Supplements and other changes to an approved application

Public meeting
Center for Drug Evaluation and Research, USFDA

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Agenda

- Points to consider
- Quality System
- Way forward

- Comments are limited to questions raised in the January 5, 2007 FR Notice for this public meeting.

Points to consider

- *Indication* and *dosage form* may be the primary considerations for a risk-based regulatory scheme.
- Secondary considerations may include:

1. length of time in the market
2. safety profile
3. compliance risk profile
4. product profile (e.g. history of meeting In-Process, release, stability specifications)

Points to consider

- The existing OTC monograph system provides a framework for regulation of drugs outside the application review process. This new approach may include change from NDA to OTC monograph status as well as enable Quality by Design.
- Number of annually reportable changes expected to increase. Preparation time may be reevaluated (adjustment to beyond 60 days after end of reporting period)

Points to consider

- If changes to § 314.70 are anticipated, related guidance documents (FDA's April 2004 Guidance for Industry entitled "Changes to an Approved NDA or ANDA", SUPAC Guidance documents, etc.) may be modified or eliminated.

General points

Simplicity

- The revision may provide clarity and consistency of concepts
- Reduce complexity
- Logical categorization
- Provide interpretation relative to the FD&C act, a process and establish expectations in line with the act
- Identify areas of core competency to support science based decisions.

Flexibility

- Use general language consistent with SEC. 116 and knowledge/science based flexibility

- Minimize reliance on opinion, hearsay and precedence.

Transparency

- Use Risk management to support decisions.
- Allow risk management methods to determine the change category
- Involve stakeholders in developing and implementing the new rule
- Compel fact and data based decisions

Continual Improvement

- Acknowledge organization - customer dynamics
- Meet the challenge to be sufficiently detailed to meet public health protection goals and sufficiently general not to impede implementation (enforcement, innovation).

Continual Improvement

- Use risk management, science and technology to systematically institutionalize and integrate public health objectives into the rule.

- Allow the stakeholders the freedom to exercise expertise and discretion within said frame work

Continual Improvement

- Provide industry with the incentive to innovate and maintain effective Quality.
- Allow language to encourage adoption of new science and technology.
- Support the development of manufacturing science

Details on some general points

Provide interpretation relative to the FD&C act, a process and establish expectations in line with the ACT (simplicity)

- There are a number of triggers in 314.70 under "changes to conditions":
- Prospectively or retrospectively compiled information during development and manufacturing subjected to scientific examination and risk based reasoning can serve to determine "conditions".
- The decision to notify may be determined by risk assessment.

Reduced complexity and provide logical categorization. (simplicity)

- Catalogue changes:
- PA
- CBE 30
- CBE 0
- AR
- N/A: no filing
- Identify criteria for process inputs

The revision may provide clarity and consistency of concepts (simplicity)

Example:

Paragraph 314.70 (b)

"…Substantial potential…..".

Allow risk management methods to determine the change category (Transparency)

- Assess the effects of the change to evaluate the effects on the identity, strength, quality, purity, and potency of a drug.

- Assess the effects as these factors may relate to the safety or effectiveness of the drug.

Quality System

Contributions of a Quality system

- Quality system provides the organizational frame work to manage change:

1. Risk management uses the content of a quality system to function.
2. Processes within a Quality system serve to gather data and build knowledge
3. Measurable quality relies on flexible systems and processes dealing with variable inputs.

Benefits of a flexible quality system

1. Leads to the Development of a suitable system using product and risk knowledge
2. Leads to the Development of an effective system
3. Flexible customer and product focused quality system supports organizational objectives.
4. Life cycle approach to quality may fill gaps and support integration.
5. Allows organizations to adapt

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- We acknowledge the Advisory committee's agreement to progress in this direction

Way Forward

- Phased approach
- Implementation
- Pilot program?

Implementation

- Adapt existing structures, organizations and systems

- Improve communication and transparency

Thank you