PQRI WORKSHOP ON EXCIPIENT TESTING AND CONTROL STRATEGIES

TENTATIVE AGENDA

Tuesday – October 10, 2006

Day 1, Morning: Introduce the Survey Results and Discussion Topics which will include the following

Industry: Excipient and Drug product manufacturers, Excipient distributors -

- List topics, and discuss issues with examples of problems
- Excipient availability as compendia grade
  - Excipient manufacturer incidents of stopping to use *USP-NF* compendial designation to their products which were formerly labeled to be of *USP-NF* compendial grade (state number of excipients and their extent of use in terms of their volume or mass).
- Present industry concerns (real, perceived or potential risks) about labeling excipients to be of *USP-NF* compendial grade.
- Discuss current regulatory burden in connection with procuring, testing, and use of excipients in drug products.

FDA: Address topics with the government point of view.

- Discuss Regulations and Guidances applicable to components used in FDA regulated drug products.

Round Table Discussion: Groups on 5 Topics. Attendees will rotate through each topic.

Lunch

Day 1, Afternoon: Continuation of Roundtable Discussion Groups on 5 topics. Attendees will rotate through each topic.

Reception

Wednesday – October 11, 2006

Day 2, Morning: Continuation of Roundtable Discussion Groups on 5 topics. Attendees will rotate through each topic.

Lunch

Day 2, Afternoon: Wrap-up by Topic Leaders
Present summary of discussion; include regulatory issues from industry, present workshop participants' recommendations for changes in FDA regulations and guidances related to use of excipients in drug products.

Topics to be covered by this Workshop are:

1. Clarify “continuous flow manufacturing” and “skip lot testing” used for excipients in the context of 21 CFR Part 211.84 regulations.
    - How is a "batch" or "lot" defined in the context of continuous manufacturing of an excipient?
    - Is skip-lot testing routinely used by the excipient industry for obtaining test results for the “Certificate of Analysis?” What are the current regulatory expectations, and any potential for skip-lot testing for excipients? What should be the criteria for skip lot testing of excipients?

2. Discuss how characterization of excipient physical and chemical properties helps build quality into the drug product.
    - How is Quality-by-Design built into a drug product by understanding critical properties of excipient(s) used?
    - What are processability issues when excipients are procured from multiple vendors and sources?
    - Should these properties be addressed in compendial monographs or registration filings?

3. Highlight advantages of increased use of third party audits.
    - How are third party audits viewed? Is this a part of building a qualified excipient? Can third party be used to develop a good qualification program for excipient suppliers? How should third party audit programs be qualified? How would small manufacturers benefit from a third party audit?
    - What qualification should a third party auditor have?

4. Discuss strategies to reduce excipients not labeled *USP-NF*.
    - What are the barriers to labeling an excipient to be of *USP-NF* grade? How can the barriers be reduced?
    - What excipients are no longer available as *USP-NF* grade, which were formerly available as *USP-NF* grade?
    - What are the implications when a non-compendial grade (not designated through labeling suffix, namely *USP-NF*, JP, or Ph.Eur.) excipient will be used, when it was previously procured as compendial grade?
    - Industry's burden to supply analytical method validation data to regulatory agency for excipients no longer labeled *USP-NF*.
    - What test methods are used when a non-compendial grade excipient is used, when it was previously procured as compendial grade?
    - What are the ongoing initiatives at the USP to address these problems?

5. Discuss when reduced testing is appropriate.
    - How should industry resolve problems with ICH Q4B interchangeability?
    - When can Industry start implementing a new signed off general chapter?
        i. Once it is published in *USP-NF*?

ii. Wait until the delayed implementation date?
iii. When ICH Q4B has been completed?

- How many tests should be performed to assure an excipients quality for global drug products when there are a number of non-harmonized tests in the global (e.g., *USP-NF*, Ph.Eur., JP) compendia?
- What are the regulatory approaches when industry uses Ph.Eur. or JP test results to meet the *USP-NF* requirements?
- How is your company filing changes to *USP-NF* excipient monographs and general chapters, to your previous submission to the FDA? 21 CFR 314.70 regulations apply, but FDA's "Guidance to Industry, Changes to an Approved NDA or ANDA; Specifications–Use of Enforcement Discretion for Compendial Changes" states discretionary enforcement, and industry uncertainty remains. What are your company's policies/practices based on FDA's 21 CFR 314.70 and the FDA's Guidance on Enforcement Discretion issued on November 19, 2004?
- How should industry make effective use of PDG harmonization in light of the resulting changed excipient monographs?