WHAT'S NEW AT Q

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FROM THE COO's DESK

It has been a long process, but the new USP/NF chapters on Elemental Impurities are ready for implementation. Effective January 1st, the old qualitative Heavy Metals Chapter 231 will no longer be utilized, and will be replaced by the much more sophisticated procedures provided by new Chapter 233. The new methodology produces quantitative results at limits of detection as low as parts per billion (ppb). Chapter 232 and Chapter 2232 (dietary supplements) provide guidelines for performing risk assessments on your products and includes formulas for determining the allowable residues of the various elemental impurities based on Permitted Daily Exposure (PDE) levels. Q Laboratories has been preparing for the new procedures and limits and we are ready to provide all the analytical support you need to meet the new guidelines. Our lab is equipped with ICP-MS as well as ICP-OES technology and we have analysts well versed in the new chapters to help you and/or your suppliers achieve compliance. Give us a call today and we can set up a testing regimen that aligns with the new USP chapters.

David G. Goins, COO

PROBIOTICS

The growth of probiotics usage has continued to trend upward with the global probiotics market reaching $41 billion in 2015 and predicted to grow at a CAGR of approximately 7.3% over the next several years, expanding the market to an estimated $74.7 billion by 2025. According to the International Food Information Council Foundation, 81 percent of Americans identify probiotics as the most important nutrient to take and 9% of US adults (15.3 million) take probiotic supplements.

DID YOU KNOW?

A 2016 Council for Responsible Nutrition (CRN) Consumer Survey on Dietary Supplements found 77% of adult women and 65% of adult males in the United States take dietary supplements. Of those who take dietary supplements, 97% take Vitamin and/or Mineral supplements, with the most popular being Vitamin D, taken by 37% of users. In addition, 36% take Herbals/Botanicals, 20% take Omega 3 or some other Fatty Acids supplement, and 13% take Probiotics.

RESIDUAL SOLVENTS?

According to USP/NF, "(a)ll USP and NF articles are subject to relevant control of residual solvents, even when no test is specified in the individual monograph. If solvents are used during production, they must be of suitable quality. In addition, the toxicity and residual level of each solvent shall be taken into consideration, and the solvents limited according to the principles defined and the requirements specified in Residual Solvents (USP Chapter 467), using the general methods presented therein or other suitable methods." Contact Q Laboratories today to assure your product(s) meet USP requirements for residual solvents.

FDA METALS

One of the reasons for the implementation delay of the new USP/NF Chapters on Elemental Impurities, which were originally introduced in 2013, but were ultimately not scheduled for implementation until January 2018, was the desire to harmonize the chapters with the International Standard, ICH Q3D, which has also been years in development. The FDA has produced a Guidance document stipulating their current view of how ICH Q3D and USP 232, 233 and 2232 should be interpreted and implemented. For both the USP and ICH guidelines, it is generally recommended to perform an elemental impurities risk assessment by, "first identifying known and potential sources of elemental impurities. Manufacturers should consider all potential sources of elemental impurities, such as elements intentionally added, elements potentially present in the materials used to prepare the drug product, and elements potentially introduced from manufacturing equipment or container closure systems. Manufacturers should then evaluate each elemental impurity likely to be present in the drug product by determining the observed or predicted level of the impurity and comparing it with the established Permitted Daily Exposure (PDE). If the risk assessment fails to show that an elemental impurity level is consistently less than the control threshold (defined as being 30 percent of the established PDE in the drug product), additional controls should be established to ensure that the elemental impurity level does not exceed the PDE in the drug product. These additional controls could be included as in-process controls or in the specifications of the drug product or components."

The new USP chapter requirements should be applied to all new NDAs and ANDAs for drug products with an official USP monograph as well as marketed compendial drug products not approved under an NDA or ANDA (e.g., nonprescription over-the-counter (OTC) drug products marketed under an FDA OTC monograph) subject to the provisions of the FD&C Act. Applicants submitting new NDAs and ANDAs for drug products without an official USP monograph should follow the recommendations for the control of elemental impurities as described in ICH Q3D.

The Chapter 233 methods are quantitative and provide for very low limits of detection. The FDA guidance states, "ICH Q3D does not describe specific analytical procedures for routine testing of materials or for performing a risk assessment. FDA recommends that manufacturers use the analytical procedures described in General Chapter 233 or, if those analytical procedures cannot be used for a specific item, analytical procedures that meet the validation requirements described in General Chapter 233. Any analytical procedure used to test for elemental impurities should be properly described, and if used for routine testing, its suitability must be verified under actual conditions of use."

Analytical procedures for both risk assessments and routine testing should be validated. Analytical procedures used during risk assessments must possess characteristics (e.g., accuracy, precision, specificity) such that the manufacturers can be reasonably certain (e.g., at the 95-percent confidence level) that the measurements can be relied upon to decide whether to include routine testing of materials in the control strategy. This decision depends on whether the amounts of the elemental impurities in the materials are consistently below control thresholds. The analytical procedures should be validated with this goal in mind.

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