

Genetic Testing Reference Material Program (GeT-RM)

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The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the views of [the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry]

Reference Materials are used for:



- Development of new genetic tests
- Validation of new genetic tests
- Assay performance- QC
- Test calibration
- Inter-laboratory comparison
- Proficiency testing samples

Reference Materials: Essential for Quality Testing

The Current Situation

Reference materials are **not publicly available** for most genetic tests; laboratories may use uncharacterized, **non-renewable** clinical materials for test development, validation and QC

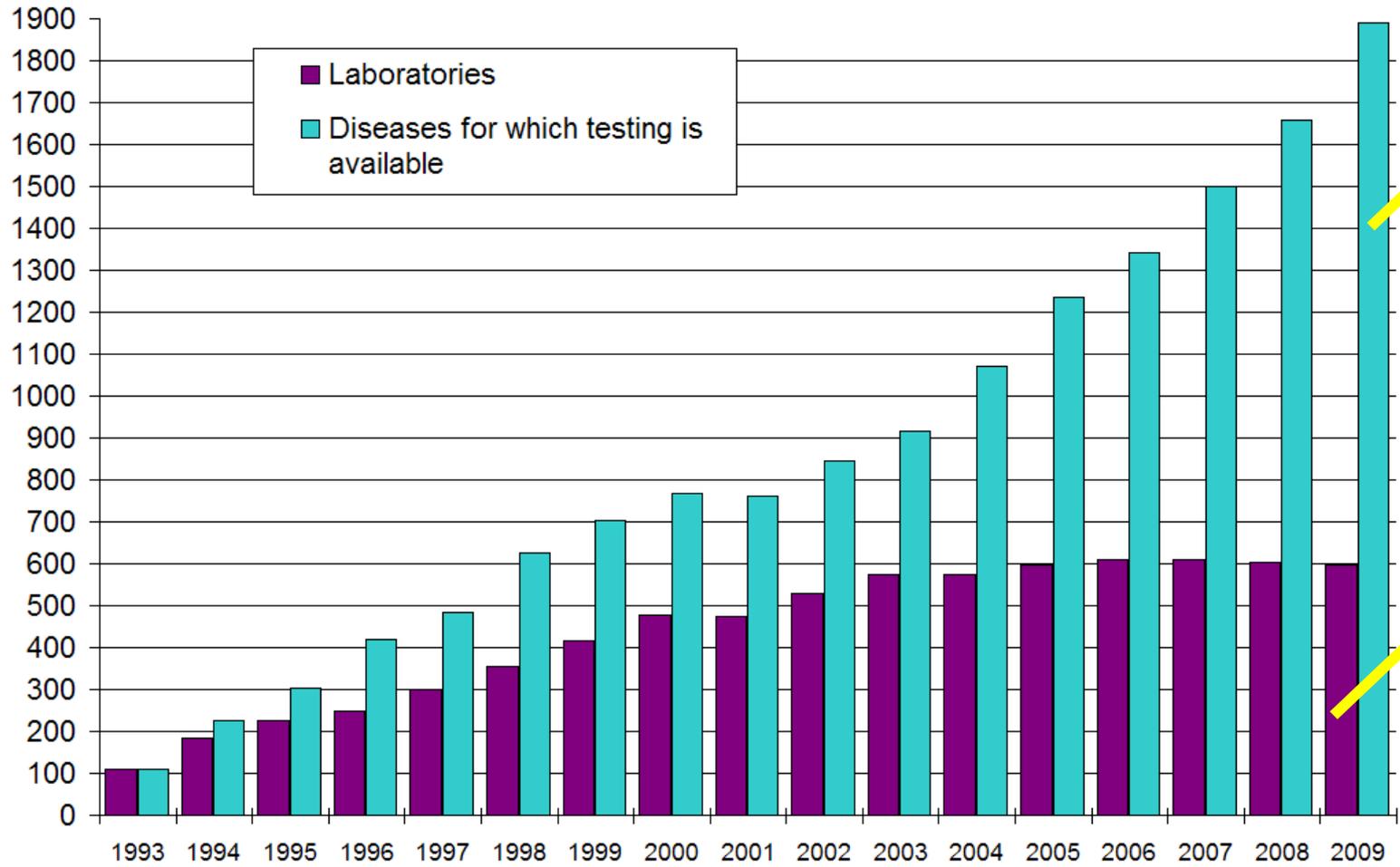
Consequences

Quality of genetic tests potentially compromised

Growth in Genetic Testing Labs and Number of Tests Offered



GeneTests: Growth of Laboratory Directory



Tests:
19-fold
increase

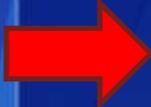
Labs:
6-fold
increase

Data source: GeneTests database (2009) / www.genetests.org

Commercial Availability of RMs:

Genetic Tests for over 2000 heritable disorders...

