

# **Cytology Proficiency Testing (PT) Regulatory Review**

**Presented by the Cytology Proficiency  
Improvement Coalition**

**Office of Information and Regulatory Affairs**

**Office of Management and Budget**

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# **Why We are Here: An OIRA Review**

# Current CMS PT Regulation

- 2 hour, 10-slide exam administered annually.
- Different grading scale for pathologists and cytotechnologists.
- Four limited interpretive categories.

# **Proposed CMS Regulation Based on CLIAC Recommendations**

- 4 hour, 20-slide exam administered every three years.
- Four limited interpretive categories with the elimination of the difference between HSIL and LSIL.
- Same grading scheme for cytotechnologists and pathologists.
- Require field validation of slides.

# **Today's Presentation Will Demonstrate...**

- The CMS regulatory scheme lacks necessary utility for rulemaking.
- The cost-benefit of CMS' regulatory scheme does not support rulemaking.
- CMS' regulatory scheme is not flexible and cannot maintain relevance in an evolving market.

# **Impact Analysis of this Revised Rule Guided by Executive Order #12866**

- In 2003, OMB published guidelines on how federal agencies should perform regulatory analysis to implement the President's Executive Order.
- This process applies to any action, “regardless of the stage of the regulatory process,” including “rulemakings that rescind or modify existing rules as well as to rulemakings that establish new requirements.”

# OMB Identifies Three Elements of “Good Regulatory Analysis”

- (1) Clear statement of **need** for regulations.
- (2) Evaluation of **costs and benefits** of the proposed action.
- (3) Examination of **alternative** approaches.

# Agencies Are Directed to Review Existing Regulations for Continued Need

- All agencies are to periodically review existing regulations **“to determine whether any such regulations should be modified or eliminated so as to make the agency’s regulatory program more effective in achieving the regulatory objective,”**[Executive Order 12866].”
- If a regulation becomes, **“unjustified or unnecessary as a result of changed circumstances,”** the OIRA works with interested entities to identify **legislative mandates** that may be appropriate for reconsideration.

# **The Current CMS-CDC Regulatory Review Process is Deficient**

- Continuing need for regulation in light of **changed circumstances** since 1992 has not been examined or established.
- The public health benefits of Cytology PT were declared “speculative” in 1992 and **continue to be unsubstantiated.**
- CMS-CDC has **blocked consideration of cost effective alternatives.**

(<http://wwwn.cdc.gov/cliac/cliac0905.aspx#t5s1>).

## The Revised Rule Should Adhere to “Good Regulatory Analysis”

- The current structure of Cytology PT adversely affects the clinical laboratory industry and **impacts a substantial number of “small entities.”**
- In CLIA HHS concluded: “We consider all clinical laboratories to be small entities ... The final rule will significantly increase the operating expense of the nation’s laboratory industry – perhaps by as much as 6 percent per year.”
- CMS-CDC has discretion to restructure requirements and establish an alternative.

# **Background on CLIA '88**

# **What Triggered CLIA '88?**

## **Wall Street Journal Exposes Bad Business Practices**

- “Pap Test Misses Much Cervical Cancer through Labs’ Errors.”
- “Cut-rate ‘Pap Mills’ Process Slides With Incentives to Rush.”
  - WSJ reported that cytotechnologists in large commercial labs were screening up to four times as many slides as recommended by the leading professional societies.
  - WSJ reported that “Pap Mills” were prospering by underbidding competing labs, and that gynecologists seeking to profit by marking up lab fees on patient bills were susceptible to these arrangements.

# Journal Article Triggered Congressional Hearings

- “Flawed system of compliance.”
- “Absence of regulation of tens of thousands of labs.”
- “Inadequate system for overseeing screening for cervical cancer.”

# **Senate Committee Report on CLIA '88 Defines Central Issue**

**“The main problem stems from excessive technician workloads and the lack of continuing medical education programs for both technicians and physicians.”**

# **CMS Enacted Congressionally Mandated National Standards for Quality Assurance**

Examples of the 21 Quality Assurance Standards Include:

- Maximum number of cytology slides that any individual can screen in a 24 hour period.
- Maintain record of number of hours devoted by each individual screener during a 24 hour period.
- Requirements that all cytology be conducted on lab premises.

# **CMS Enacted Congressionally Mandated National Standards for Quality Assurance to Address False Negatives**

Examples Include:

- Random rescreening of benign slides.
- Focused rescreening of slides from high risk groups.
- For each abnormal precancerous or cancerous slides, rescreening of all prior negative cytology slides from the patient, if available.

