

PQRI Manufacturing Technical Committee
April 19, 2007
Summary Meeting Minutes

The MTC had a face to face meeting on April 19, 2007.

Antitrust Statement

The meeting began with the reading of the following antitrust statement: "Our discussions today are subject to the anti-trust guidance applicable in the U.S. Nothing discussed at this meeting is intended to restrict the individual decision-making of any member company or to represent an agreement to coordinate marketing or sales conduct. Those participating in this meeting are instructed to avoid discussion of competitively sensitive subjects, including, confidential marketing, sales, and pricing information."

Open Action Items

Open action items from prior to the Mar. 15th meeting:

1. Follow up for a Merck participant on a teleconference to discuss the Biological Indicators for isolators work plan, then to arrange a meeting for the discussion of the need for this work.
Set up a meeting in May to discuss this. There was a question on the urgency in doing this work. Member mentioned that he could participate in the teleconference to give some perspective of how the topic came about. The current main point may be around the organisms used and the coupon to use during validation and around skip testing. The MTC also asked whether any help is needed in getting this started.
2. Check with Compliance about getting a member for the Specification WG.
FDA will try to get someone from Compliance as a team member.
3. **MTC** to review the article (attached to the minutes) and see if a work group is warranted.
Discussed below.
4. **MTC** to review the proposals (attached to the minutes) to see if the MTC would support recommending funding of these proposals.
Discussed below.

New Action items from Mar. 15th meeting:

5. **Get** a Risk Management WG update to share with the MTC.
See below. An update given at this meeting.

Work Group Proposals

The group then discussed the various work plan proposals sent to the MTC. The first one discussed was "Effect of shear on the hydrophobicity (and dissolution) of lubricated blends". The group felt that this proposal fit better with the Development Technical Committee, since it would help select the process and/or excipients to use. The MTC's

main question is how this work would benefit manufacturing. It does not appear to link dissolution testing with manufacturing processes. There was a feeling also that a lot of this work was already in the literature. There also is no timeline or work plan associated with the proposal and we can not determine how long the work is proposed to take.

The proposal “Experimental/computational approach for predicting cohesion and flow of pharmaceutical blends containing size-distributed non-spherical particles” raised the same questions as the first proposal (i.e. how will manufacturing benefit, no timeline, etc.).

The MTC felt that the proposal “Geometrically and Dynamically Induced Hydrodynamic Variability in the USP Dissolution Testing Apparatus II and its Effect on Dissolution Profiles of Solid Dosage Forms” was much more relevant to the manufacturing. The team felt there was merit to exploring this, but possibly expanding the scope to include geometry of the tablets and the hydrodynamics of that take place. The inclusion of capsules should also be considered. It was mentioned that in previous publications, the tablet was fastened to the bottom of the dissolution vessel, it was suggested that studying the affect that random motion of the tablet in the vessel during the dissolution test may have on the results. A question was also raised about possibly exploring the perturbations that could result from measuring dissolution in a development laboratory vs. a commercial laboratory and whether they would have an impact on the dissolution values. The proposal is also lacking a timeline and cost estimate. We will follow up on this proposal.

The MTC felt that the proposal “Accurate Estimation of the Equilibrium Solubility of Metastable Solid API using Finite Difference Analysis and Intrinsic Dissolution” was also a Development Technical Committee type of proposal, without a link to manufacturing.

It was decided that the MTC should develop what it sees as our Strategic Imperatives, what are the manufacturing issues as we see them. We would then share these strategies with subject matter experts to develop strategies and proposals on how to work on these issues. As part of the strategic imperatives we should also include the criteria for evaluating work plans in these areas. We agreed to discuss this at our July face to face meeting.

If we agree to fund academic proposals we will assign a liaison from the MTC to work with the University to review progress on the work plans. We also mentioned that work that we would fund would be expected to be completed in a short period of time (months rather than years).

Action Item: Draft a response on the proposals and circulate to the MTC for review.

Although this was discussed later in the agenda, I have included the discussion on Active versus Passive Air monitoring here. It was mentioned that the paper was pretty thorough

on the topic and that a work group probably wasn't warranted. However, there could be other areas that required work to be done. It was suggested that we wait until after our strategic discussion in July before we decided. One possible area that has been discussed at PDA, which is what statistical model should be used for evaluation of environmental monitoring data. Since the data is usually so low, i.e. zeroes and ones, there is no good model to use. Another possibility in this area would be around how to analyze data from instantaneous monitoring systems where the counts are usually higher and how is the data correlated and analyzed. There may be some work also that could come from the EU Annex 1 revision that is due out soon.

ASTM Standards on RFID

The group reviewed the draft proposals from ASTM on standards for determining the performance of RFID transponders on cases and pallets. If anyone has comments they should send them into ASTM.

