Bill Paulson, Editor-in-Chief

NOTE FROM IPQ'S EDITOR-IN-CHIEF: More sensitive and selective methodologies have facilitated the identification and quantification of elemental impurities (EIs) in pharmaceuticals and the movement away from the old heavy metal analytical tests to the risk-based assessment strategy of ICH Q3D.

The four parts of the story featured in the December Monthly Update *(see pp. 4-49)* review the recent Q3D implementation efforts and the support that has come from workshops, research, and guideline and pharmacopeial revisions.

Part I provides an overview of the background, scope and content of a watershed November 2020 workshop, cosponsored by the Product Quality Research Institute (PQRI) and FDA, which brought experts and policy makers from industry, health agencies, and pharmacopeias together to assess the Q3D implementation challenges and progress.

The second part focuses on the experience of FDA and European regulators with Q3D implementation and the industry issues that have been surfacing.

In the third part of our story, we shift focus onto the efforts by the US and European pharmacopeias to bring their compendial standards into alignment with Q3D, including the changes made in the recent revision to the ICH guideline.

Part IV describes the results and conclusions of the second phase of a multi-center, collaborative study commissioned by PQRI to investigate how reliably EIs can be measured in pharmaceuticals.

Significant developments in the US component of our "*Updates in Brief*" section in the December issue, with links to the information discussed *(see pp. 50-53)*, include the FDA release of a "Leadership Modernization Action Plan" as the next milestone in its technology transformation journey. Also released was additional guidance on how FDA will handle inspection and application processes, including those for generic and biosimilar drugs in the wake of the recent renewals of GDUFA and BSUFA.

In focus in Europe were updates from EDQM on the European Pharmacopeia. In the global arena, ICH released the Step 2 draft of M13A on bioequivalence studies, and the International Coalition of Medicines Regulatory Authorities (ICMRA) released an update on its post-approval change collaborative assessment pilot with a request for additional applications. Also noted is a review by India's Department of Pharmaceuticals of its 2022 activities, including its manufacturing strengthening initiative.

There were seven drug GMP warning letters posted by FDA during November *(see pp. 54-58)* — three within the US and four internationally. The US letters went to a compounder, a finished dosage form manufacturer, and to a large supplier of the excipient microcrystalline cellulose involving its response to customer complaints on the product not meeting specifications and its handling of related manufacturing deviations.

Foreign recipients of warning letters included a maker of hand sanitizers in Canada, and three letters where data integrity was a prominent issue – to a finished dosage form manufacturer in India, and to API manufacturers located in India and Brazil.

EMA, meanwhile, issued a non-compliance report to an Indian API manufacturer following a joint inspection by France's ANSM and EDQM *(see p. 59)* that found a spectrum of GMP problems, including cross-contamination control for shared production of highly potent APIs.

There were only 15 drug recalls posted by FDA during December *(see pp. 59-61)* – fairly evenly distributed across the recall categories. Warranting the Class I, serious health risk rating, were two of the three in the labeling/packaging category. One involved a defective container for which there were complaints of vial breakage and "glass flying" when being prepared for administration. The other involved a mislabeled strength on an iodine syringe.