



Department of
Health

New York State

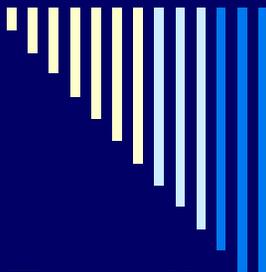
**20 Years of CLIA
40+ Years of the NYSDOH Clinical
Laboratory Reference System**

Impact on Laboratory Quality

**Richard W. Jenny, Ph.D.
Clinical Laboratory Reference System
Wadsworth Center**

Clinical Laboratory Improvement Advisory Committee

February 20, 2008

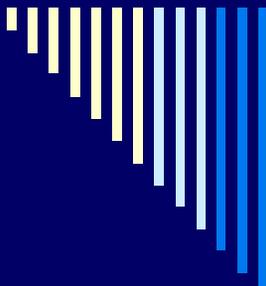


Clinical Laboratory Reference System

Established by Public Health Law (PHL) in 1964

The laboratory reference system has three components:

- inspection of laboratory facilities and distribution of proficiency test specimens for laboratory examination, or other measures of laboratory performance;
- validation and approval of standard laboratory methods and materials; and
- cooperative research relevant to advancement, development and assessment of laboratory methods and materials.

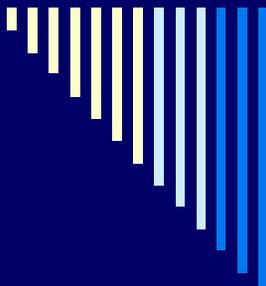


Clinical Laboratory Reference System

PHL requires reference system oversight and licensure of:

- clinical laboratories located in or accepting specimens from New York state;
- blood banks that collect, process, store and/or distribute, human blood, blood derivatives or blood components, in the State.

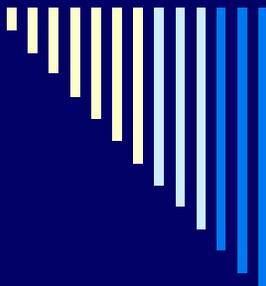
Certification of laboratory directors



Clinical Laboratory Reference System

Contributions to Laboratory Quality

Case Studies in Public Health



Clinical Laboratory Reference System

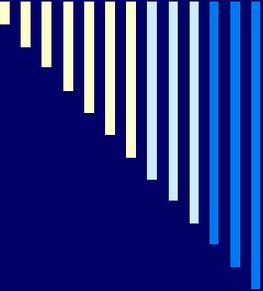
Laboratory Inspection – Standards of Practice

Medical error has been ascribed to a “failure of process.”

Too Err Is Human: Building a Safer Health System, IOM

Laboratory practice standards and inspection process grounded in expectations that the laboratory:

- Establishes specifications for sound processes;
- Develops and uses process quality indicators;
- Implements and verifies process improvement initiatives, where indicated.