# **Congress Mandated CMS to Develop Cytology PT**

CMS developed PT program based on broad statutory language below:

“Periodic confirmation and evaluation of the proficiency of individuals involved in screening or interpreting cytological preparations, including announced and unannounced on-site proficiency testing of such individuals, with such testing to take place, to the extent practicable, under normal working conditions.”

# **HCFA/CMS-CDC Struggled From 1992 until 2005 To Implement Cytology PT**

- HCFA issued RFP for contractor to procure glass slides; but agency received no responses.
- “One difficulty in implementing this program is collecting the requisite number of high-quality glass slides representing the appropriate diagnostic categories.”
- “The cost of collecting and referencing the glass slides is very high, and legal and logistical barriers to collection exist as well.”
- “For these reasons, it has proven to be an impossible task to collect and reference sufficient glass slides to conduct PT on a national scale.”

Comments by Carlyn Collins, 1993 CDC-CAP-CETC Symp. Lab. Medicine,

Vol 25, No. 4 April 1994

# **Medical Scientific Issues**

**Reducing False Negatives**  
**Assessing Screening Performance**

**Is PT the Answer?**

# **Agency Regulatory Rationale**

- 1) PT Reduces False Negatives.
- 2) PT Identifies Poor Performers.
- 3) PT Remediates Poor Performers.

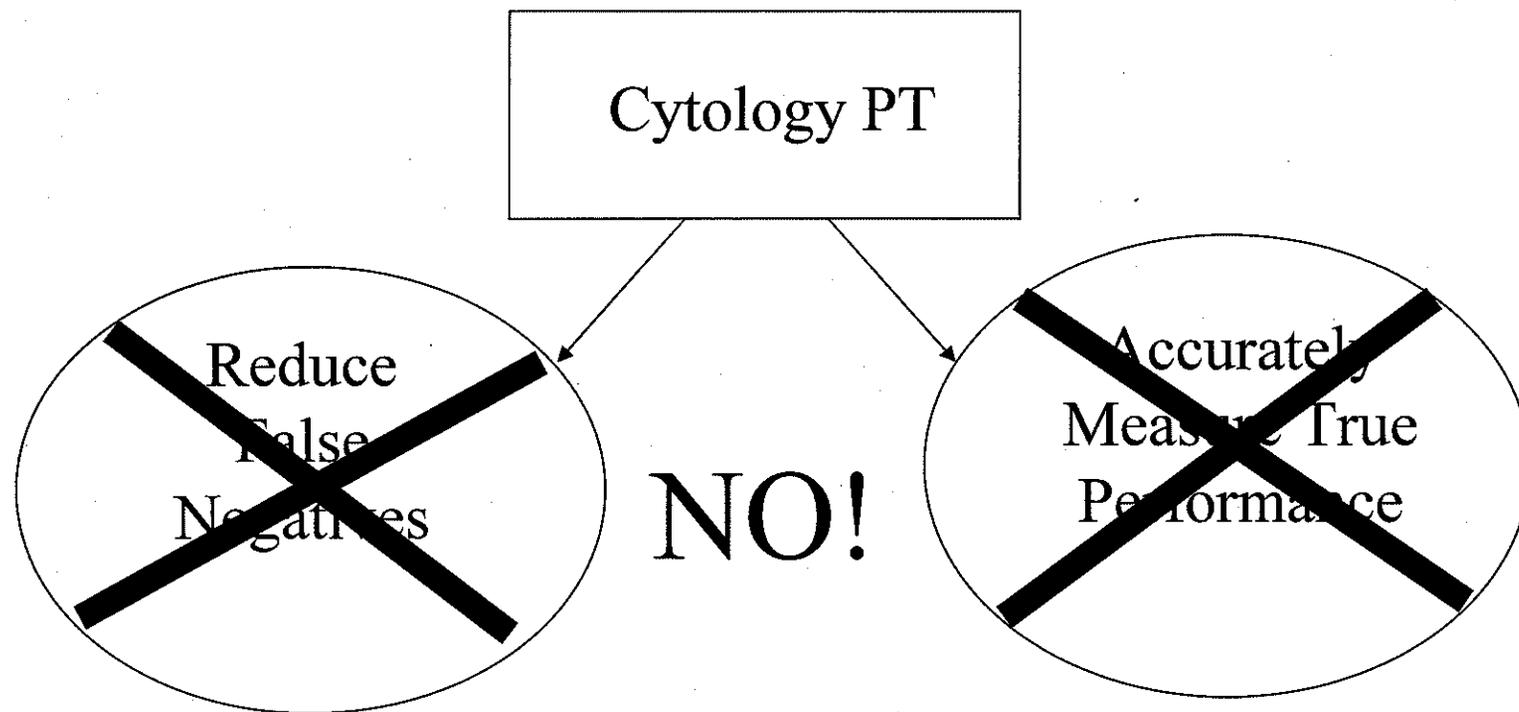
## **HCFA: Primary Purpose of PT is to Identify and Remediate Poor Performance**

“The primary purpose for PT is to identify performance problems that need correction or improvement and to ensure good performance is maintained over time.”

