



## Impurities and Contaminants in Dietary Ingredients and Dietary Supplements Open Forum

### EXECUTIVE SUMMARY

April 21, 2022

#### Overview

U.S. Pharmacopeia (USP) hosted an Open Forum on “Impurities and Contaminants in Dietary Ingredients and Dietary Supplements” on April 21, 2022. This virtual event had more than 171 attendees, including stakeholders from industry, academia, and regulatory agencies.

Specifications for impurities and contaminants are critical quality attributes of dietary ingredients and finished dietary supplements because they have the potential to affect the safety, performance, and stability of the products. At the Open Forum, subject matter experts presented the need for a USP General Chapter on impurities and contaminants in dietary ingredients and finished dietary supplements, as well as the complexity of dietary supplement identity and purity testing from a contract laboratory’s perspective. USP staff provided an overview of USP General Chapter <2760> *Impurities and Contaminants in Dietary Ingredients and Dietary Supplements*. This was followed by a panel discussion on risk assessment and management and a question and answer (Q&A) session facilitated by a USP Expert Committee member.

#### Background

For a time, USP General Chapter <1086> *Impurities in Drug Substances and Drug Products* applied to dietary ingredients and finished dietary supplements. This changed in May 2021, when General Chapter <1086> was revised to align with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) standards for drug substances and drug products. This made <1086> inappropriate for dietary ingredients and finished dietary supplements. Hence, USP recognized and committed to developing an informational general chapter to serve as a comprehensive resource on the types of impurities and contaminants associated with dietary ingredients and finished dietary supplements. General Chapter <2760> was therefore developed to help the industry accomplish the following:

- Address the unique aspects of impurities and contaminants in dietary ingredients and finished dietary supplements
- Align dietary ingredient suppliers and dietary supplement manufacturers
- Help professionals and scientists identify critical-to-quality attributes and develop specifications

## **Main Topics Discussed at the Open Forum**

USP convened the Open Forum to explain USP's thinking regarding impurities and contaminants in dietary ingredients and dietary supplements, the need for General Chapter <2760> to help the dietary ingredient and dietary supplement industry comply with good manufacturing practices, and, most importantly, to gain input from attendees in terms of questions or concerns. Some of the main points discussed were as follows:

- **Complexity of Dietary Supplement Identity and Purity Testing from the Contract Testing Laboratory Perspective**
  - Targeted screening for contaminants is an important step, but it is not the only consideration when working with a global supply chain and highly volatile market.
  - When demand exceeds supply, bad actors will develop sophisticated techniques to evade detection using standard methods.
  - Important and sometimes dangerous adulterants may be missed if a narrow-focused lens is used for contaminant testing.
  - Understanding the ingredients, how they are produced and where market conditions and use history will dictate which contaminants should be screened for.
  - Sometimes one test is not enough to detect the contamination, and the contaminants can evade detection if relied on a single test. This is especially true for botanical raw materials.
  - When choosing CROs, one must ensure that they have adequate expertise and experience in testing contaminants.
  
- **Overview and Scope of General Chapter <2760>**

General Chapter <2760> addresses the following:

  - Types of impurities, measures for the proper control of unwanted impurities, analytical procedures for detecting and quantitating impurities, and setting acceptance criteria for impurities
  - Types of contaminants including elemental contaminants, toxins, pesticides residues, persistent organic pollutants (e.g., dioxins, furans, PCBs), and polycyclic aromatic hydrocarbons
  - Risk analysis considerations, including risk assessment, risk management, and risk communication

## **Panel Discussion on Risk Assessment and Risk Management**

Dr. Richard Ko, a member of the USP Dietary Supplements Admission Evaluation and Labeling Expert Committee, facilitated a panel discussion on risk assessment and risk management. Highlights included the following:

- The largest benefit of General Chapter <2760> is that it can help align dietary ingredients and finished dietary supplement manufacturers on the unique aspects of impurities and contaminants in these ingredients and finished products.
- General Chapter <2760> provides information on available tools to help companies and industry assess, from a safety standpoint, the variety of contaminants and impurities in dietary ingredients and finished dietary supplements.
- Risk assessment relates to understanding and attempting to quantify how big the risk is and the main factors that influence the risk.
- There are a variety of risk management tools that industry and companies can employ once the risks are satisfactorily identified.

Risk communication is critical throughout the risk analysis process to promote awareness, consistency, and transparency.

### **Q&A Session**

Dr. Ko facilitated a Q&A session on risk assessment and risk management. Highlights included the following:

- Approaches that exist in FDA and ICH guidance documents can be particularly useful to industry and companies regarding certain contaminants for which data are unavailable in the literature.
- Disclosure regarding impurities and contaminants is critical in dietary ingredients and finished dietary supplements because they are sometimes taken in a range of daily servings.
- DNA testing for detecting impurities and contaminants is an important tool but requires expert interpretation; pivotal work in this area is now under investigation.
- From a safety standpoint, General Chapter <2760> may be applicable to certain food ingredients and dietary ingredients intended for use in finished dietary supplements.
- “Unknown unknowns” are a key issue; companies may put themselves and the industry at risk if they do not test for contaminants.
- Risk assessment, risk management, and risk communication should consider usage patterns because certain dietary ingredients and finished dietary supplements may be used chronically or intermittently over a lifetime.
- A basic tenet of good manufacturing practices is that companies may be able to shift to a reduced testing program.
- Certain dietary ingredients and finished dietary supplements that are not susceptible to economically motivated adulteration could be considered for reduced testing based on Certificate of Analysis to verify supplier integrity as long as the material and supplier are periodically requalified.

### **Next Steps**

USP wants to work closely with industry and provide education and resources about potential impurities and contaminants in dietary ingredients and finished dietary

supplements. USP welcomes industry input before finalizing General Chapter <2760>, particularly related to the following:

- Data on degradation products in multivitamins
- Information on the methods industry and companies use to help protect their dietary ingredients and finished dietary supplements from impurities and contaminants
- DNA-testing laboratories and services for botanicals

Please contact Dr. [Kit Goldman](#), Senior Director, USP Dietary Supplements & Herbal Medicines, or Dr. [Binu Koshy](#), Senior Scientist II, USP Dietary Supplements & Herbal Medicines, with any questions or comments.

USP is an independent, nonprofit, scientific organization based in Rockville, Maryland. USP convenes and engages a broad range of stakeholders at its Open Forum events. The main objective is to gather stakeholder input so that USPs can better understand their concerns, priorities, and questions about the topic at hand. Specifically, USP seeks feedback from stakeholders to improve the quality and relevance of USP's general chapters before they are posted in *Pharmacopeial Forum* (PF) for public comment.