Reference materials commercially available for about 20 tests....

 No characterized RMs for vast majority of genetic tests. Available RMs often do not include all variants tested in clinical assays

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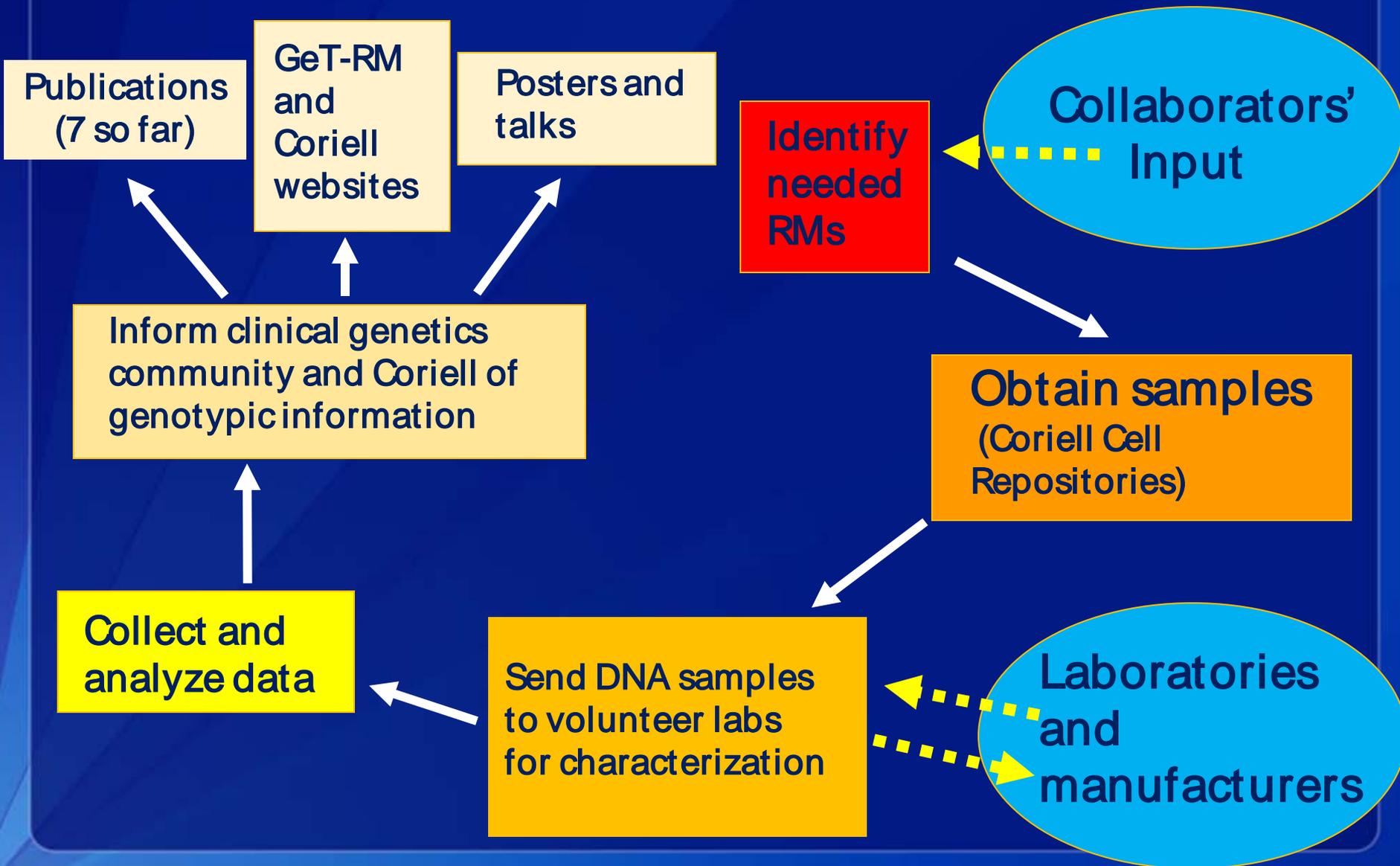
A Collaborative CDC-based program to improve the availability of reference materials for genetic testing



Roles of GeT-RM

- Information exchange about RMs for genetic testing
- Assess RM needs of laboratories
- Design and coordinate submission, development and characterization of RMs