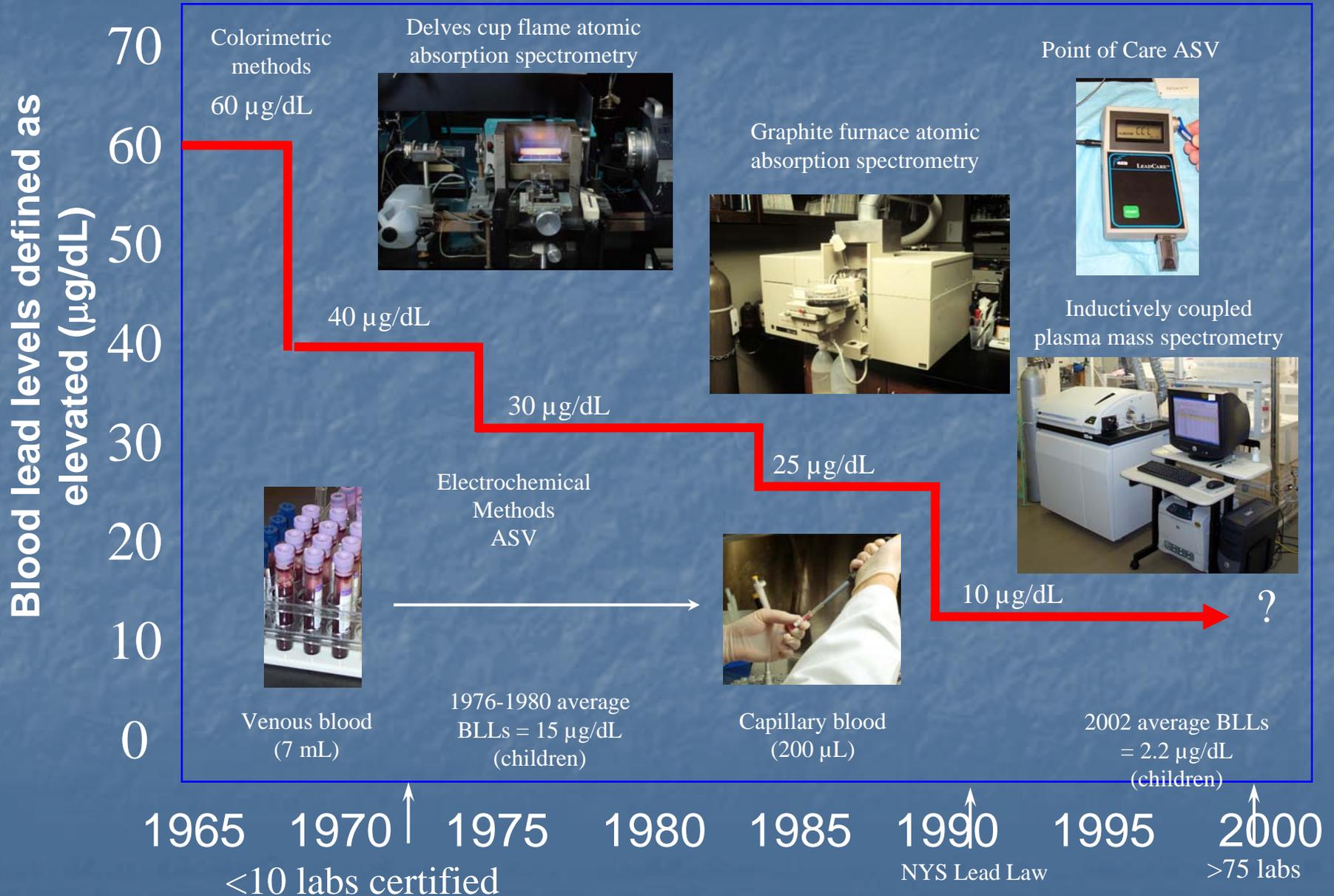
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Laboratory Inspection – Standards of Practice