# **HCFA Says Cytology PT will Reduce False Negatives but Concedes Difficulty Measuring Benefits**

- “There is no established methodology to estimate the benefits of these regulations.”
- Must, therefore, rely on “ballpark estimates.”
- “Every effort will be made to develop information on proficiency testing as quickly as possible.”

# To Date, CMS Has Not Demonstrated Program Utility



# Laboratory Community Recognizes Shortcoming of Cytology PT

“Although the value of PT as an educational tool is widely recognized, we do not know the extent to which PT measures true performance.”

Comments by Carlyn Collins, 1993 CDC-CAP-CETC  
Symp. Lab. Medicine, Vol 25, No. 4 April 1994

# **Clinical Laboratory Improvement Advisory Committee (CLIAC)**

## **Purpose:**

The Clinical Laboratory Improvement Advisory Committee (CLIAC) was chartered in February 1992 to provide scientific and technical advice and guidance to the Secretary and the Assistant Secretary for Health regarding the need for, and the nature of, revisions to the standards under which clinical laboratories are regulated; the impact on medical and laboratory practice of proposed revisions to the standards; and the modification of the standards to accommodate technological advances.

# **CLIAC Recognizes Shortcomings of Cytology PT and Advises HHS to Pursue Legislative and Regulatory Changes in 1993**

- “agrees with the CDC that a national glass slide program...is not logistically or financially feasible.”
- The full CLIAC endorsed this point.

# **CDC Study Shows Cytology PT Does Not Correlate with Work Performance of Pap Screeners**

- **1999 CDC Study found:**
  - 0.24 percent correlation between screening performance and PT test results.
  - CDC study authors readily admit 0.24 is a low correlation.
  - The 10-slide test is significantly limited to measuring performance (same point applies to 20-slide test).
  - “Cannot draw conclusions about the quality of pap smear screening in labs in the US from these results...”

–Keenlyside, R.A. et al, *American Journal of Clinical Pathology* 1999; 112, pg 769-776.

# Statistical Reliability and Validity of Cytology Proficiency Testing

- “Statistical considerations have demonstrated that the design of ‘short’ proficiency tests in cytopathology, including the current federally mandated test, fundamentally is unsound because of the lack of sufficient validity and reliability.”
- “...only the use of a 100-slide test set would ensure  $> 90\%$  confidence (exactly, 90.055 confidence) in the test results.”

-Nagy, George K. and Narshkin, Sonya.  
*Cancer Cytopathology*; 2007, pg 467.

# Further Conclusions about the Nagy PT Study

- “Knowledge acquired and changes in practice since the CLIA 88 regulations were issued 15 years ago must also be taken into consideration. Regulations should be written in a manner that anticipates innovation so that the multiyear process of updating regulations is not needed to avoid having cytology professionals evaluated on obsolete practices.”
- According to the study, “...a 20-question test...would not be long enough to meet Nagy and Naryshkin’s criteria.”
- “An education oriented approach to PT is better for assuring that practitioners learn about new concepts and technologies in a timely manner, ultimately leading to better patient care.”

