]***

Seven partner countries/jurisdictions named as "Reference Regulators" are: Australia, Canada, the EU/European Economic Area, Japan, Singapore, Switzerland, and the United States.

> **MHRA CEO June Raine recently shared her views on "the vital importance of working in partnership with other regulators" in an interview with FDA Office of Global Policy and Strategy (OGPS) staff. The interview was done in connection with a February visit to Europe by a delegation of OGPS leaders and FDA Commissioner Robert Califf *(see IPQ's Weekly Supplement for the week ending March 29, 2024)*.**

The IRP, Raine commented, "will be a very important tool in our regulatory toolbox." At the same time, MHRA intends to continue working on innovation pathways "where we add value" – particularly in areas that are challenging for regulators, where "one size does not fit all," such as products with very short shelf lives or those for rare genetic disorders.

"This is a really exciting time in the evolution of regulation," Raine said, "and my ambition is for our voice to be part of that international discussion." ***[A link to the full interview is provided below.]***

UK's IRP Will Align with Other Reliance Programs

Several MHRA leaders participated in a series of webinars to explain the IRP process following publication of the IRP guidance in August 2023. The webinars outlined the background, processes, and updates involved in the new recognition procedure as it developed.

Introducing the first webinar in September, Healthcare Quality and Access Division Interim Executive Director Julian Beach explained that the recognition framework would result in "increased capacity...to respond more quickly."

Beach maintained that it would strengthen international work with "our regulatory peers" but that the agency would retain "our sovereign powers and be a sovereign regulator." Also important, he stressed, is providing "predictability and reliability."

> **Biologics Unit Team Leader Leonard Both highlighted that recognition procedures used by other leading agencies had been considered in informing the development of the MHRA procedure, so it is "very much aligned with what other regulators are doing in this space."**

He pointed to guidance available from the Singapore Health Sciences Authority, Swissmedic, and Australia TGA, noting that Singapore has been using reliance and recognition for "several decades." HSA and Swissmedic were recently named the first WHO Listed Authorities, along with Korea's MFDS.

MHRA Deputy Director of Innovative Medicines Shirley Hopper then explained how the IRP will be an option alongside national procedures and the current collaborative initiatives such as the Access Consortium and Project Orbis. She discussed the IRP requirements and stressed that a full assessment report from the reference authority, unredacted apart from assessor names, will be needed. Product types in scope include cell and gene therapies, vaccines, and biosimilars.

NASEM Report Calls for Increased Use of Reliance

During her interview with FDA staff on agency partnerships, MHRA's Raine mentioned that much of the current focus on recognition and reliance stemmed from a National Academies of Sciences, Engineering, and Medicine (NASEM) 2020 report on "Regulating Medicines in a Globalized World," which called for increased reliance among regulators. ***[A link to the NASEM report is provided below.]***

Eminent contributors and reviewers for the NASEM report included: ● FDA Commissioner Robert Califf, then at Duke University ● EMA Executive Director Emer Cooke, then at WHO ● EDQM Director and International Pharmaceutical Regulators Programme Chair Petra Doerr, then a consultant ● EMA International Affairs Head Martin Harvey, then at Unitaid, and ● former MHRA CEO Ian Hudson.

The year-long study involved interviews with key leaders from a range of countries to share their insights at committee meetings and information-gathering sessions, culminating in a 170-plus page report.

> **The report chapters address: ● "the job of medicines regulators in today's world ● what policymakers need to know about today's regulatory environment ● stakeholder views of recognition and reliance ● removing impediments and facilitating action for greater recognition and reliance among regulatory authorities, and ● the way forward."**

The study was funded by FDA and senior agency leaders in international programs, policy, and strategy are acknowledged in the report. The Bill and Melinda Gates Foundation supported information-gathering sessions in London, and BMGF Global Health/ Integrated Development Regulatory Systems Initiatives Lead Murray Lumpkin was on the committee that led the study.

A year later, in 2021, NASEM published another report on a study commissioned by FDA on "Innovations in pharmaceutical manufacturing on the horizon: technical challenges, regulatory issues and recommendations." One of the key regulatory challenges to introducing manufacturing innovations – recognized as a "strong and recurrent theme" – was the lack of a global, harmonized approach toward regulatory expectations.

[Editor's Note: See ● IPQ January 27, 2019, for insights on the BMGF's expanded commitment to helping solve the complex CMC, regulatory, financial, and distribution challenges of providing quality medicines for low- to middle-income countries, ● IPQ August 28, 2022, for an in-depth review of the presentations and discussions at the workshop held on the NASEM "Innovations in manufacturing" report, and ● IPQ's Weekly Supplement for the week ending March 29, 2024, for current FDA Europe Office priorities in promoting global regulatory convergence around cutting-edge technologies.]

