Summary Minutes of the
Pharmaceutical Science Advisory Committee
October 25-26, 2005
Location: Center for Drug Evaluation and Research Advisory Committee
5630 Fishers Lane, Rockville Md. Rm: 1066

All external requests for the meeting transcripts should be submitted to the CDER, Freedom of Information office.

These summary minutes for the October 25-26, 2005 of the Advisory Committee for Pharmaceutical Science of the Food and Drug Administration were approved on ___November 23, 2005_____

I certify that I attended the October 25-26, 2005, meeting of the Advisory Committee for Pharmaceutical Science of the Food and Drug Administration meeting and that these minutes accurately reflect what transpired.

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Mimi T. Phan, Pharm.D.
Executive Secretary

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Charles L. Cooney, Ph.D.
Chair

Prior to the meeting, the members and the invited consultants had been provided the background material from the FDA and any written statements submitted by the public. The meeting was called to order by Charles Cooney, Ph.D. (Committee Chair); the conflict of interest statement was read into the record by Mimi T. Phan, Pharm.D. (Executive Secretary). There were approximately 80 individuals in attendance.

On October 25, 2005, the committee will: (1) receive an update on current activities of the Parametric Tolerance Interval Test (PTIT) Workgroup; (2) receive and discuss presentations from the Pharmaceutical Research and Manufacturing Association (PhRMA), the Generic Pharmaceutical Association (GPhA), and the United States Pharmacopeia (USP) pertaining to their perspectives on the general topic of Quality-by-Design (QbD) and drug release or dissolution specification setting; and (3) discuss and provide comments on the updated tactical plan under development for the establishment of drug release or dissolution specifications

Attendance:
Pharmaceutical Science Advisory Committee Members Present (voting):
Charles L. Cooney,Ph.D.(Chair), Patrick P. DeLuca, Ph.D., Carol Gloff, Ph.D., Melvin V. Koch, Ph.D., Kenneth R. Morris, Ph.D., Cynthia R.D. Selassie, Ph.D., Nozer Singpurwalla, Ph.D., Marc Swadener, Ed.D. (Consumer Representative)

Pharmaceutical Science Advisory Committee Member (Industry Representatives- non-voting):
Paul H. Fackler, Ph.D., Gerald Migliaccio

Pharmaceutical Science Advisory Committee Consultants (voting):
Judy Boehlert, Ph.D.

Guest Speakers (non-voting):
Christopher Sinko, Ph.D. (representing PhRMA), John Kovaleski, Ph.D. (representing GPhA)); Walter Hauck, Ph.D. (representing USP); Michael Golden (representing IPAC-RS)

FDA Participants at the Table:
Ajaz, Hussain, Ph.D., Helen Winkle, Moheb Nasr, Ph.D., Richard Lostritto, Ph.D., Robert O'Neill, Ph.D.

Presentations:

Establishing Drug Release or Dissolution Specifications – Quality-by-Design (QbD) Approach

(1) Topic Introduction	Ajaz Hussain, Ph.D. Deputy Director, OPS, CDER, FDA
(2) United States Pharmacopeia (USP) Perspective	Walter Hauck, Ph.D. Thomas Jefferson University (representing USP)
(3) Generic Pharmaceutical Association (GPhA) Perspective	John Kovaleski, Ph.D. Teva Pharmaceuticals USA (repsenting GPhA)
(4) Pharmaceutical Research and Manufacturers of America (PhRMA) Perspective	Christopher Sinko, Ph.D. Pfizer, Inc. (representing PhRMA)

Committee Discussions and Recommendations
Establishing Drug Release or Dissolution
Specifications – Quality-by-Design (QbD) Approach (continued)

(5) Introduction to FDA Perspective	Moheb Nasr, Ph.D. Director, Office of New Drug Quality Assessment (ONDQA), OPS, CDER, FDA
(6) *In Vivo* Relevance of Drug Release Specifications	Ajaz Hussain, Ph.D.

