IPQ
INTERNATIONAL PHARMACEUTICAL QUALITY
Inside the Global Regulatory Dialogue

CURRENT INSIGHTS FROM LEADING REGULATORS

European Commission, EMA, and Competent Authorities Lead "Coalition of the Willing" in Addressing Interfaces Between Drug/Device/IVD Regulations

At the DIA/RAPS Summit on Combination Products in the EU, held in Brussels at the end of January, European Commission Policy Officers Olga Tkachenko and Isabelle Clamou gave a joint presentation on the EC-led "COMBINE" project, which is analyzing the regulatory landscape for clinical studies involving medicinal products used in combination with medical devices and/or in vitro diagnostics. Tkachenko serves on the Directorate General Sante Unit D3, which addresses medical devices and Clamou on DG Sante D2 dealing with medicinal products. Tkachenko began the presentation by discussing the background of the project and its structure. Clamou took over to explain the timeline, actors involved, and the first two tracks of the project, which cover: • the nature of the issues, and • mapping the EU landscape. Tkachenko then finished, addressing tracks three and four, which are focusing on: • the mapping of existing work, and • analysis and proposals for solutions, and next steps.

Joining Tkachenko and Clamou for the panel discussion were the three other session speakers: AGES Biologics Quality Assessor and EMA CAT Chair Ilona Reischl, EMA Scientific Advice and Protocol Assistance Scientific Officer Stiina Aarum, and MSD Regulatory Affairs Medical Device and Digital Health EMEA Director Ruth Foster, who represents EFPIA on the COMBINE project.

UPDATES IN BRIEF: GLOBAL CMC/GMP DEVELOPMENTS

• Proposed FDA Rule on Demonstrable Difficulties for Compounding Lists • FDA Update on Plastic Syringes Made in China • WHO Development of Parallel Recommendation and Regulatory Pathways • EC and Belgian Presidency Increased Support for African Medicines Agency

FDA DRUG GMP WARNING LETTERS AND EMA NCRs

There were no FDA drug GMP warning letters nor EMA non-compliance reports posted during the week.

FDA DRUG RECALLS

Among the nine recalls posted in FDA's enforcement report during the week, none drew the most serious, Class I, rating.

OTHER IPQ CONTENT RELEASED DURING THE WEEK

Also released during the week was Part V of IPQ's in-depth story on pharma's evolution from a compliance to a risk-based mindset. Part V focuses on the Annex 1 revision and the contamination control strategy implications.

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.

EC, EMA and EU Member Agencies Take on Regulatory Interface Challenges for Drug/Device/IVD Combinations

The European Commission, EMA, and national competent authorities are leading a "coalition of the willing" to address the challenges at the interface of drug/device/in vitro diagnostic regulations and facilitate the development of innovative treatments that combine medicinal products with medical devices or IVDs.

At the inaugural DIA/RAPS Combination Products in the EU Summit, held in late January in Brussels, policy leaders from the medical device and medicinal products units of the EC Directorate General for Healthcare Products (DG Sante) reviewed the recently launched "COMBINE" project, which, they noted, is moving at the "speed of light" to bring together all the different actors involved and create an enabling environment for developers.

In a joint presentation, Olga Tkachenko from DG Sante Unit B6 for Medical Devices and Isabelle Clamou, from DG Sante Unit B5 dealing with medicinal products remarked that the Commission is "really trying to bridge across the different fields and to listen to stakeholders, to competent authorities, with EMA."

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> **The EC officials pointed out that this is the "first of a kind" collaboration across Europe – sparked by calls from both industry and competent authorities as they struggle with understanding and implementing the different regulatory pathways and IT requirements that come into play for medicinal products used in conjunction with a diagnostic, delivery, and/or monitoring device.**

While the COMBINE project is focused on the regulatory issues around clinical studies of medicinal products in parallel with a performance study of an in vitro diagnostic and/or a clinical investigation of a medical device, the increased awareness and communication the project is driving will open up pathways for more transparent and aligned regulatory processes across the medicine/device/IVD combination arena. ***[Editor's Note: See IPQ July 2, 2021, for an analysis of the combination product regulatory reform in Europe.]***

Exacerbating the challenges in the clinical trials arena are three European regulations that have recently been put in place – the Medical Devices Regulation (MDR) in May 2021, the Clinical Trials Regulation (CTR) in January 2022, and the In Vitro Diagnostics Regulation (IVDR) in May 2022 – leading to differences in interpretation of requirements and harmonization issues across member states.