GeT-RM Process



GeT-RM Website



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GeT-RM Home

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Genetic Testing Reference Materials Coordination Program (GeT-RM) - Home

The goal of the Genetic Testing Reference Materials Coordination Program (GeT-RM) is to coordinate a self-sustaining community process to improve the availability of appropriate and characterized reference materials for:



- Quality control (QC)
- Proficiency testing (PT)
- Test development & validation
- Research

The purpose of this program is:

- To help the genetic testing community obtain appropriate and characterized reference materials
- To facilitate and coordinate information exchange between users and providers of QC and reference materials
- To coordinate efforts for contribution, development, characterization and distribution of reference materials for genetic testing

We provide information about cell lines, DNA, and other kinds of materials that could be used as reference materials for molecular genetic testing. Some of these materials have been characterized by the GeT-RM program and can be divided into three categories:

<http://wwwn.cdc.gov/dls/genetics/rmmaterials/default.aspx>

GeT-RM Progress

Completed Projects

- Fragile X
- Huntington Disease
- Cystic Fibrosis
- Ashkenazi Jewish Panel
 - 9 disorders including Tay-Sachs and Canavan disease
- BRCA1/2
- MTHFR
- Multiple endocrine neoplasia Type 2A
- Alpha1-antitrypsin deficiency
- Pharmacogenetics
- Duchenne muscular dystrophy

Ongoing Projects

- Newborn Screening
- Rett Syndrome
- Angelman/Prader-Willi
- Cytogenomics
- Molecular oncology
- HLA genotyping



Over 200
gDNA RM
characterized
by GeT-RM

Cytogenetic Microarray Testing

- Detects chromosome imbalances, such as gains and losses, smaller than detected by traditional cytogenetic karyotyping
- Arrays also detect loss of heterozygosity and uniparental disomy.
- This technology is recommended first tier screen for several developmental disorders (replace karyotyping)
- No publicly available, characterized reference materials are available for CMA



Cytogenetic Microarray Testing – Need for Reference Materials

- The cytogenetics laboratory community has expressed a need for reference materials
 - Common inherited cytogenetic abnormalities
 - Validation of probe performance

Creating RMs for CMA Testing

Working with Dr. Shashikant Kulkarni, [Washington University School of Medicine in St.Louis] and

- Clinical cytogeneticists
- Assay manufacturers
- FDA
- Coriell (NIGMS Human Genetic Cell Repository)

to create needed reference materials

GeT-RM CMA RM Participants

Molecular Cytogenetics Labs:

Laura Conlin -CHOP

Julie Gastier-Foster -Nationwide Childrens

Vaidehi Jobanputra -Columbia University

Hutton Kearney -Fullerton Genetics

Shashi Kulkarni -Washington University

Charles Lee -Harvard

Brynn Levy -Columbia University

Sarah South -ARUP

Nancy Spinner -CHOP

James Stavropoulos -Hospital for Sick Kids,
Toronto

Dayna Wolf – Medical University South Carolina

Condie Carmack – Baylor College Medicine

Array Manufacturers:

Richard Shippy -Affymetrix

Darlene Solomon –Agilent

Stephanie Fulmer-Smentek -

Agilent

Harper VanSteenhouse -Illumina

Lou Welebob -Roche Nimblegen

Christine Shaw – Roche

Nimblegen

Government + Others:

Dorit Berlin - Coriell

Karen Bijwaard - FDA

Donna Roscoe -FDA

Zivana Tezak -FDA

Lorraine Toji - Coriell

Zhenya Tang - Coriell

Lisa Kalman - CDC

Creating RMs for Cytogenetic Microarray Testing

Will create 2 panels of characterized genomic DNA RMs:

Clinical Panel

- **RMs representing common cytogenetic abnormalities**
- 100+ DNA samples
- Includes : micro deletions/duplications, sub-telomeric abnormalities, LOH, UPD, common syndromes, etc.

Probe Validation Panel

- **RMs to evaluate the ability of each array probe to detect duplications or deletions**
- 200+ DNA samples
- Large deletions and duplications that cover all of the genome.

Creating RMs for Cytogenetic Microarray Testing

Progress so far:

- Selected DNA from 45 Coriell cell lines for clinical panel
- DNA being characterized using 4 commercial CMA platforms
- Raw data will be analyzed by 8 clinical cytogeneticists
- In process of selecting additional Coriell samples for characterization

Creating RMs for Cytogenetic Microarray Testing

**All of these characterized RMs will be publicly available
From the NIGMS repository at the Coriell Cell Repositories**



THANKS!!!!!!