# CAP Accreditation of Genetics Testing Laboratories

Secretary's Advisory Committee on
Genetics, Health, And Society
March 26, 2007

Gail Vance, MD, FCAP
College of American Pathologists

# Overview

- Shared Goals
- CAP Accreditation Program
  - Molecular Pathology
  - Cytogenetics
- CAP Proficiency Testing
- CAP Recommendations

# Shared Goals

- Assure that tests being offered are analytically and clinically valid
- Assure patient safety and the public health
- Assure patient access to testing
- Allow innovation and continued improvement of Laboratory-Developed Tests

# CAP Accreditation

- CMS-approved accreditor
- Higher standard than CLIA
- Scientific Resource Committees develop specialty accreditation requirements
- Specialized inspector requirements for genetics
- Labs required to report changes to testing menu

# History of CAP Accreditation

- CAP began inspecting clinical laboratories in 1961
- Program initially voluntary
- CAP initiated the first Cytogenetics Checklist in 1976
- CAP initiated the first Molecular Pathology Checklist in 1993

# CAP Accreditation Requirements

- Inspections
  - On-site inspections by external evaluator required every two years;
  - CAP uses peer inspection teams of currently practicing laboratory professionals
- Inspection Tool
  - CAP uses Inspection Checklists to guide the inspectors
  - Checklists consist of 3,500 discipline-specific laboratory requirements

# CAP Inspector Requirements

- Inspection of a genetics laboratory requires special knowledge of the science.
- The inspector should be an actively practicing molecular scientist familiar with the Checklist and possessing the technical and interpretive skills necessary to evaluate the quality of the laboratory's performance.

# CAP Inspector Training

- Live inspector training seminars
  - 2,100 participants in 2006
- Discipline-specific audio conferences
  - 7,400 participants in 2006
- On-line interactive training sessions
- Inspection Team Leader requirement for re-training every two years
  - 1,294 team leaders trained by July, 2006

# CAP Standards Exceed CLIA

- Over half of CAP requirements (1,700 questions) are additional to CLIA minimum standard
- Example special disciplines not covered by CLIA
  - Forensic testing
  - Autopsy
  - Histology processing
  - Embryology
  - Molecular Pathology
- Example sections within traditional disciplines beyond CLIA
  - Proficiency testing for non-regulated analytes
  - Computer systems
  - Lab safety & hygiene
  - Prenatal screening
  - Sweat chloride testing

# Genetics Accreditation Standards

- Assay validation
- Clinical validation*
- Universal nomenclature*
- Correlation with clinical information & other studies*
- Recommendations for genetic counseling & further studies*
- Turn-around time requirements*

* Exceed CLIA requirements

# CAP Standards Beyond CLIA

- Examples of questions from the Molecular Pathology Checklist:
  - Are the clinical performance characteristics of each assay documented, using either literature citations or a summary of internal study results?
  - Does the final report include an appropriate summary of the methods, the loci or mutations tested, the analytical interpretation, and clinical interpretation if appropriate?

# CAP Molecular Pathology Checklist

- Covers most aspects of clinical molecular testing including oncology, hematology, infectious disease, inherited disease, HLA typing, forensics and parentage applications.
- Testing that involves DNA/RNA probe hybridization or amplification constitutes molecular testing.

# Techniques with specific compliance requirements:

- Extraction & purification*
- Amplification*
- Restriction endonucleases*
- Sequencing*
- Detection*
- Real-time PCR*
- Arrays*
- In-situ hybridization*

* Exceed CLIA requirements

# CAP Cytogenetics Checklist

- Covers Chromosome analyses
  - Amniotic fluid & chorionic villi
  - Non-neoplastic blood & fibroblasts
  - Neoplastic blood and bone marrow

# Techniques with specific compliance requirements:

- Cultures*
- Cells counted*
- Karyotypes*
- Band-levels of resolution*
- Fluorescence *In Situ* Hybridization (FISH)*