LINKS:

- WHO Listed Authority Webpage
- WHO Technical Report Series 1033, 2021
- WHO ECSPP Webpage
- CIP Strategic Plan 2023-2027
- WHO April RPQ Newsletter
- CIP Terms of Reference
- MHRA International Recognition Procedure (IRP) Guidance
- FDA Interview with MHRA's June Raine
- MHRA September 2023 Webinar on the IRP
- NASEM Report on Regulating Medicines in a Globalized World




[Subscribers CLICK HERE for the WHO and EMA panelists' comments at the DIA Europe Conference.]

IPQ'S IN-DEPTH COVERAGE RELEASED SINCE 2020

The following are the headlines of the in-depth stories that IPQ has released since 2020. The topic headings for parts of a larger multipart story are included. The stories are listed in reverse chronological order. Readers of the Weekly Supplement can then click though to those that are of particular relevance to the regulator presentation, news briefs, and compliance information featured in the issue. Those of particularly high relevance to the Weekly regulator story are indicated with a red star.

2024

The Challenges of Evolving Pharma from a Compliance to a Risk-Based Control Strategy Mindset Are Drawing Conference Spotlight

- Critical Thinking in Risk Management and Data Governance
- Quality Culture/Oversight in Aseptic Operations
- Takeda's Annex 1-Based Global CCS Program
- QRM Tools in Root Cause Analysis
- Annex 1 Revisions and the CCS Implications

2023

CMC Innovation Support Programs Advance at EMA and FDA, with Distributed and Continuous Manufacturing on Front Burner

- European Regulatory Network Support for Manufacturing Innovation
- FDA's Expanding Engagement with Advanced Technologies
- Barriers to CM Adoption Explored at USP/RAPS Workshop
- Distributed/POC Manufacturing and the CMC/Quality Regulatory Paradigm

Implementing ICH Q9(R1) Will Entail a Heightened Focus on Integrating Knowledge into Risk-Based Decision-Making

- Insights from Expert Working Group Members on ICH Q9 Revisions
- Panel Discussion Among PRST Meeting KM/QRM Experts
- Risk-Based Decision-Making
- Risk Management in Drug Shortage Prevention

Industry is Urging EMA to Increase its Focus on Medicine Impact of EU Food, Chemical, and Environmental Legislation

- The Need for Pharma Stakeholder Engagement
- EU PFAS Action and Pharma Mitigation Needs
- Industry and EMA on F-gases and Hydrofluorocarbons in Inhalation Products
- DIA Europe Legislative Session Panel Discussion
- Intensified Industry Dialogue on TiO2 and Nanoparticles Ahead of More EMA Review

IPEC is Helping Marshal Expertise Across Stakeholders to Forestall a Potential TiO_2 Ban in Pharmaceuticals

USP Continues to Refine Its Strategies for Keeping Pace with and Supporting the Rapidly Advancing Biotechnology in the MAb, Vaccine and CGT Arenas

- USP Bio Stakeholder Forum Opening Remarks and Mass Spec Standards for Proteins
- USP's CGT Initiatives
- FDA and Industry Experience with CAR T Potency Testing
- Update on USP Strategies and Initiatives in the MAb, Vaccine, and CGT Arena

Government/Industry/Academia Collaborative Efforts to De-Risk and Accelerate Manufacturing Innovation Draw Strength from Pandemic Learnings

- NIIMBL and its "Going First Together" Mantra
- US Manufacturing Innovation Leaders Weigh In
- The Importance of Process and Facility Innovation in Global Health
- Charting the Advanced Therapy CMC Pathways and Other NIIMBL Projects
- CBER's Marks on Taking CGTs to the Next Level

ICH Q3D Implementation Continues with Workshops, Research, and Guideline and Pharmacopeial Revisions

- Role of PQRI/FDA Workshop in Q3D Implementation Dialogue
- Regulatory Experience and Perspectives in Implementing Q3D
- Pharmacopeial Harmonization with ICH Q3D
- Outcomes of PQRI Study on Variability in Elemental Impurity Analysis

2022

★ Strengthened European Regulator Support for Advanced Technologies Includes New EMA Quality Innovation Group

- Europe's Focus on CMC Innovation and Agile Regulation
- Innovation Issues Explored at CASSS CMC Forum in Europe
- MHRA's "New Era in Regulation"

★ EMA Toolbox on CMC Flexibilities has been Evolving to Incorporate Industry Input and Learnings from the Pandemic

- EMA Perspective on its Toolbox Guidance and OPEN Initiative
- Industry View on Efficiency Tools and CMC Flexibility Learnings from COVID
- Panel Discussion on Effective Tools for the Future

