Summary Minutes of the
Pharmaceutical Science Advisory Committee
October 5-6, 2006
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 5-6, 2006 of the Advisory Committee for Pharmaceutical Science of the Food and Drug Administration were approved on 10/24/06

I certify that I attended the October 5-6, 2006, meeting of the Advisory Committee for Pharmaceutical Science of the Food and Drug Administration meeting and that these minutes accurately reflect what transpired.

Mimi T. Phan, Pharm.D., R.Ph.
Designated Federal Officer

Carol Gloff, Ph.D.
Acting Chair (October 5, 2006)

Charles Cooney, Ph.D.
Chair (October 6, 2006)

Meeting of the Advisory Committee for Pharmaceutical Science
October 6, 2006

Prior to the meeting, the members and the invited consultants were provided the background materials 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., R.Ph. (Designated Federal Officer). There were approximately 80 individuals in attendance.

On October 6, 2006, the committee will: (1) receive an awareness presentation on risk management for complex pharmaceuticals, (2) receive presentations and discuss bioequivalence issues pertaining to highly variable drugs, (3) discuss current thinking on issues and definitions pertaining to nanotechnology, (4) discuss implementation of definitions for topical dosage forms, and (5) receive an update and discuss current strategies and direction for the Critical Path Initiative.

Attendance:

Advisory Committee for Pharmaceutical Science Members Present (voting):
Charles Cooney, Ph.D.; Carol Gloff, Ph.D.; Meryl Karol, Ph.D.; Melvin Koch, Ph.D.; Kenneth Morris, Ph.D.; Cynthia Selassie, Ph.D.; Marc Swadener, Ed.D.

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

Advisory Committee for Pharmaceutical Science Consultants (voting with noted exception):
Arthur H. Kibbe, Ph.D. (Topic: Implementation of Definitions for Topical Dosage Forms; limited to discussion only: non-voting); Marvin C. Meyer, Ph.D.

Guest Speakers (non-voting):
Leslie Z. Benet, Ph.D.; Russell M. Lebovitz, M.D., Ph.D.; Kamal Midha, Ph.D.; Jeremy Paull, Ph.D.

FDA Participants at the Table:
Gary Buehler, R.Ph.; Nakissa Sadrieh, Ph.D.; Keith Webber, Ph.D.; Helen Winkle; Lawrence Yu, Ph.D.

FDA & Guest Speakers Presentations:

Highly Variable Drugs -- Bioequivalence Issues

(1) Topic Introduction	Lawrence Yu, Ph.D. Director for Science, Office of Generic Drugs (OGD), Office of Pharmaceutical Science (OPS), CDER, FDA
(2) Therapeutic Considerations of Highly Variable Drugs	Leslie Benet, Ph.D. Professor of Biopharmaceutical Sciences University of California San Francisco
(3) Bioequivalence of Highly Variable Drugs	Kamal K. Midha, Ph.D. Pharmalytics Research Institute, University of Saskatchewan, Canada
(4) Evaluation of a Scaling Approach for Highly Variable Drugs	Sam Haidar, Ph.D. Lead Pharmacologist, OGD, OPS, CDER, FDA
(5) FDA's Proposal	Barbara Davit, J.D., Ph.D. Deputy Director, Division of Bioequivalence (DBE), OGD, OPS, CDER, FDA
Awareness Topic -- Risk Management for	Steven Kozlowski, M.D.

Complex Pharmaceuticals	Director, Office of Biotechnology Products
Nanotechnology -- Issues and Definitions	
(1) Topic Introduction/Overview	Nakissa Sadrieh, Ph.D. Science and Research Staff, OPS, CDER, FDA
(2) Applicability of Existing Regulations to the Development of a Dendrimer Nanotechnology-based Pharmaceutical	Jeremy Paull, Ph.D. Vice President, Regulatory Affairs and Quality Assessment, Starpharma Pty., Ltd.
(3) Nanotechnology in Emerging Medical and Consumer Products: Opportunities and Risks	Russell M. Lebovitz, M.D., Ph.D. Managing Partner, SUMA Partners (OBP), OPS, CDER, FDA
Implementation of Definitions for Topical Dosage Forms	
Introduction and FDA Strategy	Lucinda Buhse, Ph.D. Director, Division of Pharmaceutical Analysis (DPA), Office of Testing and Research (OTR), OPS, CDER, FDA
Conclusion and Summary Remarks	Helen Winkle

Open Public Hearing Speakers (October 6, 2006)

Laszlo Endrenyi, Ph.D. (Professor Emeritus, University of Toronto)

Questions to the Committee on Topic 3: Highly Variable Drugs

5) Does the committee agree with the use of a point estimate constraint when applying scaled bioequivalence?

YES= 8 (eight) *NO=0 (zero)* *Abstain=1 (one)*

If yes, is the 80 – 125% limit on the point estimate appropriate?

YES= 2 (two) *NO= 3 (three)* *Abstain= 4 (four)*

6) We propose a minimum sample size of 36 subjects when evaluating the BE of highly variable drugs. Does the Committee concur?

The Committee asked the FDA to rephrase the question to:
We propose a minimum sample size of subject when evaluating the BE of highly variable drugs. Does the Committee concur? If yes, what would be the minimum sample size?

YES= 6 (six) *NO=1(one)* *Abstain=2 (two)*

Four members voted for a minimum sample size of 24; three members voted for a minimum sample size of 36, and two members abstained. (Please refer to the transcript for detailed discussion)

Questions to the Committee on Topic 4: Critical Path Initiative

Due to schedule conflict, Topic 4 on Critical Path Initiative has been deferred to a future ACPS meeting.

Questions to the Committee on Topic 5: Nanotechnology- Issues and Definitions

1) Is the NNI definition of nanotechnology adequate for our needs and if not, how should we define nanotechnology?

The Committee suggested that a functional definition of nanotechnology should include the following:

a) *Definition should include the context: Drug vs. Devices;*
b) *Definition should focus on namomaterials and not nanotechnology*
c) *Nomenclatures must include the labeling implication;*
d) *Size-what size does is represented, and what risks are associated;*
e) *Recognize the complexity of the results;*
f) *Recognize the process dependence on the property;*
g) *Recognize the continuum of the sharp boundary may not be constructive and;*
h) *Recognized that it is a very precise particle (1-100). The Agency may not want qualification in the definition.* (Please refer to the transcript for detailed discussion)

2) Should we request more information from sponsors in the areas of characterization and safety of nanomaterial containing products, and if so, what type of information should we ask for?

The Committee felt the Agency should approach it like any new products and ask the sponsor for the indications, safety and efficacy of their products. In addition, if the product is recognized as a nanomaterial; the agency should ask the sponsors for their definitions and characterizations to allow to be called as a nanomaterial. Furthermore, the agency should not ask for a specific contained numbers of nanomaterials in each formulation. (Please refer to the transcript for detailed discussion)

3) Other than the steps being taken and being planned, what more can we do at this time?

The Committee felt that in addition to working groups, public meetings, research collaboration, memorandum, in house researches that are now underway, the agency can also inform the public of the ongoing process to avoid any falsify information on the products that are claimed by stakeholders. (Please refer to the transcript for detailed discussion)

4) Should we consider an ACPS nanotechnology subcommittee to help address some of our concerns?

The Committee felt that there was no need for a subcommittee on the issue, but to encourage the agency to convene the necessary expertise to identify relevant issues in accomplishing the agency's mission. (Please refer to the transcript for detailed discussion)

The Meeting adjourned for the day at approximately 16:15 hours