Pharmacogenomics
A Regulatory Perspective

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FDA Mission: Overview

- Safe Use of Experimental Products
- Assure Manufacturing Quality
- Approve Marketing Claims
  - Safety
  - Effectiveness
  - Product Characteristics

Claims Require Evidence

Pharmacogenetics:
Pharmacology meets Genetics

Genes and Pharmacology:

- Absorption
- Pro-drug metabolism / Active metabolites
- Drug induced changes in metabolism
- Toxic drug metabolites
- Metabolism mediated drug–drug interactions
- Drug–Disease/Gene interactions

Pharmacology Tool Kit

Types of Tools

- Useful to plan and conduct early trials
- Explanatory tools
- Inclusion / Exclusion tools
- Dose finding tools

Drug Development Tool Kit

- Animal Pharmacology / Toxicology
- ADME evaluation
- Therapeutic Drug Monitoring
- Pharmacodynamic Monitoring
- Toxicity Monitoring
- Adverse Event evaluation
- Therapeutic Window Determination
- Drug Interaction studies

Clinical Therapeutic's Tool Kit

- Therapeutic Drug Monitoring
- Pharmacodynamic Monitoring
- Toxicity Monitoring
- Symptom Titration

- Pharmacogenomic Evaluation

Where will Pharmacogenomics be used in clinical practice ?

- ? Select patients for therapy
- ? Exclude patients from therapy
- ? Evaluate observed toxicity
- ? Predict effective dose
- ? Follow-up unexplained high/low drug levels

  - Qualitatively ?
  - Quantitatively ?

Device Regulation Nitty Gritty

Questions:

- Is the *in vitro* diagnostic (IVD) already marketed ?
- Is this going to be a service of a single clinical lab ?
  - Will analyte specific reagents (ASRs) be purchased ?
- Is there a 510(k) predicate to your new IVD ?
- Can the drug be safely used without the IVD ?
- Will the drug and IVD be co-marketed ?
- Will the drug and IVD be combined in a kit ?

Genetic Tests in Drug Trials

If a genetic test is used to screen participants or to tailor dose or schedule for a new drug during clinical trials will labeling of the drug require the genetic test?

Analyte Specific Reagents (ASR)

Antibodies, specific receptor proteins, nucleic acid sequences, and similar biological reagents which through chemical binding or reaction with substances in specimen are intended for identification and quantification of an individual chemical substance or ligand in biological specimens

Pharmacogenomic Testing

Component	Egs.
? Collection Device	? Oral Fluid Swab
? Test Specimen Container	? 96 well plate
? Analyte Specific Reagent	? Gene probe
? Testing Equipment	? PCR equipment

HIV Testing - 'Home Brew'

Regulatory Status

- Medical devices
- FDA enforcement discretion
- Recognition of CLIA's role

Testing - ASR

Regulatory Status:

- Lab
  - Tests with ASRs are Medical devices
  - FDA enforcement discretion
  - Recognition of CLIA's role
- ASR Manufacturer
  - Required to register and list
  - Required to meet good manufacturing practices
  - Required to report adverse events
  - Restricted distribution, use, and labeling

Certificate of Confidentiality

Research Record Protection

- Must be requested before clinical trial begins
- Applies to an entire IND or IDE
- Does not alter FDA access to records
- Blocks court access to research records

Applications

- Genetic testing
- Mental Health
- Substance Abuse research
- Reproductive Research
- STD Research
- Research in the workplace

Labeling of in vitro diagnostic devices 809.10(b)

- Proprietary and established names
- Intended Use(s)
- Summary and explanation of test
- Principle of procedures
- Information on reagents
- Information on instruments
- Information on specimen collection and preparation

Labeling of in vitro diagnostic devices 809.10(b)

- Procedures
- Results
- Limitations of the procedure
- Expected values
- Specific performance characteristics
- Bibliography
- Name and place of business
- Date of the package insert


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