



# Federal Activities Involving Genetic Services

## Mountain States Genetics 2007

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# Who is Paying Attention?

- ◆ **HHS and Agencies of HHS**
- ◆ **Advisory Committees**
- ◆ **Legislators 7+ bills in Congress**
- ◆ **Providers**
- ◆ **Public**



# Oversight of Genetic Testing

- ◆ **Recent clamor over the quality of testing**
- ◆ **Task Forces -> Advisory Committees**
- ◆ **SACGT**
  - **Recommends FDA find role in genetics testing**
- ◆ **SACGHS**
  - **Task Force on the Oversight of Genetic Testing**
- ◆ **Genetic Alliance**
  - **Eyes on the Prize: Truth Telling about Genetic Testing: A Genetic Testing Summit Meeting**  
(September 20-21, 2007)
- ◆ **Genetics and Public Policy Center**
  - **Genetic Testing Quality meeting (July 18, 2007)**
- ◆ **Institute of Medicine**
  - **Genomics Translation Roundtable**



# Why is it So Contentious?

- ◆ **Overly broad definitions of genetic testing used**
- ◆ **We've done a poor job characterizing genetic testing as compared to drugs**
  - gave illusion of disagreement with oversight
- ◆ **Turf fights to keep analytical generic**



# Regulatory Overview

- ◆ **FDA**
  - **Analyte Specific Reagents**
  - **In Vitro Diagnostic Multivariate Index Assays**
  - **Clinical laboratory oversight**
- ◆ **CLIA**
- ◆ **CMS**
  - **Reimbursement as the de facto regulatory system**



## ◆ Classification scheme

**Waived – analytically idiot proof**

**1 - Low risk**

**2- Controllable assays**

**3 – Blood supply and**

**new high complexity tests (e.g., Genetics)**

**Analyte specific reagents (ASRs)**

**Least burdensome**

**Risk-based**



# Over-riding Issues in Recent FDA Guidances

- ◆ **Does FDA have the legislative mandate to regulate clinical laboratories rather than manufacturers?**
  - FDA considers it within their mandate
  - No existing precedent
- ◆ **Clinical laboratory services are regulated by CMS through CLIA under current legislation.**
- ◆ **Significant implications for reimbursement coverage**



# **In Vitro Diagnostic Multivariate Assays (IVDMIA)**

**Employs data from one or more in vitro assays and an algorithm that generates (via software or otherwise) a result that diagnoses a disease or condition, or is used in the cure, mitigation, treatment or prevention of disease.**



# Key Features that Distinguish an IVDMA 1

- ◆ **Use clinical data—including data from one or more in vitro assays and, in some cases, demographic data—to empirically identify variables and to derive weights or coefficients employed in an algorithm**
- ◆ **Employ the algorithm to integrate these variables in order to calculate a patient specific result (e.g., ‘classification’, ‘index’ or ‘score’). This result can not be independently derived and confirmed by another laboratory without access to the proprietary information used in the development and derivation of the test.**



## **Key Features that Distinguish an IVDMA 2**

- ◆ **Report this result, which can not be interpreted by the well-trained health care practitioner using prior knowledge of medicine without information from the test developer regarding its clinical performance and effectiveness.**



# Implications of IVDMIA Rule

- ◆ **Does not seem to cover prenatal analyte screening**
  - Results can be independently derived
- ◆ **Does not seem to cover CGH arrays**
  - Results (risk estimates) can be independently confirmed and is routinely done as part of external proficiency testing programs
  - aCGH doesn't factor patient factors into the test result
- ◆ **Appropriately covers gene expression assays for which underlying components of risk calculation algorithms are held as proprietary**



## **ACMG Recommendations on IVDMIAs**

- ◆ **The proposal has such a significant impact on the way clinical laboratories operate that a formal rule making process as required under the Administrative Procedures Act should be employed**
- ◆ **Proposal should be much more explicit as to how laboratories would be regulated differently than manufacturers to avoid loss of access**
- ◆ **Proposal should be more explicit as to the tests and technologies considered to be subject to FDA oversight to avoid slowing innovation**



# Analyte Specific Reagents

- ◆ **The commercially distributed IVD building blocks of laboratory tests lacking clinical claims**
- ◆ **Guidance seeks to eliminate “confusion” in original rule from 1997 on:**
  - **Combining, or promoting for use, a single ASR with another product such as other ASRs, general purpose reagents, controls, laboratory equipment, software, etc.**
  - **Promoting an ASR with specific analytical or clinical performance claims, instructions for use in a particular test, or instructions for validation of a specific test using the ASR**
  - **Clarifies that some ASRs may be considered Class II or III devices that are subject to premarket notification or premarket approval**



# What are the Characteristics of a Product Considered as Meeting the ASR Rule

- ◆ **A single moiety**
  - A forward primer for amplification reactions
- ◆ **A single endpoint**
- ◆ **No instructions or performance claims**
- ◆ **Not promoted for use on specific instruments or in specific tests or test systems**