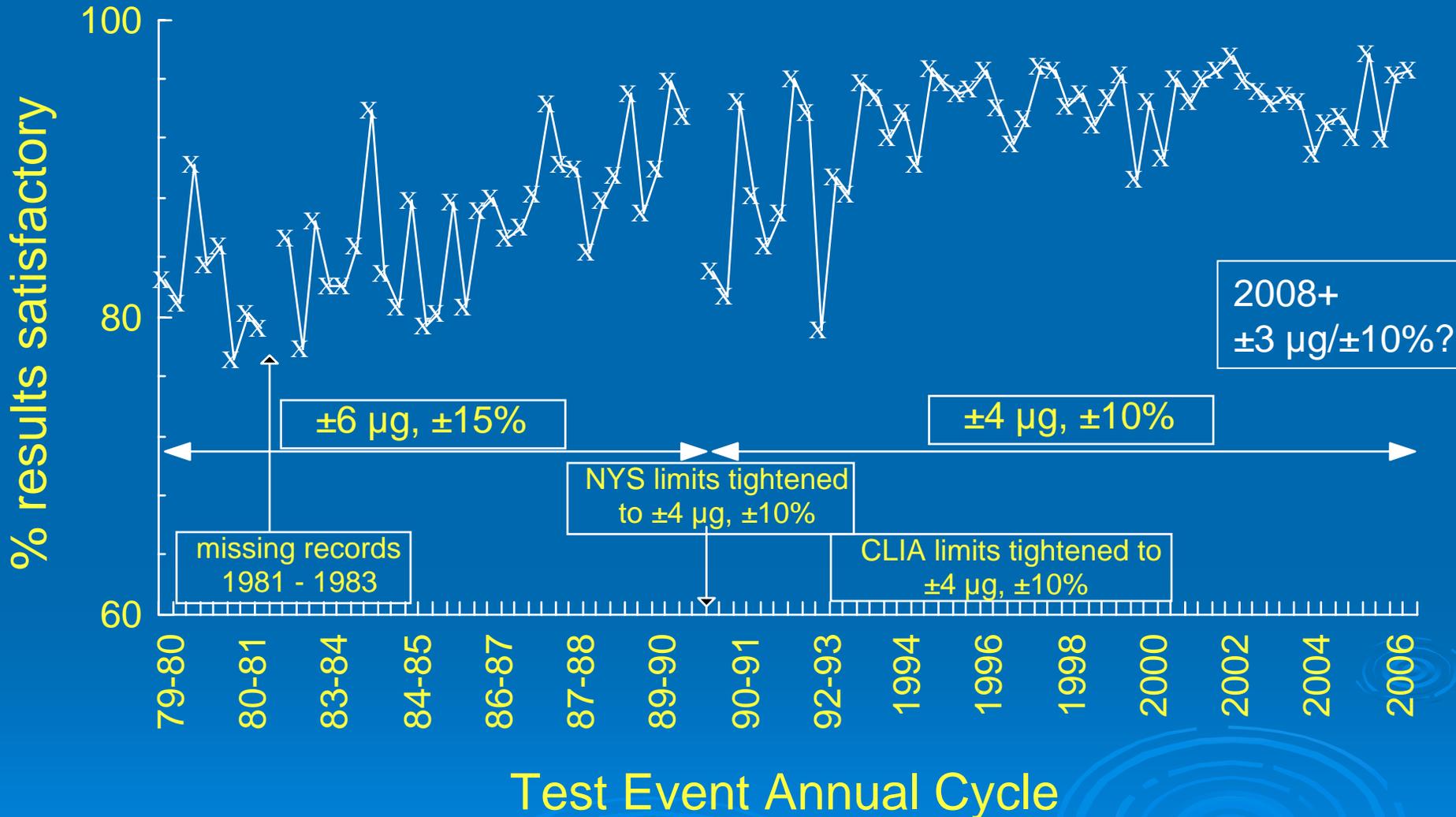
Case Study: Childhood Lead Poisoning

- Definition of risks for lead poisoning in terms of blood lead concentration has changed over time
- Continuous change in systems and processes for blood lead determinations needed to meet patient care needs
- Standards of practice drive change in the interest of patient care

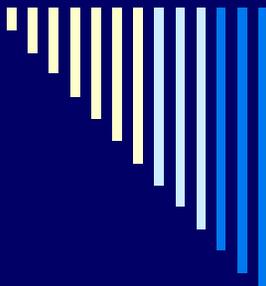
Changing Methodologies for Blood Lead Screening



NYS BLOOD Pb LABORATORY PERFORMANCE: 1979 – 2006



Source: New York State Department of Health Proficiency Testing Program for Blood Lead

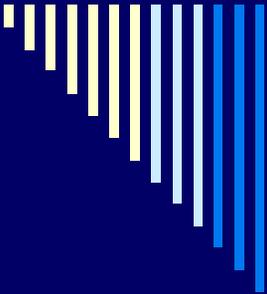


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Proficiency Testing

Case Study: Point-of-Care Blood Lead Testing

- Challenges in PT specimen design to mimic the patient specimen and test device specimen requirements
- Proven value of PT in establishing traceability to reference methods



