The Complexity of Setting Compendial Specifications for Excipient Composition and Impurities

Galina Holloway, Ph.D.
Senior Scientific Liaison, Excipients
Title: “The Complexity of Setting Compendial Specifications for Excipient Composition and Impurities”

✓ proposed:
  • the views of the Excipient Monographs 1 and 2 Expert Committees - Excipient Impurities Joint Subcommittee on the complexity of excipient composition;
  • definitions for simple excipient, complex excipient, excipient composition, and excipient impurity;
  • a proposed direction and guidance in standards setting and establishing specifications for excipient components and impurities;

✓ provided:
  • examples of challenges faced by USP in setting specifications for different components and impurities in excipients;
  • examples of the current approaches in setting specifications for excipient components (case studies and a decision tree).
The Excipient Impurities Joint Subcommittee is proposing the following set of definitions to aid in classifying excipients and to improve contrast between acceptable components of the excipients and impurities in excipients:

- **Nominal component**: Substance typically found in the excipient that is expressed by the official name and definition and/or assay provided in the USP monograph.

- **Minor component**: A component of an excipient which is not the nominal component or, where the official name does not relate to the excipient components, not the major component.

- **Simple excipient**: An excipient composed of a single main substance with a well-defined chemical structure that can be characterized well analytically.

- **Complex excipient**: Any excipient that does not fit the definition of a simple excipient.
Concomitant component: A minor component of an excipient that accompanies the nominal component which is identified either in the title or definition of a monograph. Concomitant components are characteristic of many excipients and are not considered to be impurities if there is no negative impact on drug products. Some but not all concomitant components are defined or specified in excipient monographs. Added substances are not considered concomitant components. (Any component that can be considered a toxic impurity because of significant undesirable biological effect is not considered to be a concomitant component.)

Added substances in official substances: Substances added to improve excipient handling, processing or performance, including stability (see also General Notices, 5.20.10 Added Substances in Official Substances).

Excipient impurity: Any substance that detracts from the quality of the excipient (i.e., that is not the substance appearing in the official name, or a concomitant component or added substance as defined.)
As of today, USP has received comments from six commenters including FDA.

The Excipient Impurities Joint Subcommittee is seeking feedback from stakeholders on the Stimuli article.

USP encourages all stakeholders to:
- read and comment on the article
- complete the survey questionnaire
To register for the Excipients Stakeholder Forum
Thank You

Empowering a healthy tomorrow