ADVISORY COMMITTEE FOR PHARMACEUTICAL SCIENCE
SITE SPECIFIC SUBCOMMITTEE

SEPTEMBER 22, 1999
CDER Advisory Committee Conference Room
5630 Fishers Lane
Rockville, MD

Executive Secretary:
Kimberly Littleton Topper

Academic Representatives
Garnet Peck, Ph.D.
Steven Byrn, Ph.D.
Leon Lachman

Industry Representatives
Bill Bradley
Scott Reynolds, Ph.D.
Robert Kasubick, Ph.D.
Karen Malik

FDA Representatives
Robert Seevers, Ph.D.
Eric Sheinin, Ph.D.
Roger Williams, M.D.

These summary minutes for the September 22, 1999, meeting of the Advisory Committee for Pharmaceutical Science Site Specific Subcommittee were approved on 24 Sept 99.

I certify that I attended the September 22, 1999, meeting of the Advisory Committee for Pharmaceutical Science Site Specific Subcommittee and that these minutes accurately reflect what occurred.

Kimberly L. Topper
Executive Secretary

Stephen Byrn, Ph.D.
Chairperson

3550

M1

The September 22, 1999, meeting of the Advisory Committee for Pharmaceutical Science Site Specific Subcommittee was called to order at 8:35. The Conflict of Interest statement was read for the record. The Chair asked all other participants to identify themselves.

Robert Seevers presented a brief history of the Site Specific Stability issue. He addressed the comments sent to Dockets on the Draft Guidance and broke them down into 4 specific groups. The breakdown was the scientific, regulatory, site specific stability and the logistical/economic/technical comments. He then presented three proposals:

Proposal 1	The Agency March 31, 1997 Three-tiered Proposal (see attached charts)
Proposal 2	Full ICH data on a combination 2 primary stability batches made at the Pilot Site, with 1 batch made at the commercial site
Proposal 3	Release data on 3 validation lots made at the commercial site plus a summary of the validation process, if the firm has submitted the ICH recommended primary stability data package.

The committee was then asked to discuss the merits of the proposals in terms of providing assurance of the sameness of a drug made at a commercial site and the clinical batches made at the pilot site.

Scott Reynolds presented the PhRMA view and discussed the merits of the three proposals.

Proposal 1	Site Specific Stability does not provide the best marker for success of technology transfer
Proposal 2	does not provide the best marker for success of technology transfer and there is still commercial burden to the firm
Proposal 3	Agree with the release data on three validation lots, in the form of a "Certificate of Analysis" (C of A), to be submitted prior to PDUFA date.

The committee discussed the three proposals and came up with the following suggestions for the 3 proposals.

Proposal 1	Could serve as an alternative to the PhRMA proposal with the following considerations: Clarify "Moderate -vs- Minor" Define "Complex Dosage Forms" Define "Intrinsically Unstable" Based on public comments from the docket.
Proposal 2	Decision was made to leave it to the committee to decide if it should be included as a possible method, concern was expressed that including this would make the Guidance unwieldy

Proposal 3 Better define and standardize “Certificate of Analysis” and FDA would like to see numeric values for data not the word “Passed”
Training would be held to get the FDA, Field offices and industry up to speed on the requirements
A decision would be made at the pre-NDA meeting on which dosage strengths would need the Certificate of Analysis

The Open Public Hearing (OPH) had one registration in advance and one the morning of the meeting. Anton H. Amann, Ph.D., Senior Vice-president, Manufacturing and R&D, Eon Labs, and Tobias Massa, Ph.D., DABT, Eli Lilly and Company. The following spoke from the floor: Robert A. Jerussi, Jerussi Consulting, Inc, Dr. Patricia Tway, Merck & Co., Inc., Colin Gardiner, Merck & Co., Inc., Shaun Brennan, Parke-Davis Division of Warner Lambert, Suva B. Roy, Ph.D. GlaxoWellcome, and Bob Polock of Novartis. The general consensus of the OPH was the both FDA and industry have stretched to develop a Guidance that both can live with. Consider requiring a summary of the C of A. Validation data should remain in the field to eliminate the potential of double jeopardy. If the ICH stability package is not included in an application the FDA should send a refuse to file letter.

The committee held a final discussion and made the following recommendations:

Proposals - Proposals 1 & 3 are workable and have use for different firms.
Proposal 3 is the proposal of choice. Proposal 1 is an alternative.
- Certificate of Analysis for 3 validated lots is required and numerical values should be used on the certificate for proposal 3
A summary of the validation process would not be required. Instead, certification that the process validation was completed successfully with changes reflected for regulatory in process controls would be required.

Timing: - This should be phased in from the date of release of the final Guidance.
Submission to NDA 3 months prior to PDUFA action letter with a three year phase-in (1, 2 and 3 months prior to letter in the first 3 years following implementation)
- Initial submission must have the full ICH stability package at time of submission
The Agency will use the public comments to examine which dosage forms belong in each category and they will be modified appropriately.
Post approval changes will be dealt with in the individual SUPAC's.
This applies to all dosage forms

The committee also decided that these decisions will apply to both API drug substance) and drug product)

The meeting was adjourned.