American College of Clinical Pharmacology
Annual meeting, September 11, 2005, Rockville, MD

Symposium I :
Emerging Pharmacogenomic Tools & Their Utility in Benefit/Risk Assessment During Drug Development & in Clinical Trials

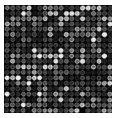
- Introduction -

Shiew-Mei Huang, PhD, FCP
Deputy Director for Science
Office of Clinical Pharmacology & Biopharmaceutics
CDER, FDA

This symposium is supported by educational grants from:

GlaxoSmithKline and Perlegen Sciences.

Personalized Medicine



"Instead of your doctor telling you that *40% of the population* responds to a drug, he can tell you that if you take this drug, *you have a 90% chance* of responding"

"There aren't bad drugs or good drugs. Instead, some drugs run into bad problems with a small subset of people"

<Janet Woodcock, BusinessWeek, September 5, 2005, cover story>

What's FDA's Role in moving towards personalized medicine?

Guidance for Industry
(transparent process)

Genomic data submission
- <http://www.fda.gov/cder/guidance/6400fnl.pdf, March 2005 >
- <http://www.fda.gov/cder/guidance/6400fnlAttch.pdf, March 2005 >

Drug Metabolizing enzyme genotyping systems
- <http://www.fda.gov/cdrh/oivd/guidance/1551.html, March 2005 >

Instrumentation for Clinical Multiplex Test System
- <http://www.fda.gov/cdrh/oivd/guidance/1546.html, March, 2005 >

Drug- diagnostic co-development concept paper
- <http://www.fda.gov/cder/genomics/pharmacoconceptfn.pdf, April, 2005 >

Workshops/Collaborative Efforts

FDA-PhRMA-BIO-PWG Public Workshops- May 2002, November 2003, July 2004, April 2005, October 2005
- <Lesko, LJ, et al, J Clin Pharmacol. 2003 Apr;43(4):342-58 >
- <Salerno RA, et al, Pharmacogenomics 5(5):503–505 >
- <Ruano G, et al, Pharmacogenomics 5(5):513–517 >
- <Leighton JK, et al, Pharmacogenomics 5(5):507–511 >
- <Trepicchio WL, et al, Pharmacogenomics 5(5):519–524 >
- < http://www.diahome.org/Content/Events/05020.pdf >

FDA-PhRMA-Hopkins Educational Workshops- Sept 2004, July 2005
- <http://www.fda.gov/cder/offices/ocpb/workshops.htm >
- <Andersson, et al, Clin Pharmacol Ther, in press >

Other partnerships- cooperative agreements, consortia (under "critical path")
- < http://www.fda.gov/oc/initiatives/criticalpath/whitepaper.html>

Translation to Drug Label (Pre-approval)

- **Herceptin (trastuzumab)**
  - **HER2 overexpression**

  <FDA approved HercepTest (IHC); additional tests (FISH) including Pathvysion, post-approval>

- **Strattera (atomoxetine)**
  - **CYP2D6**

  < FDA approved Roche's AmpliChip in 2004 (CYP2D6/CYP2C19)>

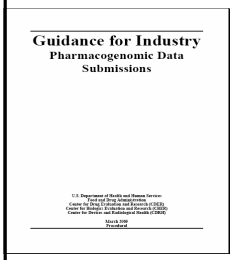
Translation to Drug Label (Post-approval)

- **Purinenthol (6-MP)- July 2004**
- **Imuran (azathioprine)- July 2005**
  - **TPMT**
- **Camptosar (irinotecan)- July 2005**
  - **UGT1A1**

< FDA approved TWT's Invader assay in August 2005>

- **others- e.g., Coumadin (warfarin)- ?**
  - **CYP2C9, VKORC1**

<Advisory Committee for Pharmaceutical Science - Clinical Pharmacology subcommittee meeting, November 14, 2005; 2Q 2006>



Guidance for Industry
Pharmacogenomic Data Submissions

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

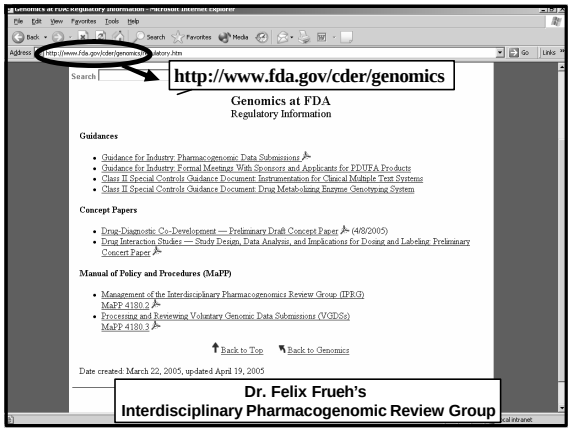
March 2000
Provisional

Voluntary Submissions

Recent examples---

- **Candidate gene approach vs. whole genome SNP scan**
- **Gene expression profile in peripheral blood**
- **Gene expression pattern as genomic biomarker to predict responders and non-responders**

Required Submissions



Dr. Felix Frueh's Interdisciplinary Pharmacogenomic Review Group

Agenda

- **Introduction:** ***Shiew-Mei Huang, PhD, CDER, FDA***
- **Clinical Pharmacogenetics- Why We Don't Have It, How to Get It -** ***David Flockhart, MD, PhD, Indiana University***
- **Whole Genome Association Study & Risk Assessment -** ***David Cox, MD, Perlegen***
- **Pharmacogenetics- Lessons from Anti-Epileptic Drugs-** ***David Goldstein, PhD,*** **Duke**
- **How Pharmacogenomics Will Revolutionize Oncology Clinical Trials-** ***Richard Pazdur, MD,*** **CDER,** ***FDA***

Agenda (2)

- **Presentation of Case Studies and Audience Discussion (Interactive Case Discussion)** ***Susan T. Hall, PhD, Moderator*** **,** ***GlaxoSmithKline***
- **Commentary: Follow-up on the Case Studies and Key Strategic Considerations on the use of Pharmacogenomics in Improving the Efficiency of Drug Development** ***Susan T. Hall, PhD, Moderator***
- **Additional Panelists:**

  Steve Gutman, MD, CDRH, FDA
  Lawrence J. Lesko, PhD, CDER, FDA
  Robert Temple, MD, CDER, FDA
  Allen Roses, MD, GlaxoSmithKline
  Roland Valdes, PhD, University of Louisville