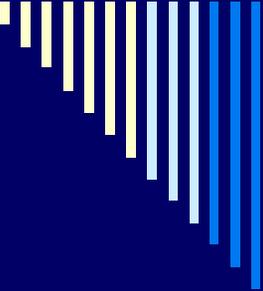
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ESA LeadCare® Specimen Requirements

- Blood must be fresh (<24 hrs old)
- Cannot refrigerate blood

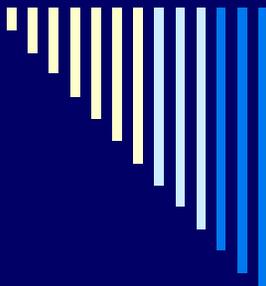
PT Program Design

- Most US-based PT programs circulate aged blood that has been previously frozen or has been refrigerated;
- Peer-group grading is typically practiced by US-based PT programs for blood Pb by LeadCare®



Clinical Laboratory Reference System

- NYSDOH reference system circulates blood from lead-dosed animals, unfrozen and unrefrigerated.
- PT samples delivered within 24 h; validated for the evaluation of LeadCare® against AAS, ASV (bench) and ICP-MS methods; and
- LeadCare® performance in PT demonstrated a negative bias greater than 20% from reference method values



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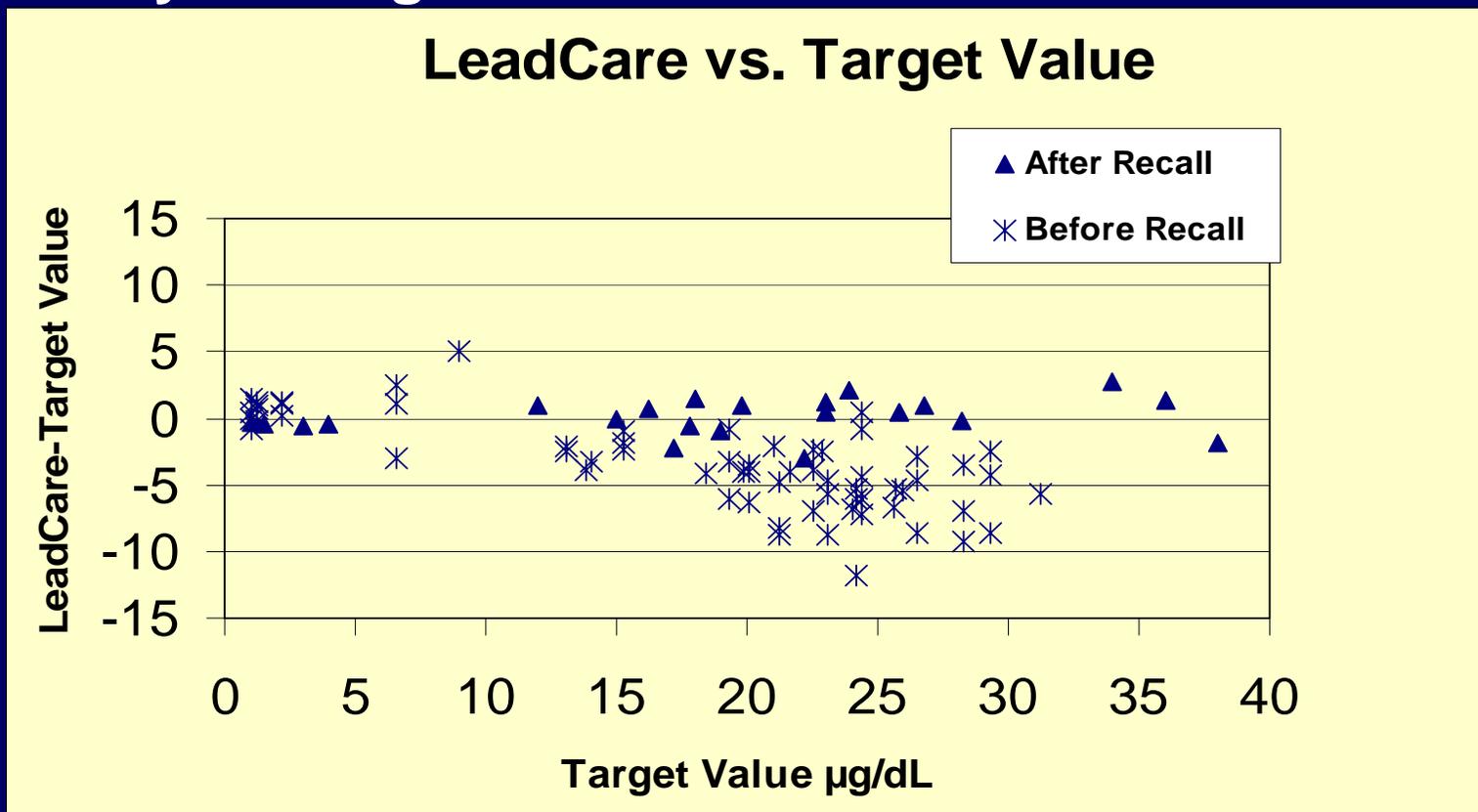
Consequences of defective LeadCare® sensors as detected by PT program:

