Stakeholder Meeting on PDUFA V Reauthorization
January 11, 2011, 2:00 – 5:00 PM
Hubert H. Humphrey Building, Washington, D.C.
Room 800

Purpose

To discuss FDA's conduct of post-market epidemiology initiatives in PDUFA IV and PDUFA V proposals related to development of drugs for rare diseases, benefit-risk and patient-focused drug development, and biomarkers and pharmacogenomics.

Participants

FDA

Wade Ackerman	OCC	Theresa Mullin	CDER
Ed Cox	CDER	Anne Pariser	CDER
Gerald Dal Pan	CDER	Judy Staffa	CDER
Patrick Frey	CDER	Andrea Tan	CDER
Debbie Henderson	CDER	James Valentine	OSHI
John Jenkins	CDER	Issam Zineh	CDER
Brian Kehoe	OL		

Stakeholders

Julio Abreu	Mental Health America
Jeff Allen	Friends of Cancer Research
Jason Barron	National Organization for Rare Disorders
Cynthia Bens	Alliance for Aging Research
Dave Bernstein	American Society of Clinical Oncologists
Marcie Bough	American Pharmacists Association
Marc Boutin	National Health Council
Pam Bradley	American Association for Cancer Research
John Brockman	American Medical Student Association
Paul Brown	National Research Center for Women & Families
Rebecca Burkholder	National Consumers League
Lauren Chiarello	National Multiple Sclerosis Society
Adam Clark	FasterCures/The Center for Accelerating Medical Solutions
Barry Dickinson	American Medical Association
Diane Dorman	National Organization for Rare Disorders
Christin Engelhardt	Pancreatic Cancer Action Network
Eric Gascho	National Health Council
Steve Gibson	The ALS Association
Amanda Grimm	American Academy of Dermatology
Suzanne Henry	Consumers Union
Darby Hull	Consumer Federation of America
Campbell Hutton	Juvenile Diabetes Research Foundation
Julia Jenkins	Kakkis EveryLife Foundation
Nik Johnson	Academy of Managed Care Pharmacy
John Kamp	Coalition for Healthcare Communication

Madoussou Kane	Academy of Managed Care Pharmacy
Stephanie Krenrich	Cystic Fibrosis Foundation
William Lang	American Association of Colleges of Pharmacy
Lisa McGiffert	Consumers Union
Martha Nolan	Society for Women's Health Research
Angela Ostrom	Epilepsy Foundation
Mark Pascu	Leukemia and Lymphoma Society
Kate Ryan	National Women's Health Network
Drew Saelens	Men's Health Network
John Schall	Parkinson's Action Network
Andrew Sperling	National Alliance on Mental Illness
Brad Tallamy	National Patient Advocate Foundation
John Thornton	Blue Cross and Blue Shield Association
Mellanie True Hills	StopAfib.org
Gretchen Wartman	National Minority Quality Forum
Michael Werner	Alliance for Regenerative Medicine
Celia Wexler	Union of Concerned Scientists
Patrick Wildman	The ALS Association

The following topics were discussed at the January 11 stakeholder meeting:

Post-Market Epidemiology Initiatives

FDA discussed the agency's ongoing efforts in post-market safety and pharmacoepidemiology during PDUFA IV. FDA conducts feasibility studies to determine if a sufficient number of patients have been exposed to a drug and if it is possible to ascertain outcomes in any given database. In-depth formal epidemiologic studies are then conducted to assess risks and/or risk factors associated with a drug and outcome. From 2008 to mid-2010, FDA launched 27 feasibility studies and 28 in-depth studies. FDA noted that PDUFA IV commitments allowed for expanded database and staff capacity including the establishment of federal partnerships to conduct this work.

Development of Drugs for Rare Diseases

FDA discussed the development of drugs for rare diseases and the recently established Rare Diseases Program in CDER's Office of New Drugs. The program was established due to the growing number of drug applications for rare diseases and the difficulty in developing drugs for rare diseases where few patients are available for study and the natural history of the disease is not well understood. FDA stated that during the 2008-2010 period, 30-40% of new molecular entity approvals were of drugs for rare diseases. The program focuses on regulatory science, scientific development, external (scientific investigator) and internal training, and communication. The proposal to address rare diseases in PDUFA V includes development of a staffing and implementation plan, guidance and policy development, a public meeting regarding clinical development complexity, staff training, and development of an evaluation tool for the program.