Post Approval Changes for Sterile Products

An update on the work group was given. They will update the document to include the minor comment from PDA. We then discussed what should be done with the document. It was agreed that we should send it to PDA for publication. We also mentioned that the paper should be sent to the FDA also. We will draft a cover letter for sending the document to the FDA. FDA rep mentioned that he would look into submitting the document to the docket for post approval changes. It was agreed this would be great way of getting the work out.

Action Item: Draft a cover letter to submit the document to the FDA.

Action Item: Look into submitting the document to the post approval changes docket.

Action Item: Work on submitting the document to PDA for publication in some format.

It was mentioned that the group has completed their work and many stated that they would like to be involved in future PQRI working groups if possible. A list of current members will be submitted so that PQRI can send out thank you letters to the WG.

Action Item: Forward a list of current members to chair. PQRI will send letters of thanks to the work group once they have the list of members.

It was asked if this work has shown any areas where new work groups might be useful. There may be some need for work groups in the areas where the changes could not be assessed, i.e. changes in media fills and raw material testing. They mentioned that we would see about getting draft work proposals for these areas.

The MTC also encouraged that we publicize the work that was completed. We will look into getting a presentation into this falls PDA/FDA Joint Conference. We will also look

to draft a news item on the work for the PDA Newsletter. It was suggest to the other members of the work group, that if they get a chance to present the work at a conference they should present the work of the WG.

Action Item: See if we can get a presentation on the PAC Sterile Products at the PDA/FDA joint conference in the fall.

Action Item: Draft a news brief for the PDA Newsletter and to communicate to the WG members the desire to have them present the data at conferences.

Risk Management Work Group

Reviewed the progress the work group has made to date. Matrix for this analysis was sent to the MTC. They are beginning to get some good case studies from the new members from Wyeth and J&J. There are some gaps with case studies for materials system, product system, and laboratory control. WG Chair will be put in touch with the chair of the PDA risk management support group to see if there are some possibilities for case studies there also.

Action Item: Provide WG chair with contact information for the Chair of the PDA risk management support group.

Specification Design & Lifecycle Management Work Plan

Updated the MTC on the progress of the Specifications work group. The WG is looking for a clinician as a member of the work group. The WG has a possibility for a member. It was mentioned that the group might want to consider the addition of a pharm tox person also, since the move is towards specifications with not only clinical relevance, but on a safety (tox) basis also, this would be a good addition. WG will explore the possibility of adding a pharm tox specialist to the team also. The WG is currently working on a glossary. They plan to have a June face to face meeting where they will review a straw man on the glossary and definitions that have been drafted. They then plan a second face to face meeting the end of July where they hope to complete their “high level process” and start on the detailed process.

Biologicals Inspection Survey Work Group

The survey results would be published in the May/June addition of the PDA Journal. They are awaiting the final proofs after making some minor editorial revisions. They will send names of current members so thank you letters may be sent to the work group. It was felt it might be better to send the thank you letters out after the publication of the article so it may be acknowledged in the letter.

Action Item: Send a list of the current work group members to MTC chair. He will have PQRI send out thank you letters to the work group.

It was mentioned that it would be good to present the results of the work group at conferences. It was felt that the FDA would reference the work in presentations that they make, but we should also look to present results. We will look to see whether we can get a presentation at the PDA/FDA conference this fall.

Action Item: Explore the option of having a presentation on the biologicals survey included on this falls PDA/FDA conference agenda.

Action Item: MTC to be on the lookout for conferences where presentations on the biologicals survey work group results could be made.

Steering Committee Update

The DPTC and DSTC are being combined into one, the Development Technical Committee. The DPTC and DSTC are being disbanded and new members selected for the DTC. Members from the DPTC and DSTC could be on the DTC. Chair said he would forward the rationale drafted for the reorganization that is being sent to the member organizations.

Action Item: Forward rationale for reorganization of the DPTC and DSTC to the MTC. (**Post Meeting Note:** rationale is attached to email for these minutes.)

It was mentioned that the QbD for Drug Release work group is proposing a work shop to gather information to help them with their work plan. It was mentioned that there have been several conferences on this and it may be difficult to get participation.

In discussing the use of work shops (small number of invited subject matter experts) versus conferences (large number of attendees) it was mentioned that we will have to think about how we will attract the SME's to attend our workshops.

It was also suggested that we review the output from the ISPE/AAPS/FDA workshop that was held in Feb./Mar. to see if there are ideas there for work groups.

Next Meeting

The next teleconference is scheduled for May 17th from 9:00 to 11:00 AM (EDT). An agenda and call information will be issued prior to the teleconference.

Also note we have changed the date for the July face to face meeting to July 12th it will be at Pfizer's Peapack, NJ facility.

Schedule of meetings:

2007

May 17th Teleconference

June 21st Teleconference

July 19th Face to Face

August 16th Teleconference

September 20th Teleconference

October 18th Face to Face
November 15th Teleconference
December 13th Teleconference