May 3-4, 2005
ACPS
Hilda F. Scharen

Summary Minutes of the
Advisory Committee for Pharmaceutical Science
May 3-4, 2005

This is the final report of the Advisory Committee for Pharmaceutical Science meeting held on May 3-4, 2005. A verbatim transcript will be available in about 2 weeks, sent to the Division and posted on the FDA website at http://www.fda.gov/ohrms/dockets/ac/cder05.html#PharmScience

All external requests should be submitted to the Freedom of Information office.

The Advisory Committee for Pharmaceutical Science of the Food and Drug Administration, Center for Drug Evaluation and Research, met on May 3-4, 2005, at the Advisors and Consultant Staff Conference Room, 5630 Fishers Lane, Rockville, Maryland. Charles Cooney, Ph.D., chaired the meeting.

Advisory Committee for Pharmaceutical Science Members (voting):
Charles L. Cooney, Ph.D., Patrick P. DeLuca, Ph.D., Michael S. Korczynski, Ph.D., Kenneth Morris, Ph.D., Cynthia R.D. Selassie, Ph.D., Marc Swadener, Ed.D., Nozer Singpurwalla, Ph.D.

Advisory Committee for Pharmaceutical Science Consultants (voting):
Carol Gloff, Ph.D., Thomas Layloff, Ph.D., Arthur H. Kibbe, Ph.D., Marvin C. Meyer, Ph.D.,

Industry Representative (non-voting):
Paul H. Fackler, Ph.D., Gerald Migliaccio

FDA Guest Speakers:
Lucinda Buhse, Ph.D., Kathleen A. Clouse, Ph.D., Jerry Collins, Ph.D., Ajaz Hussain, Ph.D., Robert Lionberger, Ph.D., Mehul Mehta, Ph.D., Robert O'Neill, Ph.D., Vibhakar Shah, Ph.D., Keith Webber, Ph.D., Helen Winkle, Lawrence Yu, Ph.D.

FDA Participants:
Gary Buehler, R.Ph.

Open Public Hearing Speakers:
May 3, 2005: Will Brown, USP

May 4, 2005: None

These summary minutes for the May 3 and 4, 2005 of the Advisory Committee for Pharmaceutical Science of the Food and Drug Administration were approved on ____May 20, 2005_____.

I certify that I attended the May 3 and 4, 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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Hilda F. Scharen, M.S.
Executive Secretary

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Charles L.Cooney, Ph.D.
Chair

On May 3, 2005, the Committee discussed and provided comments on the general topic of establishing drug release or dissolution specifications. An update from the Clinical Pharmacology Subcommittee was provided at the end of the day. On May 4, 2005, the committee received an update on current activities of the Parametric Tolerance Interval Test (PTIT) Workgroup. The Committee discussed and provided comments on the general topic of considerations for assessment of pharmaceutical equivalence and product design, and discussed criteria for establishing a working group for review and assessment of Office of Pharmaceutical Science (OPS) research programs.
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Charles L. Cooney, Ph.D. (Committee Chair), called the meeting to order at 8:30 a.m. on May 3, 2005. 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:

Day 1: Tuesday, May 3, 2005

Introduction to Meeting OPS Update	Helen Winkle Director, Office of Pharmaceutical Science
Welcome and Opening Remarks	Charles Cooney, Ph.D. Chair, ACPS

Establishing Drug Release or Dissolution Specifications

(1) Topic Introduction	Ajaz Hussain, Ph.D. Deputy Director, OPS
(2) Dissolution Measurement System: Current State and Opportunities for Improvement	Lucinda Buhse, Ph.D. Director, Division of Pharmaceutical Analysis, Office of Testing and Research (OTR), OPS

Break

(3) Overview of Current Guidance Documents and Decision process: Biopharmaceutics Section	Mehul Mehta, Ph.D. Director, Division of Pharm. Evaluation I, Office of Clinical Pharmacology and Biopharmaceutics
(4) Establishing Dissolution Specifications: Current Practice (CMC)	Vibhakar Shah, Ph.D. Chemist, Division of New Drug Chemistry II Office of New Drug Chemistry

Lunch

Open Public Hearing

Establishing Drug Release or Dissolution Specifications

(5) Factors Impacting Drug Dissolution and Absorption: Current State of Science	Lawrence Yu, Ph.D. Director for Science, Office of Generic Drugs
(6) Summary of Tactical Plan	Ajaz Hussain, Ph.D.

Break

Committee Discussions and Recommendations

Subcommittee Reports

Clinical Pharmacology Subcommittee (via teleconference)	Jürgen Venitz, M.D., Ph.D. Chair, Clinical Pharmacology Subcommittee

The meeting was adjourned at approximately 4:41 p.m. on May 3, 2005.