Benefit-Risk and Patient-Focused Drug Development

FDA discussed the proposal to develop an enhanced structured approach to benefit-risk assessment and communication that would include a series of public workshops throughout PDUFA V for obtaining patient and other stakeholder perspectives to better establish the clinical context for certain therapeutic areas. FDA stated that its assessment of benefits and risks is a qualitative approach that is grounded in

quantification of various data elements. FDA also noted that the evaluation of benefits and risks evolves over time as new information emerges after a product is marketed. The agency further stated that the proposal to engage the patient perspective to obtain a clearer understanding of patients' views on a disease area and the adequacy of the existing treatment armamentarium for that disease would yield valuable information to help inform review decisions. The proposal for patient-focused drug development would provide resources to support additional program staff in order to expand activities dedicated to eliciting patient input; convene meetings with review divisions and relevant patient advocates; and hold public workshops focusing on diseases areas and unmet need.

Biomarkers and Pharmacogenomics

FDA discussed the use of biomarkers and pharmacogenomics in drug development and regulatory decision making. Through increased development and utilization, biomarkers have the potential to streamline medical decision-making by reducing reliance on a trial-and-error approach that may lead to poor patient response to therapies, patient dissatisfaction, non-compliance, and poor outcomes. FDA explained that a biomarker qualification is the conclusion that a biomarker measurement can be relied upon to have a stated interpretation and value within a stated context of use. Once qualified, all review divisions must accept that determination which improves the efficiency of the drug review process. The agency stated that its biomarker and pharmacogenomic workload has increased, with 56, 139, and 210 submissions reviewed in 2008, 2009, and 2010, respectively. FDA also noted that as pharmacogenomics has increasingly become a part of drug review, the agency has published several guidances on this topic, such as a recent guidance on the context, structure, and format of biomarker qualification submissions. The proposal to address the increased use of biomarkers and pharmacogenomics in PDUFA V would provide additional resources to review the increasing number of applications with a biomarker component, review biomarker qualification submissions that are not currently part of normal application review, develop additional guidances, and conduct meetings with sponsors on the use of biomarkers in development programs.

Input from the Patient, Consumer and Public Health Coalition

The Patient, Consumer and Public Health Coalition is comprised of Consumers Union, the National Research Center for Women and Families/Cancer Prevention and Treatment Fund, the National Women's Health Network, and the Union of Concerned Scientists/Scientific Integrity Program. This Coalition submitted a document to FDA outlining proposals to address its concerns. The PDUFA Stakeholder meeting on January 11 reserved time for presentation and discussion of the areas identified in the Coalition document. In making its presentation, the Coalition noted that many of its concerns and suggestions were addressed by the discussions during this January 11 meeting. The Coalition offered additional suggestions for consideration:

- Ensure that the Sentinel Initiative is sufficiently funded in PDUFA V with the capacity to query databases and to utilize electronic health records and e-prescribing
- A 50% preservation of efficacy in a non-inferiority trial is too large; limit efficacy losses in these trials to 10% of the control drug
- Issue guidance to require that meta-analyses be consistent with best practices described in a forthcoming Institute of Medicine study [Refer to prior stakeholder discussion of the PDUFA V meta-analysis proposal]
- Ensure that FDA maintains flexibility for determining the appropriate REMS components in the proposal to standardize and integrate Risk Evaluation and Mitigation Strategies (REMS) in the healthcare system
- Encourage stakeholder involvement in consultations on well-defined and reliable patient-reported outcomes and other endpoints

- Increase number of foreign clinical research site inspections

The Coalition also discussed its proposal related to off-label prescribing where observational research would be conducted to determine the safety and efficacy of the practice and to inform regulatory action (e.g., REMS), if necessary. However, other stakeholders at the meeting expressed concern about restricting off-label prescribing practices, noting that this is the standard of care for many diseases with few available approved therapies, particularly rare diseases.

Input from the National Organization for Rare Disorders

The National Organization for Rare Disorders (NORD) stated its support for the proposal to advance development of drugs for rare diseases.