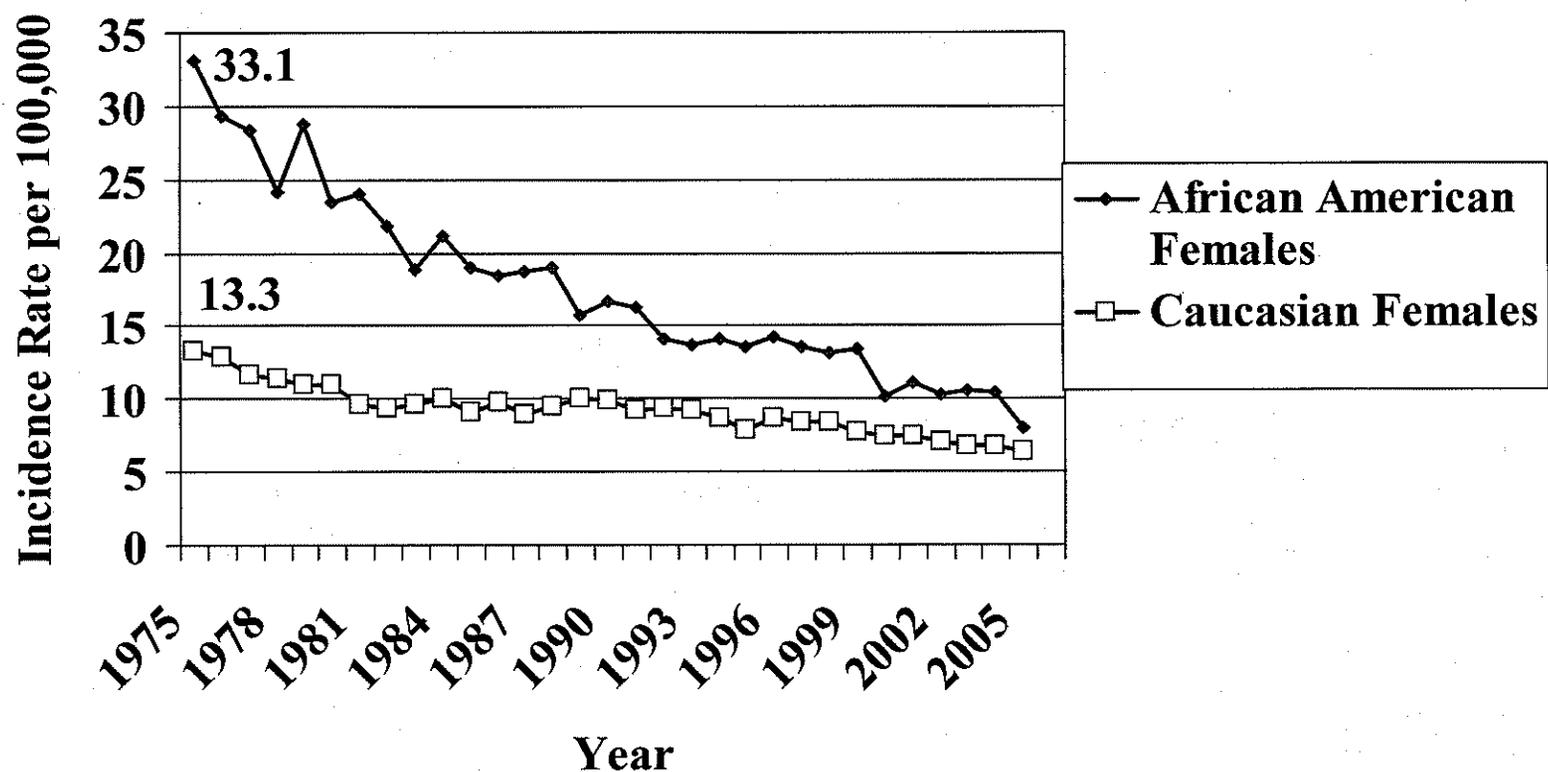
-Birdsong, George G. *Cancer Cytopathology*; April 10,  
2007, pg 463.

# **Cervical Cancer Screening**

# Facts About Pap Test

- Sensitivity is 51% with conventional Pap Smear (now only about 5% of the US market).
- Specificity is 98%.
- Two-thirds of false negative Pap tests are due to sampling problems. A majority of sampling errors are attributed to lack of cell harvest in physician office.
- The test characteristics have been proven adequate because cervical pre-cancer is usually a slowly progressing and often self-resolving condition.
- The estimated progression time from cervical pre-cancer to invasive cancer is 10 to 15 years.
- Effectiveness of Pap test is based on repeated screens.
- More than 60% of women diagnosed with cervical cancer have never been screened or haven't received a Pap test in the last five years.