* Exceed CLIA requirements

# Accreditation Process

- If a deficiency is cited, lab must respond with corrective action within 30 days of on-site inspection
- Two-tier review process to determine adequacy of action plan and lab's ability to maintain sustained compliance
- Accreditation decision is rendered by a committee of lab experts
- On alternate years, self evaluation is required

# Most Common Deficiencies - Molecular Pathology

- In cases where there is no commercially available PT, does the laboratory at least semiannually 1) participate in external PT, or 2) exercise an alternative performance assessment system for determining the reliability of analytic testing? [3.9%*]
- Are temperatures checked and recorded appropriately for equipment in which temperature is critical? [3.5%*]
- Is there a summary statement, signed by the laboratory director or designee, documenting review of validation studies and approval of the test for clinical use? [3.3%*]

*% of inspections deficiency cited

Deficiencies must be corrected for accreditation.

# Most Common Deficiencies - Cytogenetics

- Is the final report for tests requiring rapid reporting of results available within 7 calendar days of specimen receipt in at least 90% of cases? [7.6%*]
- Is the final report for neoplastic bloods and bone marrow analyses provided within 21 calendar days of specimen receipt in at least 90% of cases? [6.8%*]
- Are reagents and solutions properly labeled, as applicable and appropriate? [Missing at least one element - 4.2%*]

*% of inspections deficiency cited

Deficiencies must be corrected for accreditation.

# CAP Accredited Labs

- 6600 CAP Laboratories Accredited
- 250 labs with Cytogenetics discipline
- 700 labs with Molecular Pathology discipline
- 98 of the Top 100 Hospitals
- Majority of the large commercial reference labs, i.e., Quest & Lab Corp

