MEMORANDUM

TO: Members, ACPS

FROM: Helen Winkle
Director, Office of Pharmaceutical Science, CDER, FDA

DATE: September 8, 2006

RE: ACPS Meeting October 5-6, 2006

Dear Committee Members and Invited Guests,

We look forward to meeting with you on October 5-6, 2006, to discuss several important issues for the Office of Pharmaceutical Science (OPS). This meeting follows the separate one-day joint meeting between ACPS and the Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) to discuss variability of levothyroxine sodium products. You will be receiving separate information from the Advisors and Consultants Staff pertaining to that meeting.

At the start of the meeting on October 5, I will outline the goals and objectives for our meeting and I will also provide to you a brief update on OPS ongoing initiatives and activities.

DAY 1 (October 5, 2006)

DAY 1 (Topic 1)

Following my opening remarks, our meeting will begin with a series of presentations to update the committee on the ongoing ICH Quality Topics. Specifically, updates will be provided on Q8 (Pharmaceutical Development), Q9 (Quality Risk Management), Q10 (Pharmaceutical Quality Systems), and Q4B (Regulatory Acceptance of Analytical Procedures and Acceptance Criteria). Current directions and interface into ongoing OPS activities will be discussed.

DAY 1 (Topic 2)

At many venues over the last year, we have discussed the quality-by-design (QbD) topic at a conceptual level. These discussions were essential to establish a shared vision for the future and for describing the "desired state" for pharmaceutical development and manufacturing and how these changes will be incorporated into the regulatory framework. On October 5, we will provide the Committee an update specific to implementation activities that move the established vision into definable action within OPS. Each of the review offices in OPS will present how they are implementing this initiative. This will be followed by industry presentations (PhRMA and GPhA) to convey their perspectives on issues and challenges.

DAY 2 (October 6, 2006)

DAY 2 (Topic 1)

We will begin Day 2 with a discussion on the bioequivalence issues and challenges of highly variable drugs. This topic was discussed previously with the Committee in April 2004. The term "highly variable" in the context of bioequivalence evaluation has been generally applied in the scientific literature to those drugs or drug products that exhibit intra-subject variability equal to or greater than 30% CV for measure of rate (peak drug concentration [Cmax]) or extent of absorption (area under the drug concentration in blood/plasma - time curve [AUC]). High intra-subject variability poses many challenges for establishing bioequivalence. Useful background information relevant to the 2004 discussions can be obtained on the FDA Website via the following links:

Background information: http://www.fda.gov/ohrms/dockets/ac/04/briefing/4034b1.htm
Presentations: http://www.fda.gov/ohrms/dockets/ac/04/slides/4034s2.htm

After framing the topic, we will present an approach and proposal as to current thinking on the bioequivalence issues for highly variable drugs.

DAY 2 (Topic 2)

Next, an awareness topic will be presented to the Committee on *Risk Management for Complex Pharmaceuticals*. These products present unique challenges for manufacturing and regulation. Our current thinking will be presented along with ongoing approaches being developed in conjunction with ICH Q9 (Quality Risk Management -- see http://www.fda.gov/cder/guidance/7153fnl.pdf).

DAY 2 (Topic 3)

We will begin the afternoon sessions with an overview of current Agency activity on the *Critical Path Initiative*. This will be followed by a presentation to discuss ongoing implementation activities within OPS as part of the *Initiative*. We will end the topic discussion with a presentation on the next steps envisioned for OPS as we move forward with the *Initiative*.

DAY 2 (Topic 4)

We will continue our afternoon discussions with a presentation on current implementation plans for new definitions for topical dosage form products. The nomenclature for topical dosage forms was previously discussed with ACPS during its meetings in 2003. In preparation for our discussions, we have included in the background materials relevant information framing the 2003 discussions. We will discuss our current thinking on the perceived issues as implementation goes forward, to include the results of partnering efforts with the United States Pharmacopeia (USP).

DAY 2 (Topic 5)

We will conclude our Day 2 topics with follow-up presentations on the nanotechnology awareness topic originally introduced to the Committee in April 2004. Nanotechnology is a very rapidly growing area of science and technology. It is expected to lead to the development of many novel and sophisticated applications in drug delivery. As part of our discussions, the industry's perspective on nanotechnology opportunities and challenges will be presented.

We are looking forward to a very stimulating discussion with you on the selected topics. Have a safe and enjoyable journey to Rockville, MD. The meeting will be held at the 5630 Fishers Lane building in Rockville. If you need any additional information please do not hesitate to contact Bob King (Robert.King@fda.hhs.gov).