Background, State of Play, and Next Steps Explained

Tkachenko and Clamou explained: ● how the COMBINE project arose ● its four tracks ● the state of play of the different tracks, and ● the next steps, including the target time for publication of the analysis report and how the project will be taken forward. ***[Tkachenko's and Clamou's full remarks and the speaker panel discussion that followed are appended below.]***

Tkachenko acknowledged the member state competent authorities from Belgium, Ireland, and Sweden for leading the project tracks, and Denmark for "doing an amazing job of project management." She also thanked all the project participants, including EMA and stakeholder groups, stressing, "It is really invaluable to have you at the table."

In the ensuing panel discussion, the possibilities for extending the project to other regulatory interfaces were discussed. Austria's Biologics Quality Assessor and Committee for Advanced Therapies (CAT) Chair Ilona Reischl pointed to the additional interfaces for cell and gene therapies – for example, the regulations on substances of human origin (SoHO) and genetically modified organisms (GMO).

Session chair AstraZeneca Regulatory Affairs Senior Director Tim Chesworth commented on the influence of changes in other legislation impacting medicines and medical devices, such as the Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) regulations and "the really big picture piece at the macro level of how all these things connect in one another" ***(see IPQ July 21, 2023)***.

Explaining that the challenges around clinical trials had been "the most burning of the interfaces," and cautioning that expanding the project at this stage could lead to difficulties, Tkachenko reassured delegates that the Commission as a whole, including the president, "is very keen on burden reduction for industry." She stressed the current commitment to the COMBINE project, leading Chesworth to remark that it was "fantastic" to hear about this "energy within the Commission."

Analysis Report Will Propose Solutions

After addressing the background and scope of the COMBINE project, Tkachenko outlined the structure of the four tracks of the project.

Track 1, being led by Belgium, has been identifying the issues and clustering them into topics and criticality, and then determining the nature of the issues as legal/regulatory, procedural, or scientific/technical.

Track 2, led by Ireland, has been mapping out the EU landscape, which includes ● competent authorities ● ethics committees ● processes in each member state ● national legislation ● communication between the different entities, and ● indication of the volume of studies.

Sweden has been leading on Track 3, which is collating existing work related to the CTR, IVDR, and MDR – taking into account both published and draft official documents, guidance, Q&As, and presentation materials.

Track 4, again led by Ireland, is the analysis and proposals for solutions track, which will be divided into solutions to address challenges around: ● coordinated assessment ● alignment ● guidance and clarity, and ● communication and dialogue.

Summing up the next steps, Tkachenko emphasized that the analysis report will propose solutions, which will then be taken forward by the different authority groups to make a roadmap and plan based on which solutions are considered the most important to implement and which of them "are feasible in terms of resources."

Competent Authority and CAT Chair Perspectives Shared

Opening the session on "medical devices in medicinal product clinical trials" at which the two EC officers spoke was CAT Chair and AGES assessor Reischl, who shared her personal perspective and experience, which has included service as Head of Clinical Trials for both medicines and devices at AGES.

She began by describing the challenges at the Austrian agency, noting that there had been a "reluctance by applicants to acknowledge requirements" expected by AGES – with the common refrain that other agencies had not had the same expectations. Pointing to the current reality of separate legislations and overlapping assessments, Reischl acknowledged that there "is a lot we can do in the current framework," but that communication and "joining of expertise" is needed.

Emphasizing the need for a "joint, big picture view," she stressed that "for the sake of patients, we need solutions for development and life cycle of complex innovative products in Europe, and we need them fast."

In the panel discussion, where Reischl had the opportunity to bring attention to the additional challenges for advanced therapy medicinal products (ATMPs), she highlighted that work was progressing on the second version of the EMA/CAT draft guideline on quality, non-clinical, and clinical requirements for investigational ATMPs in clinical trials.

