Nonclinical Studies Subcommittee (NCSS)

Report

Background Information

Advisory Committee for Pharmaceutical Science Meeting

November 15, 2000

Rockville, MD

Nonclinical Studies Subcommittee of The Advisory Committee on Pharmaceutical Science

Objectives

The principal goals of this Subcommittee are to recommend approaches and mechanisms 1) to provide the most effective nonclinical safety data base for optimizing selection of candidates for pharmaceutical development, rapidly advancing development of these candidates, and maximizing the favorable impact of pharmaceutical use on public health, 2) to improve the predictivity of nonclinical tests for clinical outcome and to improve the linkage between nonclinical studies and clinical trials, and 3) to facilitate collaborative approaches to advancing the science and regulation of pharmaceutical development and usage among the FDA, industry, academia, and other government and private institutions.

Subcommittee

John Doull, M.D., Ph.D., Chairperson
Nancy Chamberlin, Executive Secretary

Academic Representatives
John Doull, M.D., Ph.D.
Jay Goodman, Ph.D.

Consumer Representative
Gloria L. Anderson, Ph.D.

Industry Representatives
Joy Cavagnaro, Ph.D.
Jack H. Dean, Ph.D.
Jack Reynolds, D.V.M.

NIEHS Representative
Raymond Tennant, Ph.D.

FDA Representatives
David M. Essayan, M.D.
James MacGregor, Ph.D.

Meetings
1. Tuesday, December 14, 1999
2. Thursday, March 9, 2000

December 14, 1999

AGENDA

8:30	Call to Order/Conflict of Interest	John Doull, M.D., Ph.D. (Chair)
8:40	Introduction and FDA Objectives	James MacGregor, Ph.D.
9:10	Industry Perspective	Jack Reynolds, DVM
9:30	**Discussion of Focus Areas**	John Doull, M.D., Ph.D.
9:30	Positron emission tomography imaging	Jerry Collins, Ph.D.
9:55	Positron emission tomography imaging	Richard Frank, M.D., Ph.D.
10:20	**Break**	
10:35	Magnetic resonance imaging	Dave Lester, Ph.D.
11:00	Magnetic resonance imaging	Allan Johnson, Ph.D.
11:25	Subcommittee Discussion	
12:00	**Lunch**	
1:00	Public Comments	
2:00	Biomarkers	Frank Sistare, Ph.D.
2:25	Biomarkers	Gwyn Morgan, Ph.D.
2:50	**Break**	
3:05	Efficient advancement to clinical trials	Jack Reynolds, DVM
3:30	Efficient advancement to clinical trials (safety issues)	Joseph DeGeorge, Ph.D.
3:55	Efficient advancement to clinical trials (quality issues)	Eric Sheinin, Ph.D.
4:20	Subcommittee Discussion	
	Adjourn	

December 14, 1999 Meeting Summary

Dr. Jim MacGregor introduced FDA objectives for the subcommittee. FDA is looking to work in the areas of defining science - not Regulatory issues, bridging technologies, (animal to human) and asked the question, “What should we be doing with opportunities and limited resources?”

Dr. Jack Reynolds provided industry perspective stating the need to focus on those technologies that allow us to make the bridge, measure the same thing in laboratory models and then make key measurements in the clinic. He defined the general classes of biomarkers and sees value in partnering with regulatory agencies as a win/win situation.

Academic, industry, and FDA experts made presentations on prospective nonclinical studies focus areas: (1) positron emission tomography imaging, (2) high-resolution magnetic imaging, and (3) interspecies biomarkers of toxicity.

FDA presentations were made on the topic of efficient advancement to clinical covering safety and quality issues. It was concluded that there are areas where nonclinical and clinical research could shape agency and industry guidance. Decisions and identification of focus and approaches to address the research questions would necessitate broad cooperative efforts.

Subcommittee discussions resulted in the following consensus:

1) FDA should establish a standardized approach for use of biomarkers in nonclinical studies in collaboration with representatives from ongoing biomarker initiatives.

2) Broader expert groups should be formed for biomarkers and imaging and bring decisions back the NCS Subcommittee - focus on specifics.

3) Bring together experts in imaging technology and clinical application area and the experts should identify knowledge gaps in imaging and should help facilitate communication on technology.

4) The committee should work with stakeholders to bring this project into the forefront.

March 9, 2000

AGENDA

8:30	Call to Order/Chairman's Remarks/ Conflict of Interest	John Doull, M.D., Ph.D. (Chair)
8:45	FDA Objectives	James MacGregor, Ph.D.
9:00	Biomarkers, Introduction	Frank Sistare, Ph.D.
9:05	NIH Perspective on Biomarkers	Gregory Downing, Ph.D.
9:25	Establishing Biomarkers of Toxicity for Safety Assessment - A Focus on Cardiac and Skeletal Muscle Toxicity	Malcolm York, M.Phil.
9:50	Proteomics and Safety Biomarker Discovery	Gordon Holt, Ph.D.
10:10	Proteomics Technology	Leigh Anderson, Ph.D.
10:30	**Break**	
10:45	Applications of SELDI to Protein Biomarker Discovery Strategies	E. Chip Petricoin, Ph.D.
11:05	Applications of Gene Expression Analyses in Peripheral Blood Cells to Safety Assessment	Spencer Farr, Ph.D.
11:25	TaqMan Gene Expression Arrays for Accurate Quantification of Toxicity Targets	Frederico Goodsaid, Ph.D.
11:45	Recommendations for Biomarkers Projects	Frank Sistare, Ph.D.
12:00	Subcommittee Discussion	
12:30	**Lunch**	
1:30	Open Public Hearing	
2:30	Subcommittee Discussion	
3:00	Micro-PET: Experiences with Small Animal Imaging	Simon Cherry, Ph.D.
3:20	**Break**	
3:35	NIH/NCI Initiatives to Stimulate Applications of Imaging Technology	James Tatum, M.D.
3:55	Proposal to Form Expert Working Group on Imaging	Jerry Collins, Ph.D.
4:10	Subcommittee Discussion	
	Adjourn	

March 9, 2000 Meeting Summary

Academic, industry, and NIH experts made presentations on current advances in the areas of: (1) Biomarkers, (2) Proteomics Technology, (3) Gene Expression, (4) Micro-PET, and (5) NIH/NCI Initiatives in Imaging Technology

Outcome

The NCSS endorsed establishing working groups in accordance with the following draft focus statements:
(1) Multi-disciplinary working group to identify biomarkers to better predict drug-induced cardiotoxicity.
(2) Multi-disciplinary working group to identify biomarkers to better predict drug-induced vasculitis.
(3) Working group for PET imaging to evaluate PET as a nonclinical tool to enhance the linkage of nonclinical with clinical studies, with emphasis on the utility of probes for imaging replicating cells.

Expectations for Working Groups

To identify: 1) appropriate areas for focusing research, and 2) areas in which collaboration would be beneficial.

Mechanism to Establish Working Groups
1) FR Notice to solicit nominations to docket #00N-0930.
2) Letters to societies and other appropriate organizations requesting nominations to docket #00N-0930.