# Declines In Cervical Cancer Due to Increased Screening



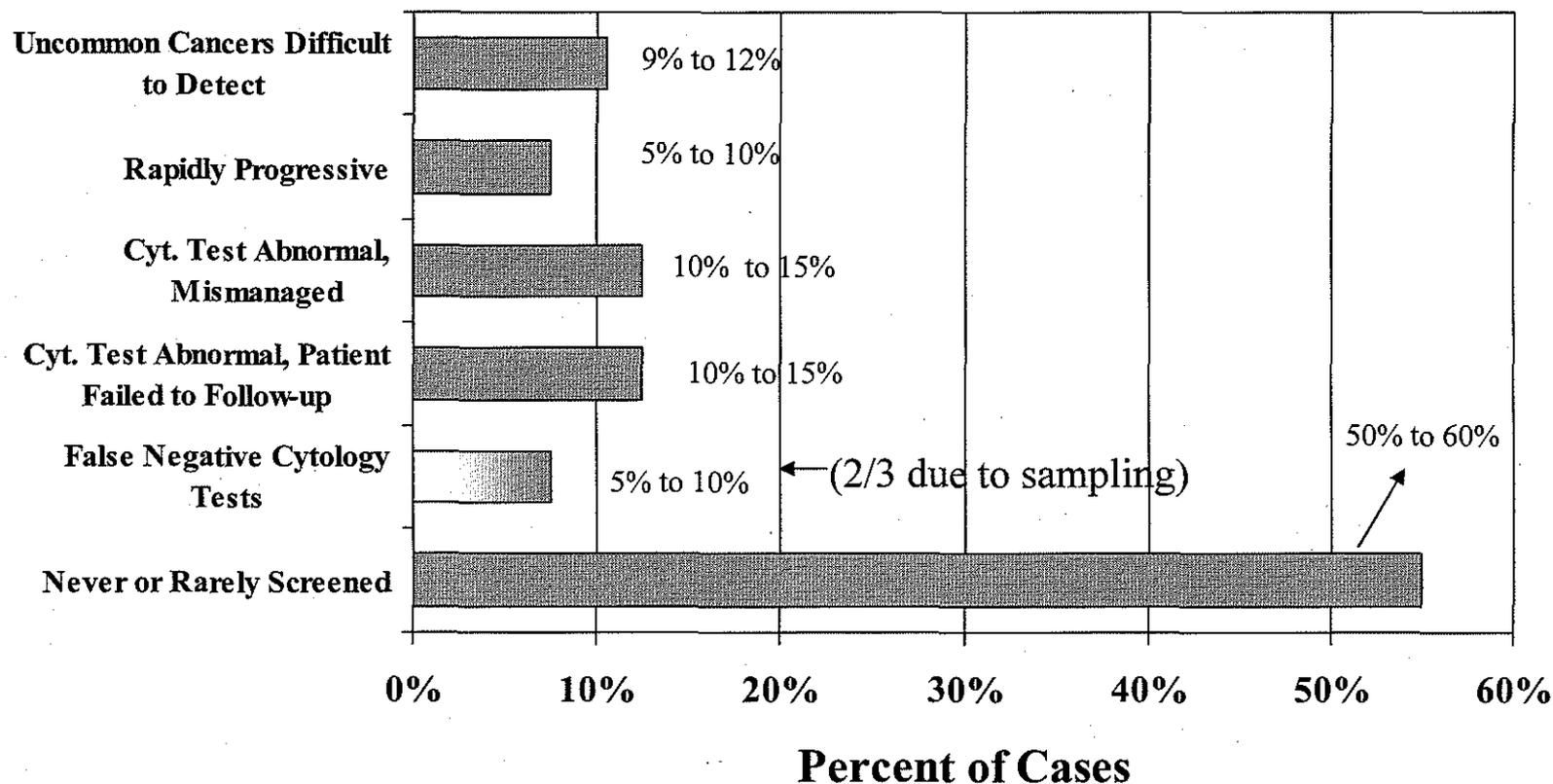
Source: SEER Cancer Statistic Review, National Cancer Institute

# **Cervical Cancer Mortality Due To Other Factors**

- Uninsured or absence of a usual source of health care.
- Less likely to receive preventive services including cancer screening.
- Have low incomes.
- Have high rates of breast cancer, colorectal cancer, and infant mortality.

**Source: Freeman, HP and BK Wingrove. "Excess Cervical Cancer Mortality: A Marker for Low Access to Health Care in Poor Communities," NCI, May 2005. NIH Pub. No.-5-5282**

# Factors Contributing To Cervical Cancer- False Negatives Small Part of Problem



Source: NIH Consensus Conference, Reported in CLIAC  
June 2006 Presentation by CDC

# Potential Benefit of Reduction in False Negatives On Treatment Costs

- Cancer caught at later stages may lead to increased treatment costs.
- As previously highlighted, the estimated progression time from severe dysplasia or carcinoma in situ to invasive cancer is 10 to 15 years.
- “Thus repeated screening builds in redundant opportunities to detect abnormalities (Cuzick, et al. 1999).”

## **CLIA Standardized Quality Controls Already Help Minimize Laboratory False Negatives**

- **WorkLoad Limits:** Individuals who manually screen cytological preparations may examine no more than 100 slides per day (24 hour period) in no less than 8 hours.
- **Rescreening of Negative Cases:** 10% of gynecological specimens from each cytotechnologist be rescreened and that both randomly selected cases and those from “high risk” individuals be included in the rescreened specimens.
- **Cytological-histological correlation:** The laboratory must compare all gynecological cytology reports with an interpretation of HSIL or carcinoma with the histopathology report, if available, to determine the cause of any discrepancy.