★ CBER's Advanced Technologies Program Growing Stronger with Increased Funding, Expertise, and Collaboration

mRNA-LNP Vaccines Spur Global Dialogue on Nanomaterial Standards and Regulatory Approaches

- Pfizer/BioNTech Lipid Challenges with mRNA-LNP COVID Vaccine
- FDA's Novel Excipient Review Pilot Program and Nanomaterials Guidance
- USP's Draft Guideline and Other Efforts on mRNA Vaccine Quality
- The EDQM Nanomedicines Dialogue and WHO on Regulating mRNA Vaccine Quality
- Potency Assays for mRNA-LNP Vaccines

★ NASEM-Led Study for FDA is Helping Drive Industry/Regulator Agenda on Innovation Needs

- The NASEM Study and FDA Reflections
- Existing Mechanisms to Enable Innovation
- Challenges and Opportunities
- The Path Forward

★ Pandemic Experience Showcases the Potential for Faster Innovation, More Collaboration, and Workplace and Operations Modernization

- The Evolving Landscape of Pharmaceutical Operations
- Government-Industry Collaboration in This and Future Pandemics
- Reducing the Cost of Vaccine Manufacturing for Broader LMIC Access

Progress in Addressing Impurity Challenges in Focus at USP's 2022 Peptide/Oligo Workshop

- US and European Regulator Perspective on the CMC Challenges of Oligonucleotides
- USP Standards Development Efforts for Peptides and Oligos
- Peptide and Oligo Analytical, Manufacturing and Raw Material Considerations

Pandemic Experience and Supply-Chain Risk Management Expectations Increase Attention on Excipient GMP Third-Party Auditing

Janet Woodcock and Jeff Baker will Continue to Play Key Manufacturing Innovation Roles in New FDA and NIIMBL Positions

★ **FDA's KASA and Related PQ/CMC Initiatives on Improving CMC Data Structuring and Sharing Will Help Support ICH M4Q Revision**

- The Advancing Knowledge-aided Assessment Component of KASA
- Bringing Biologics into the KASA System
- The Progress of FDA's PQ/CMC Initiative
- The Goals of Accumulus Synergy in CMC Data IT and Regulatory Communication
- The Drivers for Revising ICH M4Q and Evolving the CMC Regulatory Process

Key GMP Focal Points in Europe Include Guidance Revisions, New Vet Regulations, and Adaptive Assessment/ Inspection Approaches

- Update on EMA GMP-related Activities
- MHRA Innovation Pathway and Proposal for Point-of-Care Regulatory Framework
- Insights from Europe and ICMRA Regarding Onsite Inspection Alternatives

2021

USP and Ph. Eur. Initiatives in the Biologics Arena Continue to Bear Fruit; FDA Joins the Pharmacopeias in Upgrading Particulate Guidance

- Update on USP's Evolving Role and Current Initiatives In the Biologics Arena
- European Pharmacopoeia and FDA Join USP in Focusing on Particulate Control

★ **COVID Vaccine Industry Project Leaders Are Sharing Insights on How the Daunting CMC Challenges Were Addressed**

- Implementing the Pfizer/BioNTech mRNA Vaccine Development Plan
- New Digitalized Facility as Springboard for Moderna's mRNA Vaccine
- Oxford University/AZ Partnership for Global Adenovirus Vaccine Access
- J&J's Experience in Handling the Supply Chain Challenges
- Novavax's Approach to Assuring Comparability for its Protein-based Vaccine
- Inter-Company Panels at DIA and ISPE Meetings on Vaccine Experience

Biomanufacturer Raw Material Control on Regulatory Front Burner as Analytical Power and Formulation Challenges Intensify

- Biotech Regulator Vantage Point on Raw Material Control
- The Added Challenges of Materials Management for CGTs
- Biomanufacturer Use and Control of Polysorbates

Manufacturing, Impurities, and Characterization Methods Are Key Regulatory Focal Points for Peptides and Oligonucleotides

- Recent CMC/Regulatory Challenges of Oligonucleotide Drugs
- Comparability Challenges in Crossing Over to Generics
- Comparing Peptide and Oligonucleotide CMC Issues
- Starting Material Specifications for Oligonucleotides

A Confluence of Forces Is Now Spurring Combination Product Regulatory Reform in Europe

- EU Pharma Strategy Roadmap, Comments from Industry, and Related Agency Strategies
- Culture/Structure/Process Change and Global Alignment
- HPRA CEO Lorraine Nolan on HPRA and EMA Strategy
- EMA's Zaïde Frias and NB/Industry Perspectives on EU Regulatory Transformation

★ **Pandemic Urgencies Highlight Constraints in Manufacturing Change Regulatory Paradigm and Where Adjustments Are Needed**