- Under reporting of lead exposed children
- Product recall
- Company recommended all children previously tested with defective sensors and found to be $>6 \mu\text{g}/\text{dL}$ be re-tested by another method.
- Source of error identified and test kits quickly replaced



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Proficiency Testing





Clinical Laboratory Reference System

Test Approval

Reference system scientists have reviewed more than 3000 SOPM and validation submissions for laboratory developed and FDA-cleared assays modified for intended use.

Laboratories must establish analytical and clinical validity

- 55% of submissions required revision to procedures and/or validation protocol
- 1.5% rejected where clinical validity was not proven

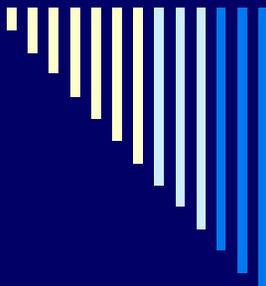


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Test Approval

Case Study: UNOS Prevention of transmissible diseases in organ transplants

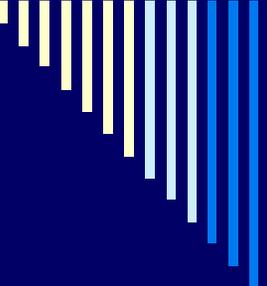
- Laboratory developed molecular assay for CMV
- Intended use included testing of organ donors
- Submitted to NYSDOH for approval for use in NYS



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Test Approval Case Study: Molecular CMV Assay Design

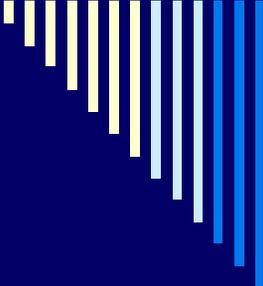
- DOH virology reviewers received SOPM and validation data for the laboratory developed molecular CMV assay, which targeted the gB gene
 - Reviewers aligned the primer sequences with the four subtypes of gB and found one primer contained a major mismatch with one subtype
 - The mismatch would have prevented detection of that subtype, which is estimated to cause CMV disease in 20-25% of transplant recipients in the USA
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Test Approval Case Study: Molecular CMV Assay Design