The revised draft, along with an overview of the comments on the first version, was published on March 25, 2024, and is open for consultation until the end of May 2024. Over 270 pages of comments were received on the previous version, with 170 pages of comments on quality sections. ***[A link to the draft guideline is provided below. IPQ will be reviewing the comments and revision in an upcoming story.]***

EMA Develops Focus Group for Combination Products Advice

EMA Product Development Scientific Support Department Senior Scientific Specialist Stiina Aarum followed Reischl to the podium and spoke about EMA activities, particularly the development of a focus group to provide scientific advice for drug-device combinations and drug-companion diagnostic combinations. ***[Editor's Note: Aarum gave a similar presentation and participated in the panel discussion at the US AFDO/RAPS Combination Products Summit in November 2023. See IPQ Weekly Supplement for the week ending January 26, 2024.]***

Focus group participants include the EMA Scientific Advice Working Party, national competent authority (NCA) medical device and IVD experts, industry representatives, notified bodies, and EMA staff. Five meetings were held in 2023 to analyze nine case studies of DDCs and drug-IVDs.

DDC focus group cases discussed involved: ● stability strategy for a co-packed product ● clinical trial design for a new on-body delivery system (OBDS) with bridging from pre-filled syringe (PFS) to OBDS ● clinical development of medical device software to be used in combination with a medicine, and ● a line extension of a product already commercialized as a PFS where an autoinjector is under development.

Specific follow-up actions include a scientific publication "to keep the discussions going" and looking at the opportunity for bridging with medical device expert panel advice and involvement of NCA medical device/IVD expertise.

In terms of the EMA activities on digital health technologies – where the agency is rapidly developing experience – Aarum pointed to a number of publications and workshops throughout 2023, noting that "the challenge is to respect the EMA remit while being prepared for evolving technologies/methods." A draft reflection paper on the use of AI in the medicinal product lifecycle will be finalized in 2024, she confirmed. ***[A link to the current draft is provided below.]***

In the final part of her presentation, Aarum spoke about an EMA scientific advice pilot for "certain high-risk medical devices" intended to administer and/or remove medicinal products. EMA took over the coordination of medical device expert panels in March 2022 as part of its extended mandate on crisis preparedness and management.

EFPIA Provides Input and Case Studies to COMBINE

MSD Medical Devices and Digital Health Products Director Ruth Foster shared the work that the European Federation of Industries and Associations (EFPIA) has been doing to contribute to the COMBINE project as one of the stakeholder groups.

She began by visualizing scenarios for delivery methods of medicinal products in clinical trials, then shared EFPIA member companies' experience to date, and outlined some of the major challenges. For each of the critical challenges listed, EFPIA offered proposed solutions for consideration by the project group.

The three major issues identified by EFPIA are: ● applying inappropriate notified body opinion (NBOp) requirements at the clinical trial stage ● inconsistent interpretation of which trials require applications under the EU MDR ● the lack of a clear regulatory framework, and the clinical investigation process and documentation requirements not being consistent across member states.

Foster noted that of particular concern and a "very important issue for EFPIA members" is the use of a CE-marked device outside its intended use or a non-CE-marked device where there is no intention to collect data on the device. Supporting Reischl's earlier point, she noted that there are inconsistent interpretations of which trials require applications under the MDR.

For each challenge, both short and mid-term solutions were proposed, and in her "key takeaways," Foster stressed that a "motivated, engaged and experienced group of stakeholders" have come together to identify and address issues to "ensure the EU continues to be an attractive region for clinical research with innovative combined drug device technologies."

In the Q&A panel discussion that followed the presentations, UCB Global Regulatory Affairs CMC and Medical Devices Associate Director Isabelle Mingam raised two issues that her team had experienced during the clinical trial stage.

One related to the device part of an agency trying to find standalone device information and not being aware it was in module 3. To resolve this issue, Mingam advised providing a "reviewer's guide," which UCB also provides for marketing authorizations, pointing to where device information can be found.

The other issue, relating to the use of a delivery device in a different tissue than the one it has been CE marked for, drew extensive comments from Reischl, Tkachenko, and Foster and was one of the challenges highlighted in the EFPIA presentation ***(see remarks appended below.)***

DIA/RAPS Summit Addresses Other Key CP Issues

Other sessions at the DIA/RAPS Combination Product Summit included an opening plenary panel on how to help keep innovative combination products in Europe, with speakers in leadership roles from the Commission, EU Heads of Medicines Agencies network, EMA, BSI notified body, Zealand Pharma, and GSK.

UCB's Mingam then presented in a workshop session addressing the challenges around the development of medicinal products with co-packaged devices/cross-referenced devices, setting the scene along with EMA Regulatory Affairs Senior Officer Christelle Bouygues. Chaired by Roche Device and Combination Products Regulatory Group Director Andreas Emmendoerffer, the panel discussion considered output from a roundtable exercise, with BSI Technical Specialist and Scheme Manager Theresa Jeary joining the panel.

