

## **Minutes of PQRI MTC Teleconference 1/22/04**

**Participants:** Mark Altman (CHPA), Bruce Bird (Pharma), Jon Clark (FDA), Linda O'Connor (GPHA), Nick Maselli (GPHA), George Millili (ISPE), Margaret Szymczak (AAPS), Sylvia Gantt (PQRI), Fred Razzaghi (CHPA)

The purpose of the teleconference was to inform the MTC members of the recent PQRI steering committee meeting, and to solicit feedback from the MTC members, regarding future projects for the group, focusing on the FDA's GMP Initiative. The proposals must be developed for presentation at the February 12 steering committee meeting.

### **Overview**

Nick Maselli provided a brief overview of the steering committee discussions namely that 3 working groups were proposed – manufacturing science, risk management, regulatory process. A possible fourth WG to address specifications was also suggested. It is recommended that the groups start with solid oral dosage forms.

Jon Clark provided additional direction of the GMP initiative from an FDA perspective: ideally when a firm is in control, review divisions would like to have increased confidence in the products and firm, to allow regulatory relief to post approval changes. Now, GMP aspects are relegated to the districts, and a significant body of knowledge resides in annual product reviews, which are subject to district but not review division review. Integrating these areas to demonstrate control, and providing FDA increased confidence in a product's quality is the challenge for the working group. Assessing risk is integral to the initiative. Firms should demonstrate that there is enough science behind their products, resulting in higher confidence. Consistency is expected.

### **Risk Management**

A detailed discussion of risk ensued. To develop the risk criteria, a workshop is recommended to define what is risk and what models apply, followed by formation of a WG, and publication of a white paper.

The MTC will develop an agenda for the workshop focusing on risk concepts and risk models. Experts will be asked to speak to the various models, and how they apply to pharmaceuticals. Pharmaceutical industry experience with the models should be shared. Experts will be asked to educate us how they are applied. Ideally the MTC working group would propose one model rather than firms choosing a model. The goal is to have a draft proposal for the next steering committee, by 1/30 including identification of specialists. Jon Clark was asked to solicit feedback at Arden House Conference this month.

### **Manufacturing Science:**

The MTC is asked to give some definition and direction to this category. The concepts of robustness, predictability and life cycle management were discussed. To narrow the category and achieve short-term progress, solid oral dosage forms will be addressed first. The goal is to “define product and process (attributes?) , and ways of defining robustness for those operations.”

A working plan will be developed for the steering committee, followed by population of a working group, if approved.

Volunteers: George Millili, Margaret Szymczak, Fred Razzaghi

**Regulatory Process / Change Management:**

The MTC will develop the criteria to lower the hurdles (reporting levels), and how to get to that level. The annual product review is recognized as the lowest reporting level (no submission necessary), followed by annual report, CBE, and prior approval. We should develop the relationship between the reporting categories. Case studies would be helpful, noting a product's quality attributes. The regulators need to know that product is under control. Currently development reports, validation data, and APR data is not filed. How do we provide or integrate this information to give the reviewer a comfort level about the product?

A work plan is required incorporating quality by design, specification life cycle, and specification setting concepts.

Volunteers: Bruce Bird, Nick Maselli, Fred Razzaghi

**Specifications:**

This category crosses a few technical committees, but clearly falls within the purview of the MTC as well. Cross-fertilization of ideas within the MTC working groups is needed, as they all relate to specification setting. The concept of interim specifications needs development. Specifications need to be based on the product's safety and efficacy, and should be appropriate for the product, and not rote application of prior criteria. We can then hone in on in process controls. Specifications need to be addressed within the concept of manufacturing science. What is the basis for the specification? Over time the specification will evolve and grow. This category is recommended as a Phase II exercise after we lay the groundwork by better defining manufacturing science and risk.

To insure cross-fertilization – a member of MTC will serve as a liaison to the working groups.

Volunteer: Margaret Szymczak

**Follow-ups:**

A teleconference will be held on February 9<sup>th</sup> at 8AM to finalize the work plan proposals, which will be presented to the steering committee on 2/12. In the interim, the volunteers should develop their work plans and forward to Nick and Bruce, for dissemination prior to the 2/9 telecon. Any additional assistance from other MTC members is welcome. Please call the volunteers directly.

Prepared by Nick Maselli