# **CLIA Made Laboratory Director Responsible for Periodic Competency Reassessments**

- **Individual Performance Assessment:** The laboratory director must establish work-load limits for each individual every 6 months based upon capabilities and performance using evaluations of 10% negative quality control screens and cytotechnologist-pathologist interpretation correlation data.
- **Documentation of Performance:** The laboratory must evaluate individual performance in comparison to overall performance and document discrepancies and corrective action if appropriate.

# **Extensive CLIA Record Requirements Facilitate Competency Assessment of Lab and Individuals**

Statistical records must be maintained, including:

- The annual number of cytologic specimens.
- Number processed by specimen type.
- The volume of cases by interpretation.
- Number of unsatisfactory cases.
- Number of cases where rescreen results in reclassification to abnormal (pre malignant or malignant).
- Number of cases where cytology and histology is discrepant.
- Number of HSIL and malignant cases in which histologic follow-up is available.

# **Existing CLIA Quality Standards Improve Real Patient Outcomes**

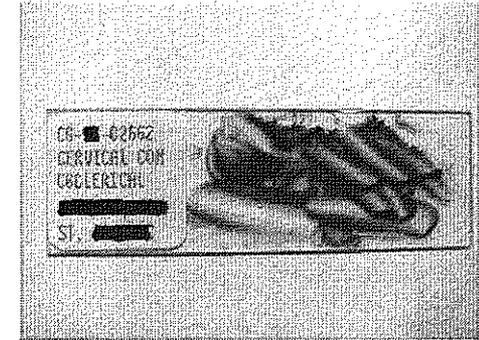
- Continuous monitoring of performance.
- Reviews of actual outcomes.
- Performance reviewed in context of actual laboratory work environment.
- Records are subject to regular unannounced accreditation inspections.

## **New Technologies\* Widely Implemented In Cervical Cancer Screening Since 1992**

- Enhanced sampling with liquid-based cytology.
  - 3 FDA approved products: ThinPrep, SurePath, and Monogen (over 90% of 2006 Pap Tests)
- Enhanced screening with computer-assisted screening.
  - 2 FDA approved products: ThinPrep Imaging System and FocalPoint (40% to 50% of 2006 Pap Tests)
- Enhanced interpretation of abnormalities with objective molecular testing for HPV DNA in women with indeterminate (ASCUS) cytology results (preferred method of testing in 2002 NCI guidelines).

\* All Technologies Covered by Medicare

# Pre-CLIA '88



**Available Technology:**

Conventional Pap  
“Smear”; Multiple layers of cells  
and other matter.

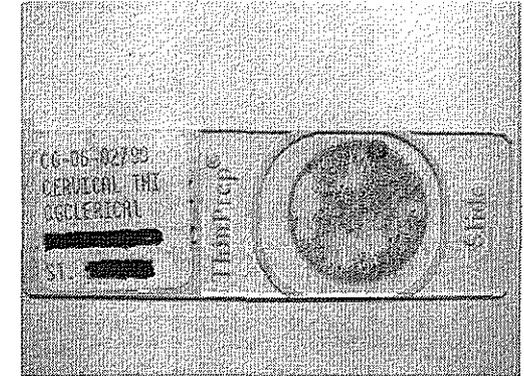
**Operating Environment:**

Pap Mills (Volume  
over quality).

**Federal Oversight:**

No Federal  
Cytology Quality  
Standards.

# Post-CLIA '88



**Available Technology:**

Liquid based cytology, monolayer slides, computer-assisted screening, location-guided screening, digital imaging, HPV testing, cervical cancer vaccine.

**Operating Environment:**

Pap Mills Eliminated; Emphasis on collaborative nature of pathology.

**Federal Oversight:**

Extensive and rigorous oversight through national quality standards and bi-annual lab inspection and accreditation.

Examples of the standards include:

- 10% of all slides diagnosed as negative require rescreening
- All individuals reading Pap tests are subject to workload limits
- Five years worth of previous negative slides are pulled on all current high grade diagnosis

# **Regulatory Impact Analysis**

# Clear Statement of Need for Regulations

Consistent with Executive Order 12866:

- CMS cannot demonstrate clear need for regulation, i.e. reduction false negatives, measure of performance.

Therefore...

As stipulated in OMB Circular A-4, OIRA must work with interested entities to identify legislative mandates for reconsideration.

# Evaluation of Costs and Benefits of the Proposed Regulation

The CMS Cannot:

- Link or correlate regulatory actions and associated costs with expected benefits.
- Identify a baseline to measure benefits or provide a comparison with alternatives.

Therefore, OIRA should direct CMS to eliminate the current regulatory program for a more effective alternative approach, i.e. H.R. 1237/S. 2510.