Charles L. Cooney, Ph.D. (Committee Chair), called the meeting to order at 8:30 a.m. on May 4, 2005. The conflict of interest statement was read into the record by Hilda Scharen, M.S. The agenda proceeded as follows:

May 3-4, 2005
ACPS
Hilda F. Scharen

Day 2: Wednesday, May 4, 2005

Parametric Tolerance Interval Test for Dose Content Uniformity	Robert O'Neill, Ph.D. Director, Office of Biostatistics (OB), Office of Pharmacoepidemiology and Statistical Science
Current update on the Working Group	
Quality-by-Design and Pharmaceutical Equivalence	
(1) Topic Introduction	Ajaz Hussain, Ph.D.
(2) Using Product Development Information to Extend Biopharmaceutics Classification System-based Biowaviers	Ajaz Hussain Ph.D.
Break	
(3) Using Product Development Information to Address the Challenge of Highly-variable Drugs	Lawrence Yu, Ph.D.
(4) Using Product Development Information to Support Establishing Therapeutic Equivalence of Topical Products	Robert Lionberger, Ph.D. Chemist, OGD, OPS
Lunch	
Open Public Hearing	
Quality-by-Design and Pharmaceutical Equivalence	
(5) Topic Introduction (Cont'd)	Ajaz Hussain, Ph.D.
Committee Discussion and Recommendations	
Break	
Criteria for Establishing a Working Group for Review and Assessment of OPS Research Programs	
(1) CBER Peer Review Process for Researchers/Reviewers	Kathleen A. Clouse, Ph.D. Acting Director, Division of Monoclonal Antibodies, Office of Biotechnology Products (OBP)
(2) CDER Peer Review Research	Jerry Collins, Ph.D. Director, Laboratory of Clinical Pharmacology, Office of Testing and Research (OTR), OPS
Committee Discussion and Recommendations	
Conclusion and Summary Remarks	Ajaz Hussain, Ph.D. Helen Winkle

***Questions to the Committee**:*

Topic #1

Are the tactical steps outlined consistent with the QbD goals we seek to achieve?

The Committee agreed with the outlined tactical steps and the members felt that this is one additional step in moving towards Quality by Design while moving to Desired State. The members expressed some concerns with the current dissolution tests that are used, as the dissolution specifications are not tailored to specific scenarios and there is substantial variability with the methodology. In addition, the Committee felt that in light of the complexity in understanding this system, the proposed approach will lead to a mechanistic understanding of the manufacturing process and the relationship of the process and product. The members unanimously voted in agreement to adopt and move forward with the tactical plan and the proposed steps to be incorporated in the recommendations.

Yes: 11
No: 24
Abstain: 0

What additional steps and/or changes would you recommend to improve this plan?
The Committee emphasized it is important to think through the implications this plan will have for the regulatory process. The members expressed some desire that this plan helps move away from a "check the box" process for reviewing and approval, and will enable continuous learning and ultimately improve the process.

What additional scientific evidence is necessary to support the development and implementation of this plan?
The members recognized the rational for the currently used release test b y the FDA and emphasized it is important to keep in mind that the ultimate point of the release test is the patient.. Finally, the Committee felt it is important for the implementation plan to consider the impact on both the regulator and the manufacturer.

The Committee added that it is essential to incorporate in its work an adequate communication plan, to inform a broader community about the implementation of the tactical plan.

General considerations for identifying and developing statistical procedures
Any other specific recommendations
Prioritization
The members discussed the implications that exist with using the same dissolution specifications for generic as for pharma. Also, some members emphasized the difficult position the generic drug industry is in while trying to comply with both FDA specifications and USP standards. The Committee agreed that it is important to give particular attention to generic products, while developing this strategy. Some member felt that this could be achieved by revising the requirements and standards and submitting them to USP. However, some members noted the long time required for a USP change and the financial burden this places on industry.

Topic #2

How can pharmaceutical development information help to extend the applications of BCS-based waiver of in vivo studies for immediate release products?
How can pharmaceutical development information be utilized to address the challenge of highly variable drugs?
Establishing therapeutic equivalence of topical products?
The members felt that a better understanding of the scenario of formulation design will lead to improved product quality with reduced variability, which they agreed is the foundation of Quality by Design. The Committee highlighted that it is a scientific hypothesis, which will allow for clearer decision-making and ultimately, hopefully create more flexibility.

In addition, the Committee added that the implementation of Quality by Design will require for additional information on the product development process, e.g. the Product Development Report. However, the members emphasized it was important that while Industry shares additional information, that this risk-based system reduces their burden and adds more relevancy to the questions asked, as well as, reduces the number of approval cycles.

The members understood that FDA wants to use the Product Development Report to: (1) extend BCS-based waiver for immediate release products, (2) facilitate approval of Highly Variable Drugs, (3) facilitate pharmaceutical equivalence of topical products.

The Committee believes it is important to add clarity on what information is needed and how additional information will be used to establish bioavailability and bioequivalence. Additionally, the members felt it was essential for the

system to be receptive and advised there was a need for FDA to work with both the reviewers and Industry to ensure and educate them so that the new information provided will be used effectively.

Some members underlined the importance of having the generic drug industry well engaged during the development phase of the decision trees for the proposed hypothesis.

In conclusion, the Committee recommended that FDA continue to address Quality by Design and define its use to facilitate its use in the regulatory approval of drug products.

Topic #3

Does the ACPS support the creation of a subcommittee under ACPS to develop the criteria and the process for review of OPS research programs?
The members agreed with the concept of creating a subcommittee under the Advisory Committee for Pharmaceutical Science in order to review the Office of Pharmaceutical Science research programs. The Committee unanimously endorsed the recommendation for the creation of this subcommittee under the main Advisory Committee for Pharmaceutical Science.

Yes: 11
No: 24
Abstain: 0

The meeting was adjourned at approximately 3:41 p.m. on May 4, 2005.