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NOTE FROM IPQ'S EDITOR-IN-CHIEF: The four-part story featured in our September/ October Monthly Update *(see pp. 4-121)* explores the significant effort underway, led by FDA and EMA, to deepen the regulator/industry/academia communication needed to realize the potential for technological advancement in the manufacturing and control arena – with continuous and distributed manufacturing up-front priorities.

The first part of the story highlights the evolution of regulatory support for biomanufacturing in Europe, sharing insights from two leading European biotech CMC reviewers. Included are the outcomes of the first year of operation of EMA's Quality Innovation Group and its inaugural "Listen and Learn Focus Group" meeting on continuous and decentralized manufacturing, in which European, U.S. and Japanese regulators, industry, and academia participated.

Part II provides an update on FDA's efforts in the advanced manufacturing arena, with insights from key leaders in the Office of Pharmaceutical Quality (OPQ) and Office of Regulatory Science and Innovation (ORSI) that were shared at an October workshop on continuous manufacturing (CM) of nanomaterials.

The third part homes in on the discussions that took place at a USP/RAPS workshop in July, which brought together a variety of pharma stakeholders to explore the issues in adopting continuous manufacturing. Emerging into clear relief were the potential benefits that CM implementation could offer in terms of flexibility, efficiency, and quality, as well as the challenges, such as knowledge gaps, start-up costs, ROI, and global regulatory uncertainties.

The last part of the story takes a deeper look at how the new wave of biotherapeutics and personalized medicine is driving a paradigm shift toward distributed manufacturing and the adaptations that are needed in CMC/ regulatory processes to accommodate a DM/point-of-care (POC) approach.

CMC/GMP regulatory developments during September and October highlighted in our *"Updates in Brief"* section *(see pp. 122-131)* include more from FDA on its: • quality management maturity initiative • remote evaluation toolset, and • sponsor meetings and research under PDUFA and GDUFA, and OTC monograph requests under OMUFA.

In Europe, briefs cover EMA on manufacturing synthetic peptides, nitrosamines, and pre- and post-authorization issues, and how EFPIA is working with Ukraine on EU accession and regulatory alignment.

Moving to the broader international arena, the Indian Pharmacopoeia commission has joined the Pharmacopoeial Discussion Group. WHO, meanwhile, has: • reported on its biological standardization program • created an electronic prequalification system • updated its drug QC lab good practices guidance, and • designated the agencies of Singapore, Korea and Switzerland as WHO-listed authorities, Turkey as maturity level 3, and Saudi Arabia as level 4.

There were 16 drug GMP warning letters posted by FDA during September and October — ten addressing US operations and six to foreign facilities *(see pp. 132-138).*

In the US, seven of the letters went to finished dose drug manufacturers, and one each to makers of APIs, HCT/Ps and compounded drugs. Three of the US finished dose letters involved a lack of or inadequate response to FDA's inquiries, and two included data integrity concerns.

Among the foreign recipients were three South Korean manufacturers, one located in China, which did not respond to FDA's inquiry, one in India, and one in Switzerland, where data integrity was at issue.

Component testing continued as a significant finding in the warning letters, with 8 of the 12 to companies for which the FDA investigations were allowed to proceed citing the problem. Four of these pointed specifically to lack of DEG/EG testing and one the testing of ethanol for methanol.

Eight of the 38 product recalls posted by FDA during the two months *(see pp. 140-143)* received the most serious Class I rating.

Two of these involved microbial contamination of non-sterile liquid products — one with *Candida parapsilosis* and one with *Bacillus cereus.* Another two involved labeling/packaging issues — one with the presence of foreign oxycodone tablets in bottles of betaxolol, and another with the wrong strength on the label of digoxin tablets. A third pair involved products marketed without an approved NDA/DNA containing sildenafil. Crystals in bottles of a cyclosporine oral solution and potential API cross-contamination were the cause of the other Class I recalls.