(7) Measuring and Managing Method Variability	Lucinda Buhse, Ph.D. Director, Division of Pharmaceutical Analysis, Office of Testing and Research (OTR), OPS, CDER, FDA
(8) A CMC System-based Approach for Pharmaceutical Quality	Vibhakar Shah, Ph.D. Chemist, Division of New Drug Chemistry II, ONDQA, OPS, CDER, FDA
(9) ICH Q8 Considerations	Ajaz Hussain, Ph.D.
(10) Summary of Current Plan Status -- Next Steps	Moheb Nasr, Ph.D.

Committee Discussions and Recommendations

Parametric Tolerance Interval Test for Dose Content Uniformity

(1) Update -- FDA Perspective	Moheb Nasr, Ph.D.
(2) Update -- IPAC-RS Perspective	Michael Golden GlaxoSmithKline (representing IPAC-RS)

Committee Discussion and Recommendations

Open Public Hearing Speakers (October 25, 2005):
Bryan Crist, Varian Analytic Instruments also USP
Biopharmaceutics Expert Committee

Questions to the Committee on Quality-By-Design (QbD) TOPIC:

1) Are there relevant scientific areas of disagreement among the stakeholders that would impact moving forward with QbD approach?

Question rephrasing: Is there an agreement among the stakeholder to go forward with QbD approach?

Yes – 0 *No – 9* *Abstain – 0*

The Committee interpreted this question as saying that a vote of No means to positively move forward with the QbD approach, while a vote of Yes meant that the committee had reservations with this approach.

2) Should FDA develop a new guidance on a QbD approach to the setting of dissolution specifications? If so, what critical elements should be included in the proposed guidance to distinguish it from the current regulatory approach to setting dissolution specification?

Yes – 8 *No – 0* *Abstain – 1*

The Committee indicated that it is an appropriate time to move forward with the development of new guidance. The critical elements were, how the specifications would relate to clinical safety and efficacy, the patient and understanding the scientific foundation; and that there should be a dialogue with the industry prior to a drafted guidance.

3) What additional considerations are necessary to leverage these efforts further to make this proposed approach a model for setting specifications of other critical quality attributes?

The committee felt that there is a need to develop clarity in of the underlining science. The key points are the need for the early development of the dissolution design specifications, as well as other products attributes in order to relate these specifications to the safety and efficacy.

4) Does the committee agree with the development of a Compliance Policy Guide for use in compliance enforcement activities?

Question rephrasing: does the committee agree with the development of a Compliance Policy Guide to provide clarification for use in compliance enforcement activities for mechanical calibration in dissolution?

Yes – 9 *No – 0* *Abstain – 0*

Questions to the Committee on Parametric Tolerance Interval Test (PTIT) for Content Uniformity Topic:

The addressing of this question was deferred until the following day due to a misinterpretation of underlying assumptions used in the analysis by IPAC-RS

The Meeting adjourned for the day at approximately 17:30 p.m. and reconvened on October 26, 2005 at 8:30 a.m.

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On October 26, 2005, the committee will: (1) discuss and provide comments on the general Quality-by-Design (QbD) topics of question-based review and alcohol-induced dose dumping; and (2) receive and discuss an update on the establishment of a workgroup for the review and assessment of Office of Pharmaceutical Science research programs. Following those items, an awareness topic will be introduced concerning the need to enhance the pharmaceutical education system in the United States.

Attendance:

Pharmaceutical Science Advisory Committee Members Present (voting):

Charles L. Cooney,Ph.D.(Chair), Patrick P. DeLuca, Ph.D., Carol Gloff, Ph.D., Melvin V. Koch, Ph.D., Kenneth R. Morris, Ph.D., Cynthia R.D. Selassie, Ph.D., Nozer Singpurwalla, Ph.D., Marc Swadener, Ed.D. (Consumer Representative)

Pharmaceutical Science Advisory Committee Member (Industry Representative- non-voting):

Paul H. Fackler, Ph.D.

Guest Speakers (non-voting):

Michael Golden (IPAC-RS); Larry Augsburger, Ph.D., Raymond Scherzer

FDA Participants at the Table:

Ajaz, Hussain, Ph.D., Helen Winkle, Moheb Nasr, Ph.D., with Rotating FDA members Richard Lostritto, Ph.D., Robert O'Neill, Ph.D.; Rober Meyer, M.D., Keith Webber, Ph.D., Elizabeth Shores, Ph.D.

