Personalized Medicine
Past, Present & Future Challenges

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Past

First Medical diagnosis and treatment

• Physicians would
  ● observe with their ears & eyes, smell and taste (Hippocrates) of specimens
  ● Use palpitation and auscultation.

• **Industrial Revolution**
  • Development of Clinical laboratory
  • Increased knowledge on Biochemistry and cellular processes

“You may takes notes for twenty years at the bedside of the sick, and all will be to you only a confusion of symptoms...a train of incoherent phenomena.” (Bichat on traditional Diagnosis)” – 18th century
Present

- Human Genome Sequencing
- Stunning Scientific Milestone
- **Genomic Revolution**
- New Paradigms & Applications in Medicine
- Diagnosis and treatment based on Molecular biology, Genomics, Genetics, Proteomics, Gene Expression
- Personalized Medicine
“Personalized Medicine”

Refers to the tailoring of medical treatment to the individual characteristics of each patient.

It is not the creation of drugs or medical devices that are unique to a patient, but rather the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment.

President’s Council of Advisors on Science and Technology “Priorities for Personalized Medicine” Sept 2008
FDA Commissioner Hamburg notes challenges of changing regulatory models to advance personalized medicine. But "we will establish a clear and illuminated pathway for product approval."

"When everything has changed our thinking must change as well. Shifting Paradigms and creating new models is not easy, but I believe that a future that provides safer and more effective therapies for all of us is well worth the effort," she concluded.

The genomics revolution has not yet unleashed a wave of newly targeted therapies in part because regulatory science has to catch up with the breakthroughs of basic science, FDA Commissioner Margaret Hamburg suggests.
Personalized Medicine Bill
Regulation, Reimbursement and Translational Research

Creation of Office of Personalized Healthcare in HHS

- Coordinate activities between government agencies
- Create translational research agenda
- Ensure coverage and reimbursement (use of best data available)
- Identify evidence gaps, whether genomic technologies are cost effective and improve outcomes
- Clarify regulation of PM products to reduce inter agency oversight conflicts
- FDA regulatory oversight over companion tests (AE reporting)
- Investigate DTC genomics industry.
- Develop a test registry (analytical & clinical validity info for LDT)
- Create a national biobank for use in PM research

Genomics and Personalized Medicine Act of 2010 (HR5440)
Personalized Medicine
Use of Companion Drug-Diagnostics

- **Efficacy** – identify patients most likely to respond beneficially to a targeted treatment
- **Safety** – identify patients most likely to respond adversely to a targeted treatment
- **Dosing** – identify patients’ specific dosing to optimize benefit or minimize risk to a targeted treatment
- **Monitoring** – monitor the effect of therapy after treatment is initiated and/or reoccurrence of the disease/condition
Dawn for Personalized Medicine
Test recommended/required in drug label

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Safety/Dosage</th>
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<tbody>
<tr>
<td>Herceptin- Her 2</td>
<td>Carbamazepin- HLA B1502</td>
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<tr>
<td>Gleevec- Bcr-abl</td>
<td>Abacavir- HLA B5701</td>
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<td>Gleevec- c-Kit</td>
<td>Warfarin-2C9,VKORC1</td>
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<td>Erbitux- EGFR</td>
<td>Camptosar- UGT1A1</td>
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<tr>
<td>Tamoxifen- 2D6</td>
<td>6MP- TPMT</td>
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<td>Rituxan- CD20</td>
<td>Codeine- 2D6</td>
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<tr>
<td>Maraviroc- Tropism</td>
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<tr>
<td>Vemurafenib-BRAF V600E</td>
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Personalized Medicine for In Vivo Diagnostics?

**Efficacy**
- EEG-(Depth of Anesthesia)
  - Response to Certain Anesthetic Agents
- EEG-(ID depression)
  - Predict Response to SSRIs
- PET Scan
  - Response to Schizophrenia drugs

**Safety**
- ECG (Long QT)
  - Procainamide
  - Cisapride
  - Terfenadine
Introduction of Innovative Products

When the Diagnostic Becomes Integral to Approval of the Drug

- Diagnostic approval is needed in parallel with the drug (labeling implications).
- FDA review centers (CDER/CBER/CDRH/OCP) work with collaborating sponsors (drug-diagnostics companies) to coordinate review processes and tandem approval.
- “Predictive” claims for companion diagnostics rely on understanding the effect of the drug in both biomarker positive and biomarker negative patients.
- Companion diagnostics are at the heart of personalized medicine, and carry the same risk profile as the drug.
Future

- Drug and Diagnostics: better understanding of regulatory framework and product development life cycles
- Create Personalized Medicine (Dx/Rx coordinated) consultation programs to harmonize practices
- Development of a feedback loop to capture outcome on innovative targeted medicines (comparative effectiveness)
- Will regulatory incentives be created for personalized medicine
- Cumulative process approval based on growth of data for Diagnostics/Therapeutics
- Recognize multi drug-diagnostics strategies- eg. bundle
- Can PM facilitate development of “preventive medicine” rather than “treatment medicine”
“The good physician treats the disease; the great physician treats the patient who has the disease”

William Osler
The Father of Modern Medicine
(1849-1919)
Thank you!

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Addendum
Model for Personalized Medicine

Parameters to consider for a “good medicine and diagnostics”:

<table>
<thead>
<tr>
<th>Good Medicine</th>
<th>Good Diagnostics</th>
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<tbody>
<tr>
<td>Safety and Efficacy</td>
<td>Safety and Effectiveness</td>
</tr>
<tr>
<td>Patients Quality/Quantity of Life improved</td>
<td>Patients are diagnosed correctly</td>
</tr>
<tr>
<td>Reduction of Cost Care</td>
<td>Proper subsequent clinical treatment decision</td>
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*Improved Health Care Outcomes/Adherences based on Diagnostics to Select Right Drug/Dosage. Eliminating/Decreasing Wasteful Spending*
Iterative nature of science causes an established or new drug associated with an old diagnostic test to be used with an improved diagnostic test. Changes are possible in either the drug or diagnostic and a variety of interactive changes may be established each requiring unique attention to study design.
Speed up Introduction of Innovative Products: Overcoming Potential Regulatory Barriers

- Harmonization between FDA Reviewing Centers
- Adequate guidance to clarify options from FDA
- Increased dialogue between FDA and Industry
- Encourage sponsors to work with FDA as science develops
- Least burdensome and creative FDA review and approval process
- Make regulatory process transparent, efficient and still preserve FDA’s public health mandate
Current Challenges

- Regulatory framework for companion drug-diagnostics is nascent and evolving.
- Clarity on IVD regulation of medical devices, LDTs
- FDA has published a companion diagnostics draft guidance but not published drug-diagnostic co-development guidance
  - Industry and regulators have learned a great deal since publication of the concept paper
- Still a great deal of confusion and controversy about evidence base needed for adoption of an individualizing test into clinical practice-
  - Clinicians dislike information without instructions
- PM success depend on safe and effective Dx-Rx