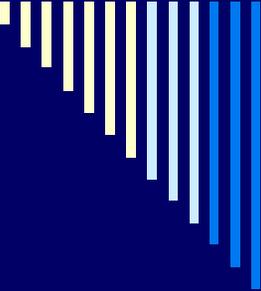
- Molecular biologist in submitting laboratory concurred that the assay design was fundamentally flawed
 - Submitting laboratory was intending on marketing the test to major transplant centers
 - Submitting laboratory designed a new CMV assay to a completely different target gene, which was reviewed and approved by reference system reviewers.
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Cooperative Research

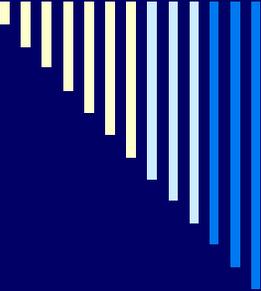
Case Study: Serodiagnosis of Lyme Borreliosis



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Cooperative Research Case Study: Serodiagnosis of Lyme Borreliosis

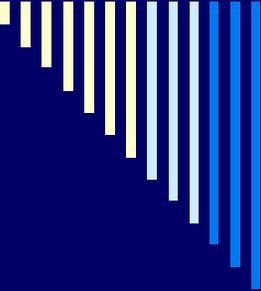
- 1994 2nd Dearborn Meeting, ASTPHLD recommended two tier testing protocol
 - First tier optimized for sensitivity, to give quantitative measure via immunoassay of antibodies to cultured *Borrelia*
 - Second tier (immunoblot) to provide a qualitative result which improves specificity
 - Two tier protocol has 60% sensitivity in early acute infection (during erythema migrans)
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Cooperative Research Case Study: Serodiagnosis of Lyme Borreliosis

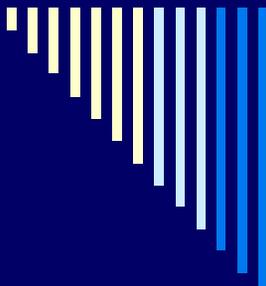
- Antigen used for FDA approved kits was *in vitro* cultured *Borrelia*
 - *Borrelia* up regulates different genes and express different proteins when infecting humans
 - ❖ Cultured bacteria not the best antigen source for diagnosis of human infection
 - Western blots are subject to interpretation
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Cooperative Research Case Study: Serodiagnosis of Lyme Borreliosis