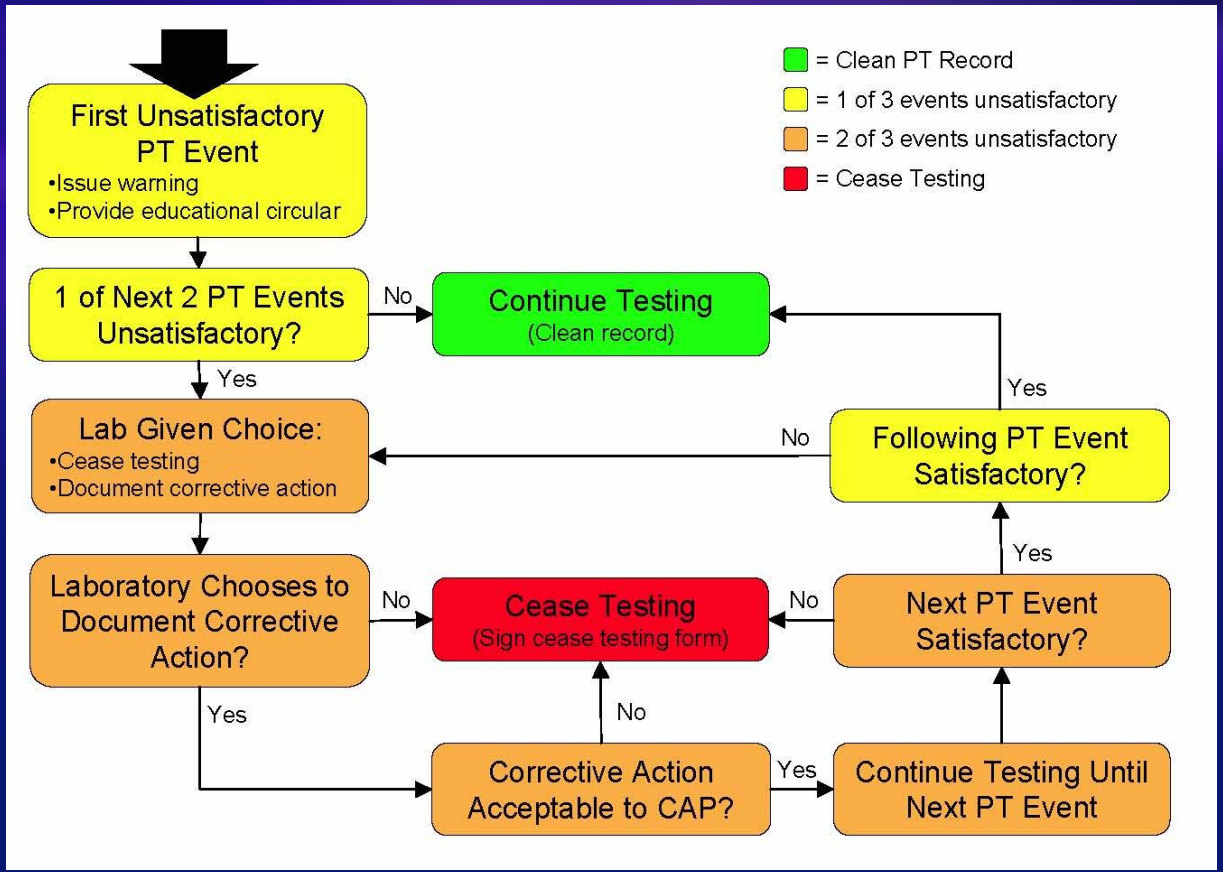
# CAP Proficiency Testing

- Allows laboratories to regularly evaluate their performance and improve the accuracy of the patient results
- Provides individual laboratories with unknown specimens for testing
- Participants analyze the specimens and return the results to the CAP for evaluation
- Results evaluated using comparable peer groups from comprehensive database of laboratories

# CAP Proficiency Testing for Genetics Tests

- CAP contribution
- Products available
  - Chromosome abnormality identification
  - FISH using chromosome-specific DNA probes
  - Biochemical genetics for metabolic diseases
  - Molecular analysis of lymphoma & leukemia

# PT Monitoring by Accreditation Program



# 2006 MGL PT Performance

| Analyte | 2006A correct | 2006A total | 2006A % correct | 2006B correct | 2006B total | 2006B % correct | 2006 A+B % Correct |
|---|---|---|---|---|---|---|---|
| FVL | 778 | 784 | 0.992 | 831 | 834 | 0.996 | 0.994 |
| FVL interp | 782 | 786 | 0.995 | 833 | 835 | 0.998 | 0.996 |
| PT | 758 | 764 | 0.992 | 789 | 798 | 0.989 | 0.990 |
| PT Interp | 756 | 765 | 0.988 | 799 | 808 | 0.989 | 0.989 |
| MTHFR | 454 | 458 | 0.991 | 476 | 482 | 0.988 | 0.989 |
| MTHFR Interp | 424 | 457 | 0.928 | 472 | 491 | 0.961 | 0.945 |
| FMR1 | 223 | 229 | 0.974 | 256 | 260 | 0.985 | 0.980 |
| FMR Status | 245 | 246 | 0.996 | 261 | 265 | 0.985 | 0.990 |
| FMR Interp | 247 | 247 | 1.000 | 262 | 267 | 0.981 | 0.990 |
| PW Interp | 169 | 170 | 0.994 | 178 | 180 | 0.989 | 0.991 |
| HH | 337 | 339 | 0.994 | 348 | 348 | 1.000 | 0.997 |
| HH Interp | 319 | 338 | 0.944 | 341 | 343 | 0.994 | 0.969 |
| DMD | 21 | 21 | 1.000 | 21 | 24 | 0.875 | 0.933 |
| Hb S/C | 72 | 72 | 1.000 | 72 | 75 | 0.960 | 0.980 |
| HB S/C Interp | 72 | 72 | 1.000 | 72 | 75 | 0.960 | 0.980 |

# Conclusion

The CAP Laboratory Accreditation Program can serve as a model to improve the quality of laboratory-developed tests thru the accreditation process in a way that:

- Improves patient care
- Protects the public's health
- Does not stifle innovation and test improvement

# CAP Recommendations

- Private organizations and laboratories should continue to build on their 15 years of work with CLIA developing quality systems.
- CAP believes that the goal of assuring analytical and clinical validity for all high complexity laboratory tests can best be achieved through the CLIA inspection process.
- In order to achieve this goal, CAP understands that statutory changes to CLIA may be needed.


# Questions!