In a session on the Notified Body Opinion MDR Article 117 "challenges and possible ways forward," chaired by Novo Nordisk Global Regulatory Affairs Devices Director Thomas Wejs Møller, speakers from large and small pharma participated in a panel discussion with EC, EMA, and NB representatives to explore how collaboration could help provide "a well-regulated environment which encourages progress."

Wejs Møller, who previously served as Medical Devices Director at the Danish Agency, also chaired the following session, exploring the impact of the new EU General Pharma Legislation (GPL) on combination products. The session included presentations by the GPL lead, EC Policy Officer Lilia Luchianov, and AZ's Tim Chesworth, as well as a panel discussion with participants from previous sessions.

Day two of the summit began with the session on medical devices in clinical trials, followed by another workshop, this time on device-led combination products. This workshop focused on the MDR re-consultation requirements, post-opinion changes, and challenges when device manufacturers try to meet medicinal product expectations.

The closing plenary session and panel discussion addressed the topics of driving convergence on regulations and the global impact on the diversity of regulations, with presentations by TÜV SÜD Global Director Regulatory Strategy Medical Health Services Sabina Hoekstra-van den Bosch, and Qserve Group Chief Scientific Officer Gert Bos, who previously served as Head of Notified Body at BSI. ***[An upcoming IPQ story will address the global challenges for combination products.]***

Dialogue on the COMBINE Project Continues at DIA Europe

At the DIA Europe Annual Conference held in Brussels in mid-March, EC officials Clamou and Tkachenko co-chaired a session on medical devices in clinical trials, in which more players from the COMBINE project were able to provide their perspectives and updates.

Representatives from both EFPIA and MedTech Europe outlined the challenges their members had been experiencing and commended the authorities leading the COMBINE project for the effective and efficient way it was progressing.

The experience of mapping the issues was shared by the Irish Healthcare Products Regulatory Authority (HPRA), and the Danish Medicines Agency (DKMA) presented proposals for solutions and next steps.

The rapid progress of the project team in sharing and taking onboard feedback on the proposed solutions was discussed. The target timeline has been extended slightly into Q2 2024, with the aim of releasing the final analysis report "soon."

A Stepwise Approach Will be Taken

DKMA Senior EU Project Lead and project manager for COMBINE Ditte Andersen stressed that the analysis report will focus on the "what" rather than the "how" to avoid the project getting stuck in the analysis phase and enable it to "move forward fast."

Regarding communication and dialogue, she pointed to the cross-functional challenges, and the "need to understand each other's languages" through training. Although trying not to prioritize issues at this stage, there is a "clear priority of coordinated assessment," which directly addresses the highest number of issues.

Moving onto "next steps," Andersen highlighted the recognition that there is too much work to manage in one project and that a stepwise approach is needed for implementing solutions.

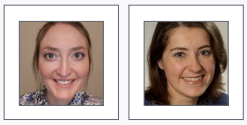
Currently, the project is focused on "reshaping the collaboration into a stepwise approach," which is expected to be agreed upon and endorsed by expert groups around May. The plan is to provide an overview of ongoing activities and a basis for prioritization and coordination of new activities, and to leverage the established COMBINE structure to develop a framework to continue collaboration, ensuring multi-stakeholder input to the solutions. The EC webpage provides information on the progress of the COMBINE project. ***[A link to the webpage is provided below.]***

> **In their closing comments, both HPRA and DKMA speakers expressed confidence in the successful outcome of the COMBINE project, highlighting the current momentum and the "very useful" dialogue and collaboration so far, which has resulted in a "significant benefit" already.**

In response to a question about the greater regulatory requirements for medical devices in Europe than in other markets, Tkachenko shared that the Commission would conduct an evaluation of the impact of the MDR and IVDR in 2024 and invited delegates to contribute to it.

LINKS:

- EC Webpage for COMBINE Project Updates
- EMA Guideline on Requirements for Investigational ATMPs
- EMA Reflection Paper on the Use of AI in the Medicinal Product Lifecycle



[Subscribers CLICK HERE for Tkachenko and Clamou's full remarks at the DIA/RAPS summit.]

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.

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 Titanium Dioxide 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