- NIH/CDC sponsored 2nd Banbury Conference on Laboratory Diagnosis of Lyme Disease, Sept 10-12, 2007
 - Reference system scientist presented evaluation of a duplex assay using recombinant proteins which has potential to improve diagnosis of Lyme disease. Further testing is required in specimens from patients whose clinical status is well documented
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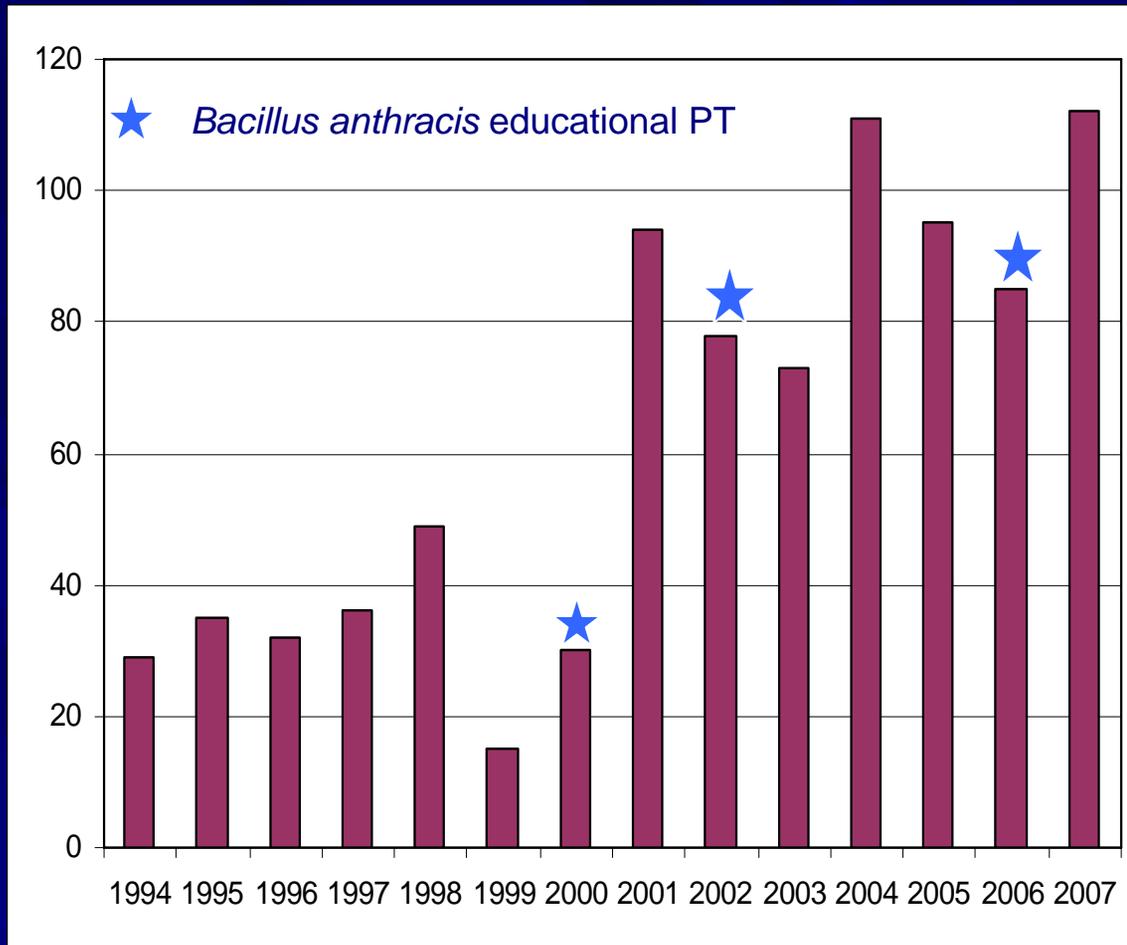
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Public Health

Case Study: Laboratory response network

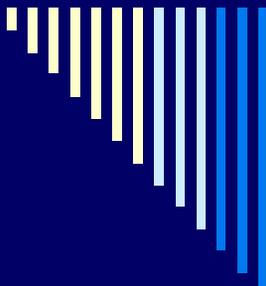
- Sentinel laboratories play a key role in the early detection of biological agents.
- Sentinel laboratories provide routine diagnostic services, rule-out, and referral steps in the identification process.

Bacillus anthracis Rule-Out Specimens Received in the NYSDOH Public Health Laboratory



Key Points

Reference system and Laboratory Response Network staff strive through practice standards, educational PT and outreach to continually improve the analytical and communications protocols needed to protect the public health. Cases of *B. anthracis* rule-out samples submitted by sentinel laboratories have demonstrated conformance to rule-out protocols and specimen referral algorithms. (star indicates educational PT event)

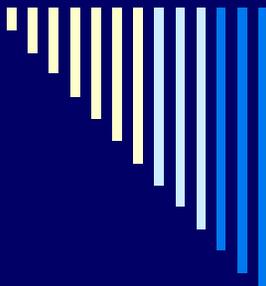


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Conclusions

Standards of practice that remain consistent with consensus requirements for delivery of clinically useful services promote continuous improvement of laboratory quality.

PT/EQA schemes provide objective measures of laboratory and examination procedure performance, and promote the remediation of substandard performance.



Clinical Laboratory Reference System

Conclusions

Approval of laboratory developed assays provides impartial assessment for analytical and clinical validity, similar to that provided by the FDA for commercial assays, limiting laboratory services to the use of *proven* assays.

Cooperative research advances the analytic and clinical validity/utility of diagnostic methods.

Laboratory quality is the product of a partnership among laboratory professionals/organizations, industry, accrediting organizations, and government