OMB Circular A-4

# Examination of Alternatives

OMB Must Direct CMS to Replace the Current PT regulation with a program that:

- Can adapt to changing technology.
- Allows for improvement through examining challenging, complex cases.
- Provides a testing regiment that is more reflective of real world laboratory practice.
- Provides feedback to allow for locator and interpretive skill improvement.
- Is consistent with other CLIA quality assurance standards.
- Allows for the identification of poor performers and improvement of skills over time.
- Is statistically valid and allows for correlation between performance and test results.

# Cytology PT is NOT a Quality Improvement Measure

- No evidence that PT reflects true performance.
- PT does not reflect **normal working conditions**.
- “There is no established methodology to estimate the benefits of these regulations.”
- Must therefore rely on “ballpark estimates.”
- Performance improvements in overall laboratory results are the outcomes that impact public health.
- Agency analysis cannot measure how individual cytology PT impacts laboratory outcomes.
- CDC concluded information from cytology PT should only be used carefully in conjunction with other performance measures as part of a laboratory's quality assurance program.

# Shortcomings of HHS Estimate of Benefits of Cytology PT in '92 Rule

- HHS conceded that there was no empirical evidence to support the 1992 estimate of benefits analysis.
- HHS assumed, based on no data, that PT testing reduced false negatives and reduced unnecessary care.
- HHS Did NOT:
  - Provide measure of extent of problem of false negatives (i.e. baseline)
  - Provide quantifiable evidence to support their assumptions that PT reduces false negatives
  - Provide quantification of impact on health outcomes (i.e. mortality and morbidity)
  - Look at cost effectiveness of possible alternatives
- For newly proposed rule, need to take a more rigorous approach.
- **Key Point: Proposed revisions to the regulation cannot demonstrate these benefits.**

# Costs of Proficiency Testing Are Substantial For Minimal Benefit

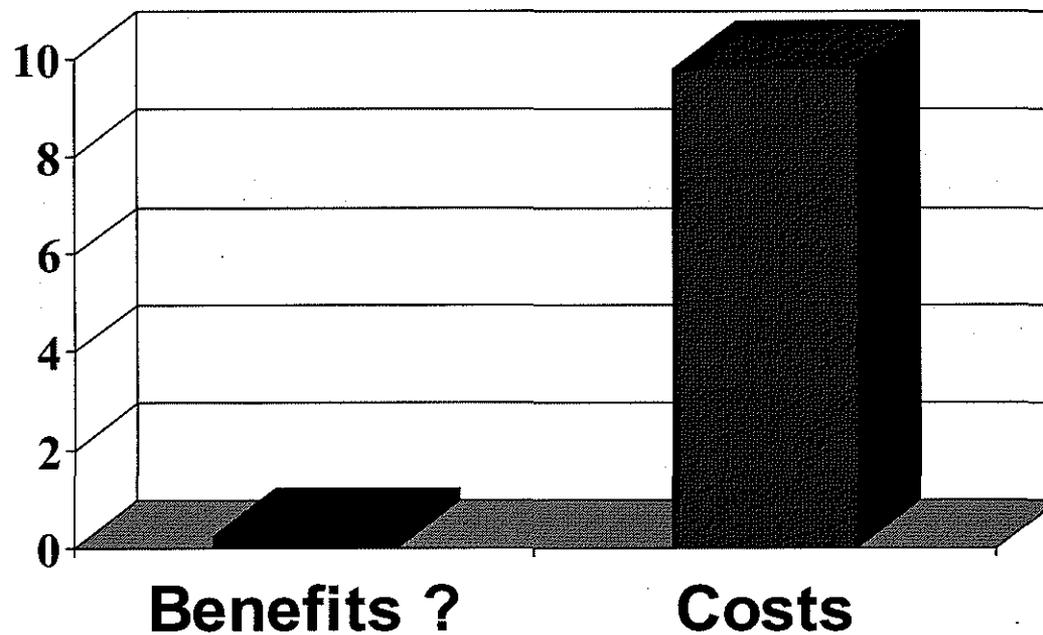
- Costs Include:
  - Slides and Material
    - Must obtain adequate slide material through field validation and a separate nationwide CME program
    - Labor Costs to produce test slides
    - Shipping Costs
  - Lost Productivity
    - Laboratories forced to shut down operations to take proficiency test
- Costs do not necessarily decline for 20 slide test every 3 years because:
  - There will continue to be new applicants
  - Test material must be continuously updated and replenished with slides field-validated in CME program

# CAP Estimate of Annual Costs of PT Program

	10 slide test 2 hours
Cost Per Laboratory	\$1,250 per* 3,800 labs = \$4.75 mil
Cost Per Test Taker	\$75 * 12,826 = \$961,950
Opportunity Cost of Taking the Test	Cytotechnologists \$21 per *13,056 hrs =\$274,176  Pathologists and Other MDs \$134 per * 13,056 hrs =\$1.75 million
Total Cost	\$7.7 million

Source: CAP Analysis

# Utilizing Cytology PT To Reduce False Negatives Is Not Cost Effective



Source: CAP Analysis

# **Regulatory Alternatives**

# **Premise for CLIAC Consideration of Regulatory Alternative**

- In 2005, the House of Representatives approved H.R. 4568 to suspend the cytology proficiency program.
- To counter the possible passage of this legislation, CMS-CDC handpicked the CLIAC workgroup to consider alternatives.

