September 17, 2003
Manufacturing ACPS
Hilda F. Scharen

Summary Minutes of the Manufacturing Subcommittee
Advisory Committee for Pharmaceutical Science
September 17, 2003

The Manufacturing Subcommittee of the Advisory Committee for Pharmaceutical Science of the Food and Drug Administration, Center for Drug Evaluation and Research met on September 17, 2003, at the Advisors and Consultant Staff Conference Room, 5630 Fishers Lane, Rockville, Maryland. The meeting was chaired by Judy Boehlert, Ph.D.

Manufacturing Subcommittee of the Advisory Committee for Pharmaceutical Members (voting):
Patrick DeLuca, Ph.D. (ACPS), Robert (Gary) Hollenbeck, Ph.D. (ACPS)
Judy Boehlert, Ph.D., Daniel Gold, Ph.D., Thomas Layloff, Jr., Ph.D., Garnet Peck, Ph.D., G.K. Raju, Ph.D., Nozer Singpurwalla, Ph.D.

Manufacturing Subcommittee of the Advisory Committee for Pharmaceutical Science Consultants(voting):

Acting Industry Representative (non-voting):
Efraim Shek, Ph.D.

Guest Speakers:
Edmund Fry, Colin Gardner, Greg Guyer, Ph.D., Tobias Massa, Ph.D., Gerry Migliaccio, Kenneth Morris, Ph.D.

FDA Guest Speakers:
Joe Famulare, Ajaz Hussain, Ph.D., Norman Schmuff, Ph.D., Janet Woodcock, M.D.

FDA Participants:
Diana Koliatis

Open Public Hearing Speakers:
September 17, 2003:
Robert Menson, Ph.D.

These summary minutes for the September 17, 2003, meeting of the Manufacturing Subcommittee of the Advisory Committee for Pharmaceutical Science of the Food and Drug Administration were approved on _____.

I certify that I attended the September 17, 2003, meeting of the Manufacturing Subcommittee of the Advisory Committee for Pharmaceutical Science of the Food and Drug Administration meeting and that these minutes accurately reflect what transpired.

_____
Hilda Scharen, M.S.
Executive Secretary

_____
Judy Boehlert, Ph.D.
Chair

The Committee discussed Quality by Design and its relationship to Risk-based Regulatory Scrutiny. The members and the invited consultants were provided the background material from the FDA prior to the meeting.

The meeting was called to order at 8:30 a.m. by Judy Boehlert, Ph.D. (Committee Chair). The Committee members, consultants, and FDA participants introduced themselves. The conflict of interest statement was read into the record by Hilda Scharen, M.S. The agenda proceeded as follows:

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Introduction	Ajaz Hussain, Ph.D., FDA

Quality by Design and Risk-Based Scrutiny

Quality for the 21st Century: Summary of FDA/PQRI Workshop	Tobias Massa, Ph.D., Eli Lilly & Co.
Defining Quality of a Pharmaceutical Product	Janet Woodcock, M.D., FDA
Components of "Quality by Design": Performance Measurement	G.K. Raju, Ph.D., MIT
Assessing Quality-by-Design: A CMC Review Perspective	Norman Schmuff, Ph.D.
Break	

Proposals for Regulatory Assessment of "Quality by Design"

Using Manufacturing Science and Risk Management principles to achieve "Quality by Design"	Gerry Migliaccio, Pfizer Inc.
Quality by Design – A Generic Industry Perspective	Edmund Fry, IVAX Corp.
Risk –Based Development for Quality by Design	Kenneth Morris, Ph.D., Purdue University
Regulatory Assessment of Quality by Design: A CGMP Perspective	Joe Famulare, FDA
Quality by Design: Next Steps to Realize Opportunities	Ajaz Hussain, FDA
Open Public Hearing	
Lunch	
Committee Discussion and Recommendations	
Break	

Quality by Design and Risk Based Regulatory Scrutiny

Designing Quality in Design	Colin Gardner, Transform Pharmaceuticals Inc.
Use of Risk Management in Pharmaceutical Manufacturing	Greg Guyer, Ph. D., Merck & Co., Inc.
Committee Discussion and Recommendations	
Closing Remarks	
Adjourn	

Questions to the Committee:

1. Quality by Design:
    - Articulate a clear description of the term *quality by design*
    - Identify the type of information and knowledge most useful to assess *quality by design*
    - Regulatory approach for assessment of pharmaceutical development knowledge to maximize its value without impacting drug development

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The committee found general agreement that Quality by Design is a dynamic active process that continues in the development stages and post-approval of a product. The knowledge useful to assess Quality by Design is the identification of stress relevance and the critical control point, and robustness of these critical control points. The regulatory approach for assessment is output oriented.

The committee recognized the clear advantage of making progress in an existing system where the goal would be to have creative incentives for a broader development context so that the companies do it and communicate it to FDA. For process development knowledge, it is essential to first understand the boundaries and basic failure modes of this process in terms of its safety and efficacy issues, and predictability issues. They are the basis for the range of the variables and specifications. In making product development formulation it is essential to understand variability, manage variability, the critical process, and end point. The focus on post-approval changes provides a flexible means to engage industry and enhance collaboration. There was also agreement that the issues discussed helped frame this view point and were consistent with the PAT Guidance.

In summary, the committee agreed that the notion of quality is self evident. They committee further defined quality by design as being a systematic process of achieving desirable quality by a careful and methodical scrutiny of all the attributes that go into characterizing quality, from the inception of a product to its end use, involving all its stakeholders (the patient, the manufacturer, the physician, and the regulator).

2. Relationship between *Quality by Design & Risk Based Regulatory Scrutiny*
In this discussion we seek subcommittee recommendations on ways to link the concept of *risk based regulatory scrutiny to quality by design.*

The committee defined the concept as using process understanding as a means for Quality by Design. In PAT, a high level of process understanding was defined as being able to understand the change and impact, and thereby the risk assessment, on the process.

There was a general agreement among the committee members that a less burdensome change management system based on development information provided, as well as testing protocol is needed to qualify change.

The committee concluded that the post-approval change scenario offers a way forward to bring pharmaceutical development information and to learn how to better utilize that information. It was emphasized that pharmaceutical development reports are not only important for post-approval changes. The committee felt this incoming information would help in training FDA personnel, as well as starting to build a culture of "information sharing" between FDA and industry.

In summary, the committee felt that the Quality by Design and risk assessment concepts would assist in the NDA review process and help alleviate fears of delayed post-approval changes. The committee agrees that the current products being developed in ICH guidance will be run in parallel to the CDER's efforts. The committee's thought process and discussions were consistent with the information contained in the Draft Process Analytical Technology(PAT) guidance and represented a good basis for ICH deliberations.

The meeting was adjourned at approximately 4:30 p.m. on September 17, 2003.