Final question list – 29 September 2005

1. How many *approved* PAT filings are there? What are the number of total product PAT filings versus unit ops PAT filings?
    a. For those that have been turned down, what was the issue?

2. We have heard that there is some pushback on recent discussions with the agency regarding PAT applications that do not have a control component.
    b. Based on discussions with other industries (e.g. commodities), not all PAT in those industries is under feedback control.
    c. What is the expectation of the agency regarding the level of control? For example, is there an expectation that we should have continuous versus discrete control?
    d. Being overly prescriptive early on may kill innovation before it starts.

3. What are your plans for getting CBER more involved with the PAT Initiative?
    e. It is rumored that more involvement will occur after the 2nd FDA PATRIOT training class? When will that be?
    f. There are PAT successes on the biologics side which are not being reported, because CBER is not formally engaged with the PAT initiative.

4. We have heard that there is some pushback on recent discussions with the agency regarding expectations of quality impact due to PAT.
    g. For example, we are told that PAT applications that improve product yield are not considered PAT. Can you clarify?
    h. The original FDA white paper states that the current state of pharmaceutical processes is inefficient and costly, and that PAT is a remedy to this. So why not include improvements in yield or inventory costs?

5. Developing and implementing PAT steps gradually is more feasible from a practitioner's standpoint -- in other words, submitting a conventional application with one PAT step in a multi-step process.
    i. Is there an intermediate benefit between regulatory relief and no benefit?

6. What is the appropriate procedure to approach FDA regarding PAT issues, applicability, and filing?
    j. Typically who is present during these conversations? Regulatory, technical or both? Can you suggest a solution for bypassing the formality associated with clearing up technical issues from a practitioner's perspective? Currently, the paradigm is that our companies' regulatory personnel are in charge of communications with the FDA and don't favor informal communications.
    k. How many conversations are generally necessary per application?
    l. How much data is required for a PAT regulatory submission? We have heard that a two-page PowerPoint presentation is sufficient, without data. Are there differences in this requirement between NDAs and Comparability Protocols?

7. Industry is in favor of using well-established scientific principles to define sampling rates appropriate to our processes.
    i. For example, using the Deborah Number, etc.

8. Even in the absence of regulatory relief, are there resources you can provide for foundation technologies that are not ready for use in feedback control? Can the PAT team act as an internal FDA resource to “bless” unconventional analytical techniques?

9. In a PAT application, when is re-filing versus agency notification required? For example, does updating process limits fall under an annual update?

10. What happened to “Safe Harbor?” Is the concept still supported, but under another name (such as “Research Exemption”)?

11. Is FDA considering changes and evolution in the definition of PAT?

12. Can we use ASTM standards which are not in E55?