# CDC/CMS Process for Revising Rule

- CDC-CMS selected cytology professionals to participate in CLIAC workgroup, including some non-CLIAC members.
- Agency instructed CLIAC workgroup that they could not make recommendations to HHS to seek a statutory change. These instructions included the prohibition of any discussion of alternatives outside the existing regulatory framework.

# **Major Cytology PT Changes CLIAC Recommended**

- Altered testing cycle from annually to once every three years.
- Change grading scheme.
- Utilize same grading scheme for cytotechnologists and pathologists.
- Use a 20 slide test instead of 10 slide test.
- Require field validation of slides.

# **CLIAC Recommendations DO NOT Remedy Fundamental Problems**

- There is no empirical evidence of a link between individual PT and work performance.
- There is no evidence that individual PT reduces false negatives or cervical cancer mortality.
- PT is redundant to mandated quality monitors and adds no additional measurable public health value.
- PT is duplicative of required CME educational programs for cytology laboratories.
- New technologies have made the glass slide PT program obsolete.

# **CMS Failed to Recognize a More Effective Regulatory Approach**

An Effective Regulatory Approach Includes:

- An evaluation of actual laboratory outcomes utilizing the quality improvement systems put in place by CLIA.
- Ensuring competency through use of quality monitors.
- Requiring testing as part of continuing medical education for individuals, and incorporate into quality improvement system.
- Mammography Quality Standards Act more closely reflects this regulatory approach than CLIA PT.

# **H.R. 1237/S. 2510**

**The *Cytology Proficiency Improvement Act of 2007* recognizes that the regulatory approach is insufficient.**

- Introduced in the 110<sup>th</sup> Congress, H.R. 1237/S. 2510 seeks to upgrade the outdated cytology proficiency testing program to a proficiency testing program administered in an continuing medical education environment.
- H.R. 1237 passed the House of Representatives in April, 2008 with bipartisan support. 175 House cosponsors.
- S. 2510 currently has 42 cosponsors and is under consideration in the Senate Health, Education, Labor, and Pensions (HELP) Committee.

# Federal Legislation Pending to Revise Cytology PT Requirements

- Require that laboratories ensure that all individuals involved in screening and interpreting Pap tests participate annually in a continuing medical education (CME) program in gynecologic cytology.
- Require that the CME program be approved by the Accrediting Council for Continuing Medical Education or the American Academy of Continuing Medical Education.
- Require that the CME program provide each individual involved in screening or interpreting pap tests with a glass slide (or equivalent technology) examination testing and documenting their locator, recognition and interpretive skills.
- Consistent with CLIA, require the laboratory director to incorporate the results of the continuing medical education program when assessing the overall performance of individual laboratory personnel. Lab director is also required to make the CME results available to outside accrediting 61 organizations.

# **MQSA Sets Precedent for H.R. 1237/S. 2510 Alternative**

- Both MQSA and CLIA had some regulatory objective to reduce false negatives and positives.
- MQSA strikes balance and emphasizes CME and quality monitors.
- FDA considered and rejected individual PT noting that the general consensus was that “PT would be excessive, unnecessary, costly, impractical, and duplicative of examinations already in place.”
- MQSA conducted a regulatory impact analysis which established a clear link between quality standards and reductions in mortality and morbidity.

# Today's Presentation

## Demonstrated...

- The CMS regulatory scheme lacks necessary utility for rulemaking.
- The cost-benefit of CMS' regulatory scheme does not support rulemaking.
- CMS' regulatory scheme is not flexible and cannot maintain relevance in an evolving market.
- Therefore.....

# Coalition Recommendations

# Coalition Recommendations

- OIRA must review the regulatory impact analysis of revised cytology PT to evaluate:
  - Evidence of reduced false negatives due to Cytology PT
  - Evidence of improved outcome due to Cytology PT
  - Account for changed circumstances due to new technologies and existing mandated CLIA regulations
- OIRA should ask CMS to withdraw rule and:
  - Support alternative provided in H.R. 1237/S. 2510.