ISPE response to FDA-2018-D-4417 for FDA Draft Guidance for Industry: "CDER's Program for the Recognition of Voluntary Consensus Standards Related to Pharmaceutical Quality

Key Messages

- ISPE supports the continued efforts to ensure that quality pharmaceutical products (including pharmaceutical, biopharmaceutical and combination products) are available for public welfare. This includes supporting the development of appropriate guidances and communication of expectations.
- ISPE appreciates the FDA Center for Drug Evaluation and Research's (CDER) willingness to consider quality standards outside of those cited in various CDER Guidance for Industry documents, and supports the establishment of a program that will evaluate and publish informally recognized voluntary consensus standards related to pharmaceutical quality

Main Comments

- The informal recognition of "voluntary consensus standards related to pharmaceutical quality" has the potential to promote innovation in the pharmaceutical industry while creating unintentional consequences related to expectations between FDA review staff, FDA Investigators and Industry. The draft guidance is unclear as to what is meant by "informally recognized voluntary consensus standards related to pharmaceutical quality." Additionally, it is unclear if "informally recognized voluntary consensus standards" will be uniformly and consistently recognized throughout CDER and across FDA Centers. For example, could informal recognition vary between reviewers, division and disciplines? Will FDA Investigators "informally recognize" the same "consensus standards" as FDA Reviewers? Providing a definition for and scope of "consensus standards" along with examples will increase clarity.

- It is unclear what type of organizations, including who they may represent, may submit voluntary consensus standards for evaluation and informal recognition. There appears to be no qualification requirements for these organizations or safeguards to prevent organizations from promoting their own agenda that may or may not be shared by others in the Industry. Nor is there a clear definition of "openness" as it related to organization. We suggest that greater detail should be provided regarding the screening of organizations, the visibility of standards being assessed, ability for other organizations (including membership) and individuals to comment on standards under review, the evaluation process, timeliness of posting and lifecycle management of informally recognized voluntary consensus standards.

- Greater clarity is desired regarding the recognition of informally recognized voluntary consensus standards in relationship to existing voluntary consensus standards, compendial standards and FDA Guidances for Industry, and future changes to or development of new compendial standards and FDA Guidances for Industry.
- Can the process be evaluated in advance of a request to recognize a document?
- Does “openness” mean allowing participation beyond an organization’s membership?

ISPE Recommendations

1) Provide a definition for “voluntary consensus standards” and intended scope. For example, is scope limited to technical specifications or does it extend to concepts such as validation of a drug product?

2) Clarify the documentation processes and expectations for submitting “informally recognized voluntary consensus standards related to pharmaceutical quality.” For example, is the process expected to have a similar rigor as production of formal standards such as ASTM standards, or will a simpler process be employed? Also, clarify whether a proposed standard can be evaluated in advance of the request to recognize a document.

3) Clarify whether proposed voluntary consensus standards will be evaluated and/or posted one at a time or batched together.

4) Clarify whether FDA would be willing to review a document recognized as a voluntary consensus standard while it is in draft status, such that any concerns can be addressed before the formal application is submitted, or if the intention to identify and address concerns by publishing partial recognitions (lines 234-235) of voluntary consensus standard.

5) Outline provisions made to give all companies and organizations visibility to what standards have been offered - and by which organization - for recognition by FDA such that there is an opportunity for each company to connect with the standard developer on content before the standard in finalized or revised in the future.

6) Expand upon the process by which an organization’s development process is evaluated and recognized as in compliance with expectations for voluntary consensus standard development. Elaborate on whether it is performed solely by the Pharmaceutical Quality Standards Working Group (PQSWG) and whether the voluntary consensus standard can be evaluated in advance of the request for informal recognition.

7) Discuss the potential that, while not recognized as legal requirements, the informally recognized voluntary consensus standards related to pharmaceutical quality could be recognized as a part of “current” GMPs.

8) Clarify the application of informally recognized voluntary consensus standards related to pharmaceutical quality in cross-Center actions, such as reviews or inspections for combination products (e.g., drug-biologic, drug-device, kits).

9) Expand upon lifecycle management expectation for informally recognized voluntary consensus standards. For example, discuss the expectations regarding:
   a) Identification of which version of an informally recognized voluntary consensus standard is being used in an application and if references need to be updated whenever the informally recognized voluntary consensus standards is updated.
   b) An informally recognized voluntary consensus standard becomes a regulatory expectation.
   c) Monitoring/version control, maintenance, archiving, re-evaluation period and retirement.
   d) Expectation of applying or complying to new versions of previously referenced informally recognized voluntary consensus standards.

10) Discuss the process for addressing potential conflicts with compendial standards, such as USP. For example:
   a) Do consensus standard organizations need to develop equivalency/superiority to maintain recognition?
   b) What is the process if USP covers a consensus standard after FDA recognition?

11) Discuss whether voluntary consensus standard will be considered by FDA without prior recognition in the database

Concluding Comments

ISPE wishes to thank the FDA for the opportunity to comment on this important topic and applauds the Agency's recognition of Industry's concerns regarding the use of quality standards that may differ from or not be covered by current FDA Guidances. CDER's willingness to evaluate, informally recognize and publish voluntary consensus standards related to pharmaceutical quality will facilitate innovation within the Industry and greater understanding of expectations between the FDA and the Industry. ISPE appreciates the Agency's willingness to consider the transparency and timeliness of evaluating, recognizing and publishing voluntary consensus standards.