- Industry Quality Leaders on the Global PAC Regulatory Problem and Solutions
- Evolving the Quality Regulatory Paradigm at the Global Level

Regulators Are Exploring with Industry How to Strengthen Quality Risk Management Practices, with Revision of ICH Q9 a Key Focal Point

- ICH Q9 Revision Lead O'Donnell on the Evolution of QRM
- FDA's Rick Friedman on Advancing Aseptic Processing through QRM
- Industry/Academia Thought Leaders on the Evolving QRM/KM Relationship

★ **Regulators Share Pandemic's CMC Impact at CASSS Japan Forum; Guidance Output Continues Apace in Q1 2021**

- EMA Perspective
- FDA CBER Perspective
- FDA CDER Perspective
- Panel Discussion Among US, Europe, and Japan Regulators

Academia/Industry Collaboration Intensifies on Addressing the Pressing Needs in Biopharma Workforce Development

- NIIMBL's Engagement with Academia on Workforce Development Needs
- ISPE Workforce of the Future Traction at UMBC and UC Davis
- Keck Institute's Behrens on Biopharma Talent Needs and KGI/Industry Partnering
- Xavier's Phillips on Sharable Quality and Regulatory Science Curriculum
- CASSS Panel on Opening Up Biopharma Career Pathways
- European and Global Workforce Development Collaborations

Latest Improvements in FDA's Inactive Ingredient Database Include Change Log and Use of Maximum Daily Exposure

Recent Technology and Partnership Advances Made Possible Precision and Speed of Vaccine Response to Pandemic, NIAID's Graham Stresses at CASSS WCBP Conference

Pandemic Intensifies USP's Focus on Supply Chain Vulnerabilities and Vaccine Development

2020

Pandemic Spurs Deepening of Pharmacopoeia/Regulator/Industry Communication Channels

- EDQM Pandemic Actions Continue Apace in Fall 2020
- Pharmacopeia, Regulator and Industry Expert Panel Explores Pandemic and Nitrosamine Communications
- Second Panel Focuses on Pandemic Organizational Impacts and Key Learnings
- EDQM and Ph. Eur. Evolution Addressed by Leaders Keitel and Vielle

COVID Vaccine Global Distribution Challenges Explored by Bio Supply Management Alliance (BSMA) Panel of European Experts

Pandemic Stresses Increase FDA Attention on Risk Management Plans for Drug Shortage Prevention and Mitigation

USP's Global Efforts to Strengthen Standards and Accelerate Innovation for Biologics Include ICH Engagement

CBER Director Marks Traverses the Complex COVID-19 Vaccine/Therapy Regulatory Landscape at FDLI's Annual Conference

Stronger Unapproved Stem-Cell Enforcement Accompanies FDA Center for Biologics' Cell and Gene Therapy Advancement Efforts

Design-Based Development Paradigm for Cell/Gene Therapies Will Significantly Reduce Costs, Timelines and Regulatory Concerns, AGT CEO Galvin Maintains

Synthesis and Analysis Advancements Are Unleashing the Potential of Peptides and Oligos, Spurring CMC Regulatory Dialogue

USP Convention Meets Virtually in May 2020 to Review Upcoming Priorities, with Both 200-Year Legacy and Current Pandemic in Focus

COVID-19 Vaccine Urgency Throws Spotlight on Next-Gen Sequencing as Key Facilitator

- Adventitious Agent Testing in Focus at CASSS CMC Forum Europe
- Sanofi Pasteur and Ghent University Experience with NGS
- A Decade of Regulator/Industry Collaboration on NGS
- Stakeholder Engagement Begins on ICH Q5A Revision
- Effort to Reduce Animal Testing for Vaccines Includes Global Health Fund Support for NGS

NIIMBL Progress Includes Partnership with Biophorum on Buffer Mixing and Global Health Fund with Gates Foundation

Top FDA Drug Compliance Concerns during 2019 Included OTCs, Supply Chain Information Flow, Compounding, and Genotoxic Impurities

Existing Accelerated CMC, Advanced Manufacturing, and Inspection Initiatives are Supporting Regulators in Pandemic Response, FDA's Cruse Explains in Recent Field Office Updates

Attention Heightens on Creating an Independent Regulatory Pathway for Introducing Novel Excipients

- FDA'S Novel Excipient Program Proposal and Stakeholder Comments
- IPEC/IQ Thought Leaders on the Novel Excipient Drivers
- Subcutaneous Biotherapeutics, Pediatrics, and Delayed Release
- USP Initiatives Supporting Novel Excipient Development
- Assessing and Managing Excipient Risks

★ **US/EU MRA Implementation, US Congressional Hearings, and Industry Surveys Shed Light on Global GMP Inspection Challenges and Collaboration Opportunities**