Presentations:

Alcohol-induced Dose Dumping

(1) Clinical Relevance of Alcohol-induced Dose Dumping	Robert Meyer, M.D. Director, Office of Drug Evaluation II, Office of New Drugs (OND), CDER, FDA
(2) Mitigating the Risk Posed by Alcohol-induced Dose Dumping	Ajaz Hussain, Ph.D. Deputy Director, OPS, CDER, FDA

Committee Discussions and Recommendations

Implementation of Quality-by-Design (QbD) Principles in CMC Review

(1) Topic Introduction	Helen Winkle Director, OPS, CDER, FDA
(2) Office of Generic Drugs (OGD) Approach	Lawrence Yu, Ph.D. Director for Science, OGD, OPS, CDER, FDA
(3) Office of New Drug Quality Assessment Approach (ONDQA)	Chi-Wan Chen, Ph.D. Deputy Director, ONDQA, OPS, CDER, FDA
(4) Office of Biotechnology Products Approach	Barry Cherney, Ph.D. Deputy Director, Division of Therapeutic Proteins, Office of Biotechnology Products, OPS, CDER, FDA

Committee Discussion and Recommendations

Open Public Hearing Speakers (October 26, 2005):

Girish Malhotra, PE
President EPCOT International

Development of a Peer Review-based Research Program within OPS	Keith Webber, Ph.D. Deputy Director, OPS, CDER, FDA

Update as follow-up to May 2005 ACPS meeting

Committee Discussion and Recommendations

Awareness Topic: Enhancing the Pharmaceutical Education System

(1) Topic Introduction	Ajaz Hussain, Ph.D.
(2) An Academic Perspective - "Is There a Crisis in the Supply of Qualified Pharmaceutical Scientist Specialists in Product Development and Related Technologies?"	Larry Augsburger, Ph.D. University of Maryland School of Pharmacy
(3) An Industry Perspective - "The Challenge Ahead: Pharma Engineering & Technology in the Future"	Raymond H Scherzer, Ph.D. GlaxoSmithKline
Committee Discussion and Recommendations	
Conclusion and Summary Remarks	Helen Winkle

Questions to the Committee on PTIT

1) Would you accept the FDA WG proposal as outlined in slide #15
    a) PTIT applied to DDU testing in the line with FDA current initiatives; i.QbD and demonstration of product and process knowledge ii) Science and risk-based specification of drug product
    b) Goalposts are 80% to 120% of label claim
    c) 87.5% coverage within the goalposts is appropriate
    d) Sample size is determined and set by the applicant
    e) Exceptions to proposed criteria could be proposed by the applicant with adequate scientific justification.
    f) FDA proposed to update the draft MDI/DPI Guidance accordingly

After hearing from the FDA and IPAC-RS, it was clear to the committee that significant progress was made on PTIT applied to DDU testing. It was noted that the FDA is responsible for setting and maintaining drug quality standards and the committee recommended to the Agency to move forward to revise the guidance by incorporating QbD principles in-setting specification, and to seek input from other stakeholders. The committee also asked the agency to update the ACPS on its progress.

Yes – 8 *No –0* *Abstain – 0*

Question to the Committee on Topic 2

Based on the three approaches presented today, what challenges do you anticipate for OPS for ensuring that:

1) The founding scientific and risk-assessment principles adopted by these programs are based on the common principles of quality-by design

2) The implementation plans by these offices are consistent with the complexity of the products, manufacturing processes, analytical and knowledge uncertainty in the regulatory applications of products regulated.

The committee suggested that the following points to be considered by OPS.

a) New science and analytical techniques are continually emerging and need to be applied to process characterization, product characterization and the linkage to clinical relevancy
b) With the science of uncertainty continue to identify where the uncertainty is in relationship to new knowledge around therapeutic safety and efficacy.
c) To acknowledge there are opportunities for continued learning and these should lead to continued improvement and evaluation in both regulation and manufacturing.
d) To evaluate the efficacy of the scoring system for facilitating submission review on the basis of risk; assess its effectiveness going forward; and its utility to the review process.

The Meeting adjourned for the day at approximately 16:30 p.m. on October 26, 2005