SACGHS Meeting on Pharmacogenomics

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Diagnostics Industry Perspectives

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- Pharmacogenomic Test Development for Drugs on the Market
- Drug-Diagnostic Co-Development Concepts
- Need for Large Scale Clinical and Epidemiological Pharmacogenomics Studies
- Healthcare Provider Pharmacogenomics Education Needs
- Reimbursement for Pharmacogenomic Diagnostics

Pharmacogenomic Test Development for Drugs already on the Market

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- Numerous examples of marketed drugs that are known to exhibit wide variation in drug response among patients (e.g. warfarin, azathiaprine)
- Genetic factors can affect drug response outcomes (e,g, drug metabolizing enzyme polymorphisms)
- Once marketed, retrospective pharmacogenetic test development generally is not sponsored by the pharmaceutical manufacturer.
- FDA has expressed strong interest in specific PGx examples (e.g. TPMT/mercaptopurines, CYP2C9/warfarin)
- Biomarkers discovered and validated in one population may not be predictive of another of different ancestry or geographical origin. How should this be approached given the unique heterogeneity of the U.S. population?

Drug-Diagnostic Co-Development Concepts

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- FDA has held a series of Workshops/Public meetings on Pharmacogenomics and related topics
- The Agency is providing Guidance for
  - *Multiplex Tests for Heritable Markers, Mutations and Expression Patterns*
  - *Pharmacogenomic Data Submissions*
  - *Drug-Diagnostic Co-Development Concepts (Draft, April 2005)*
- Several details remain to be established, particularly around timing of diagnostic device development and drug clinical trial usage

Drug-Diagnostic Co-Development Concepts - Important Issues

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- How will the review process between CDER and CDRH proceed?
- Co-development Timing: Predictive Biomarkers may not be known prior to completion of Phase II Drug Trials. Thus a fully developed in vitro diagnostic test for Phase III clinical trials will generally not be available
- Can clinical utility be demonstrated in Phase III trials using a prototype assay with defined analytical performance characteristics, retaining samples for cross-over analytical performance validation of the in vitro diagnostic to be co-marketed?
- Are two independent Phase III clinical trials expected?
- Biomarkers discovered and validated in one population may not be predictive of a population with different ancestry or geographical origin. How should this be approached given the unique heterogeneity of the U.S. population?

Pharmacogenomics & Public Health: The Promise of Targeted Disease Prevention (CDC)

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- For pharmacogenomics to fulfill the promise of targeted interventions, clinical and epidemiologic studies are urgently needed to assess
  - (1) how drug response varies among individuals with different genotypes,
  - (2) what the prevalence of relevant genotypes is in the population and in relevant subpopulations, and
  - (3) whether and to what degree other environmental factors (such as other drugs and diet) interact with genetic factors to influence drug response.
- Clinical trials and observational epidemiologic studies are crucial for providing us with the population-based data needed to use pharmacogenomics in the practice of medicine and public health in the 21st century. (http://www.cdc.gov/genomics/info/factshts/pharmacofs.htm)
- NIH (e.g. Pharmacogenetics Research Network) support for translational clinical research to determine the utility of particular pharmacogenetic tests is warranted

Pharmacogenomics Education Needs

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- The advent of personalized medicine and its incorporation into the clinic will depend to a great extent on the educating our future physicians and health-care professionals about pharmacogenomics
- Not only healthcare professionals, but policy makers, as well as patients, need to have the necessary background knowledge for making educated treatment decisions.
- An unmet need for pharmacogenomics curricula exists in Medical, Pharmacy and Nursing Schools
- Continuing Medical Education (CME) programs should also be instituted for existing healthcare providers

Reimbursement for Pharmacogenomics Diagnostics

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- Based on the antiquated Medicare reimbursement system that is:
  - Fraught with inconsistencies
  - Subject to continual congressional budget cuts and price freezes
  - Not value based
  - In need of new coding structure
- No precedence for Pharmacogenomic tests to identify patients at risk of developing adverse drug reactions (e.g. genetically-determined poor metabolizers of drugs)