# Implications of ASR Rule

- ◆ **Ignores that some products are paired (e.g. primers)**
- ◆ **Fails to recognize that any ASR mutation probe has limited uses outside of testing**
- ◆ **Ignores that a gene may be the target, rather than a specific mutation**
  - **Should acknowledge testing of multiple mutations in a gene rather than force labs into sequencing**
- ◆ **Fails to recognize that great majority of ASRs are for orphan disease testing**
- ◆ **Fails to appreciate that ASRs could be lost from the marketplace if manufacturer can't make and distribute them cost effectively**



# ACMG Recommendations on ASR Guidance

- ◆ **The proposal has a significant impact on the way clinical laboratories operate that a formal rule making process as required under the Administrative Procedures Act should be employed**
- ◆ **Proposal should be more explicit as to the tests and technologies considered to be subject to FDA oversight to avoid slowing innovation**
- ◆ **Reconsider how different ASRs relate to intended uses in genetic testing to avoid excessively splitting up products**
- ◆ **Recognize that a majority of ASRs used in genetic testing are for orphan disease testing and consider how best to protect access to and availability of these products**



- ◆ **1998 – CLIAAC recommends to HHS that a specialty of genetics be established under CLIA**
  - Notice of public rule making given
- ◆ **1999 – 2006 Into the federal abyss**
- ◆ **2006 – CMS decides no specialty is needed**
  - Essentially defers to FDA



# Centers for Medicare and Medicaid Services (CMS)

- ◆ **Genetic counseling**
  - Is it an 'incident to' service
- ◆ **Laboratory**
  - **Technical vs. professional components**
    - Laboratory fee schedules
    - Physician fee schedules
- ◆ **Clinical**
  - **Too poorly distinguished from others using same CPT codes to argue that it's different**



# New HHS Initiatives

## NIH

### ◆ NICHD

- Newborn Screening Translational Research Network

### ◆ NHGRI/NICHD

- Carrier screening conference for Winter/Spring, 2008

## MCHB/HRSA

- ◆ Move into long term NBS follow-up and data collection
- ◆ NICHD planning to use RC/NCC system



# Legislative Overview

- ◆ **Gene Patenting**
  - **Rep. Xavier Becerra**
    - **Ban Gene Patenting bill**
- ◆ **Newborn Screening**
  - **Sen. Hillary Clinton**
    - **SHINE Act**
  - **Sen's. Christopher Dodd and Orrin Hatch and Rep. Lucille Roybal-Allard**
    - **Newborn Screening Saves Lives Act**
- ◆ **Genetic Information Nondiscrimination Act (GINA)**
- ◆ **Laboratory Developed Tests (LDTs)**



# What Are We Advocating For in Legislation

- ◆ **Training and education funding**
  - **Medical genetics provider workforce**
  - **Non-genetic providers**
    - **Point-of-care education tools for practicing providers**
  - **Medical school education issues**
- ◆ **Organized national data collection as only way to improve evidence base**



# Gene Patenting

- ◆ **Genomic Research and Accessibility Act – HR.977**
  - **Outright ban on gene patenting**
  - **Reps. Xavier Becerra and David Weldon**
  - **Seeks outright ban**
  - **Not retroactive**
    - **?Administrative solutions if bill is passed to avoid a suit based on “taking”**
    - **Declaring it a ‘mistake’ allows court action against existing patents**



# Newborn Screening

- ◆ **Newborn Screening Saves Lives Act of 2007 – S.634**
  - **Sens Christopher Dodd and Orrin Hatch**
  - **Grant programs**
    - **Education and training**
    - **Family assistance**
    - **Contingency planning**
      - **\$15 million**
  - **Expand screening to include ACHDGDNC recommendations**
    - **\$25 million**
  - **Evaluate effectiveness**
    - **\$5 million**
  - **Laboratory quality and surveillance**
- ◆ **Roybal-Allard companion bill HR.1634**



# Newborn Screening

- ◆ **Screening for Health of Infants and Newborns (SHINE) Act – S.1712**
  - **Sen. Hillary Clinton**
  - **Guidelines for States (reporting, stanardize case definitions, data collection)**
  - **Monitoring, evaluation and surveilliance**
  - **NBS information clearinghouse**
  - **Interagency grant review program**
  - **Hunter Kelly grant program**
    - **Incentives for development of new tests for new conditions in NBS**
- ◆ **Reynolds companion bill – HR.2885**



# Genetic Information Nondiscrimination Act GINA

- ◆ **Close to coming to vote with strong support**
- ◆ **Enforcement minimized**
- ◆ **Fetus language added**



# Laboratory Quality

- ◆ **Kennedy and laboratory developed tests**
- ◆ **Obama and genomics**
  - **IOM study moved into FDA PDUFA reauthorization**



# Reauthorizations Potentially Impacting Genetics

- ◆ **Title VII - Health Professions Education**
  - Training and education money for genetics
- ◆ **Medicare**
  - Defines non-physician groups with statutory benefits to be reimbursed for professional components



# Our Activities to Address Issues

- ◆ **Clinical RVU study**
- ◆ **GIS developed**
  - Payers interested in using if standards based
- ◆ **Policy work**
  - Licensing
  - Telegenetics
- ◆ **Data collection activities**
  - LTFU
  - Genetics
  - National Collaborative Study System
  - Clinical investigation
- ◆ **Emergency preparedness**