

Risk-Based CMC Review

A Generic Pharmaceutical Perspective

Advisory Committee for Pharmaceutical Science

November 15, 2000

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GPHA Position

- Supported all SUPAC Initiatives
- Supported FDAMA 97 Section 116
- Supports the FDA Initiative to further “downregulate” and establish CMC requirements on a sound scientific basis

GPhA agrees with FDA that there will be no reduction in study, data, or documentation requirements by the sponsor. All established CMC requirements are maintained

GPhA supports “Phased-In”
approach which begins with the
simplest scenario and evolves
into more complexity

Focus of Initiative should be
product quality and chemistry
and manufacturing controls

Important attributes and acceptance criteria are key questions in establishing qualification. FDA proposes 4 categories (drug substance, drug product, safety, and GMP compliance)

In renewing the FDA proposal,
GPhA has identified several issues

- Will 3 lists be required?

(Drug substance only, drug product only,
drug substance and product)

Issues (continued)

- Must all acceptance criteria for all the attributes in FDA's 4 categories be met? Will meeting only some attributes suffice?

Issues (continued)

- Will FDA develop the “list” with industry input? How will new drug substances/drug products be added?
- Many of FDA’s suggested attributes are not inherent properties (such as solubility and permeability); but rather company or process specific

Issues (continued)

- How does the safety category which FDA proposes correlate with the product quality attributes?
- What is “history” with the product? Is this the sponsor’s history or simply the product being manufactured for a number of years?
- SUPAC defines “significant body of information” as 5 years for new NMEs and 3 years for new products

Issues (continued)

- With respect to the manufacturing process, FDA suggests 2 categories: “easy” and everything else. With multiple processes available to manufacture, what is “easy” for one sponsor may not be for another

Issues (continued)

- Acceptance criteria for drug substance attributes may not be relevant once drug product is formulated (e.g., a light or moisture sensitive DS may be stabilized by the dosage formulation)

GPhA Proposal for ANDAs

- Create a concept which “downregulates” and provides relief from filing requirements on the qualification of the sponsor and its product

GPhA Proposal (continued)

- Replace concept of “Truncated ANDA” and continue the traditional filing approach. After a history of manufacturing for 3 years, sponsor submits Annual Report with reduced CMC

Advantages

- The GPhA proposal could be used for all products (with FDAMA exceptions)
- This approach rewards quality and compliance
- Does not depend on a “list” concept
- Does not require regulation to implement

Summary

- GPhA supports FDA's efforts to establish a risk-based CMC review
- Questions before the committee are all relevant and challenging to apply generally to DS, DP, and to manufacturers
- GPhA proposal attempts to implement FDA concept in a "customized" approach by DS, DP, and manufacturer; thus the attributes are created, complied with, and accepted by both the FDA and the sponsor