Need for a General chapter on Impurities and Contaminants in Dietary ingredients and Dietary supplements

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Background

- For a time, USP's General Chapter <1086> *Impurities in Drug Substances and Drug Products* was applied to dietary ingredients and dietary supplements.
  - Unfortunately, a General Chapter listing drug substances and drug products do not have much visibility to dietary ingredient and dietary supplement manufacturers.
- This changed in May 2021, when GC <1086> was revised to align with ICH standards for drug substances and drug products.
  - This makes <1086> inappropriate for dietary ingredients and dietary supplements.
  - The opportunity now exists for the industry to address the unique aspects of impurities and contaminants in dietary ingredients and dietary supplements.
- Hence, a need for a new general informational chapter was recognized and committed to by USP.

Introduction

- Impurities and contaminants are critical quality attributes of dietary ingredients and dietary supplements because they have the potential to affect the safety, efficacy, performance and stability of the product.
  - Contaminants (including Impurities) are a critical element of the Dietary Supplement GMP
    - Identity, purity, strength, composition and limits on contaminants
  - Contaminants are a critical element of cGMP in HARPC Systems for Dietary Ingredients
- Limits on Impurities and Contaminants are almost always based on public health and safety factors.
  - USP has General Chapters for dietary supplements for heavy metals, pesticides and residual solvents which establish critical limits for these objectionable substances.
  - This General Chapter for dietary ingredients and dietary supplements will supplement many of the other General Chapters and product specific monographs.

Introduction

- Dietary Ingredient manufacturers must ensure the quality, purity and consistency of the dietary ingredients that they manufacture on behalf of Dietary Supplement manufacturers.
  - Many impurities and contaminants originate from the dietary ingredients, or the excipients used in dietary supplements.
  - They must employ measures for the proper control of unwanted impurities and contaminants in dietary ingredients and they must be transparent with Dietary Supplement manufacturers on the risks associated with the probability (likelihood) of contaminants and impurities.
  - They must work with finished product manufacturers to harmonize test methods and align on specifications for contaminants and impurities.

Introduction

- Dietary Supplement manufacturers must ensure the identity, strength, purity, composition and limits on contaminants (including impurities) in incoming raw materials including Dietary Ingredients.
  - Dietary Supplement manufacturers accomplish this by performing reviews of documentation and conducting Certificate of Analysis verification activities.
  - Dietary Supplement manufacturers need transparency with respect to impurities and contaminants that are likely to be present in raw materials and thus may be of concern in the finished dietary supplement product.
  - Dietary Supplement manufacturers have the obligation to identify contaminants and impurities that are likely to be introduced from the Dietary Supplement manufacturing process.
  - Impurities and contaminants can appear in Dietary Supplements through many different routes. They can occur naturally as a result of their presence in the environment (soil, water, or air). They can occur through inadvertent cross-contact or cross-contamination in the production environment of a Dietary Ingredient or the Dietary Supplement itself.
  - Many times, they are not homogenous and since they are in trace quantities, are subject to significant measurement uncertainty or analytical variation.

Introduction

Creatine Monohydrate

- Official date November 1, 2020
- Process - Related Impurities
  - Procedure 1 – Unique list of Impurities including Dicyandiamide and Dihydrotriazine based on process used to synthesize
  - Procedure 2 – Unique list of Impurities including Dicyandiamide, Urea and Sarcosine based on process used to synthesize
- Industry is beginning to align with the USP Standard, and it all starts with the raw material suppliers

Summary

Why do we need a General Chapter for Impurities and Contaminants?

- Address Unique Aspects for Dietary Ingredients and Dietary Supplements
- To provide a comprehensive resource as to the types of impurities and contaminants that are associated with Dietary Ingredients and Dietary Supplements.
- To align Dietary Ingredients suppliers and Dietary Supplement manufacturers
- Promote better visibility and usage of USP Standards (GC and Monographs) to promote GMP compliance
- To aid Quality professionals and Scientists in identifying Critical to Quality attributes and developing specifications
- Promote standardization for Quality on the International stage

Thank You

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