

# **Proficiency Testing Schemes and Traceability: the College of American Pathologists (CAP) Perspective**

**John H. Eckfeldt, MD, PhD**

**Medical Director, Clinical Pathology,  
Fairview-University Medical Center**

**Professor, Department of Laboratory Medicine  
and Pathology  
University of Minnesota**

# **Topics To Be Addressed**

- **Brief history of PT/EQAS efforts with an emphasis on US/CAP experiences,**
- **CAP's view on the role of PT/EQAS for assessing traceability/trueness and its limitations,**
- **Why CAP committees hesitate to use reference method-assigned target values for evaluation of laboratory performance,**
- **Data from 1994 CAP “fresh frozen serum” project to assess calibration and “matrix” biases,**
- **What may happen when “accuracy based” target values are used in a “free enterprise” system,**
- **Current CAP Survey status and plans for the future.**

# **Milestones in US Inter-laboratory PT/EQAS and Traceability**

**1947 Belk & Sunderman's study of clinical lab  
measurands in PA and surrounding states,**

**1949 CAP Surveys Program begin,**

**1951 CAP "Standards Solutions" begin,**

**1961 CAP Clinical Standards Laboratory instituted  
for cyanmethemoglobin,**

**1977 CDC/FDA/NBS conference on reference  
methods and material lead to NRSCC and NRSCCL**

**1988 CLIA '88 passed: CAP Survey's perceived role  
changed to a regulatory from a primarily  
educational one.**

# **Eras of Clinical Laboratory Test Traceability**

**1940's and 1950's: discovering how bad things are,**

**1950's and 1960's: reference methods for clinical measurands and PT/EQAS are developed,**

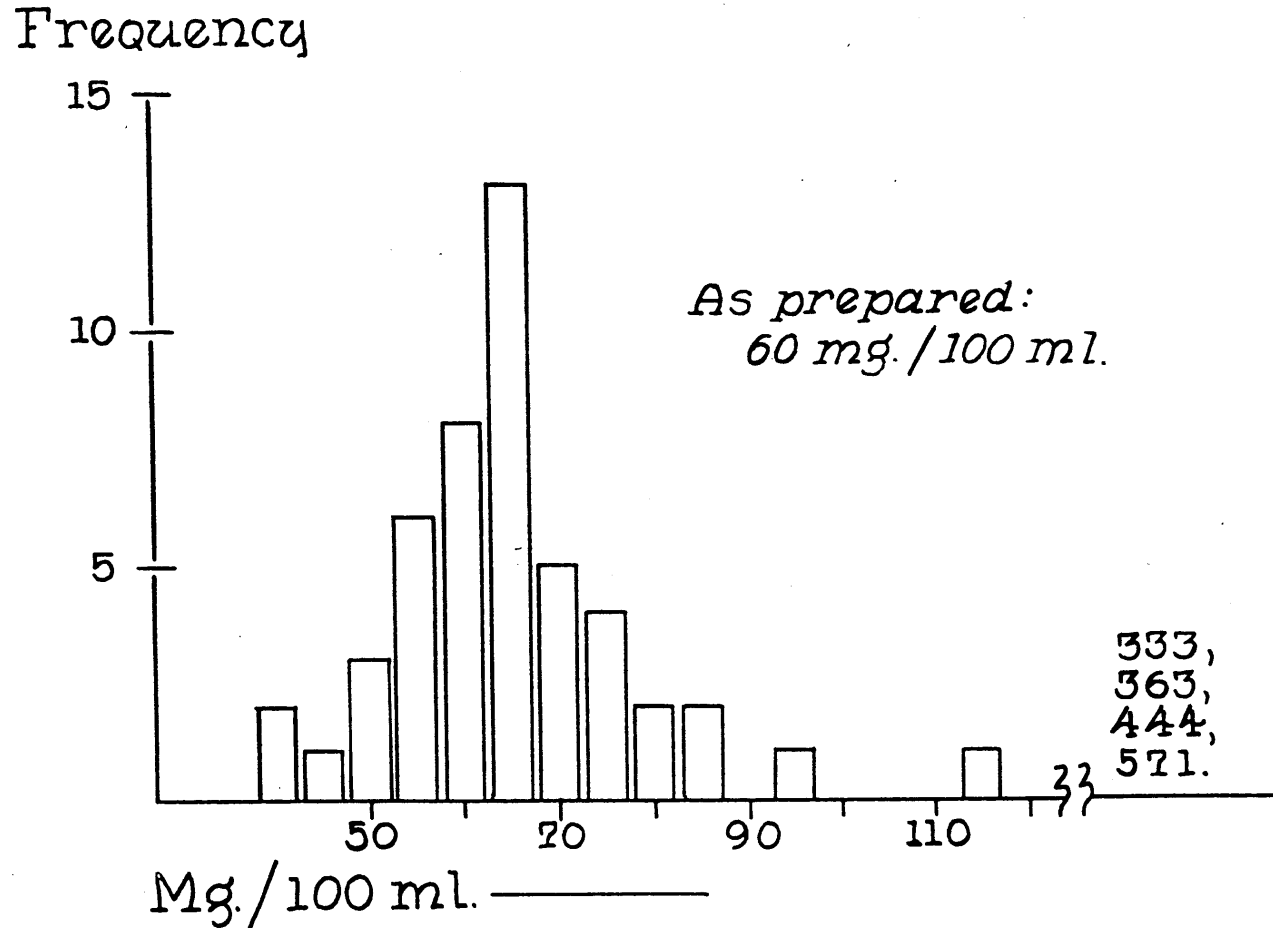
**1970's & 1980's: further development of "high level" reference methods & materials for more clinical measurands,**

**1990's: better understanding of matrix effect (non-commutability) problems, many better reference methods and materials begin to become available,**

**2000's: develop better inter-laboratory traceability for clinically important measurands???**

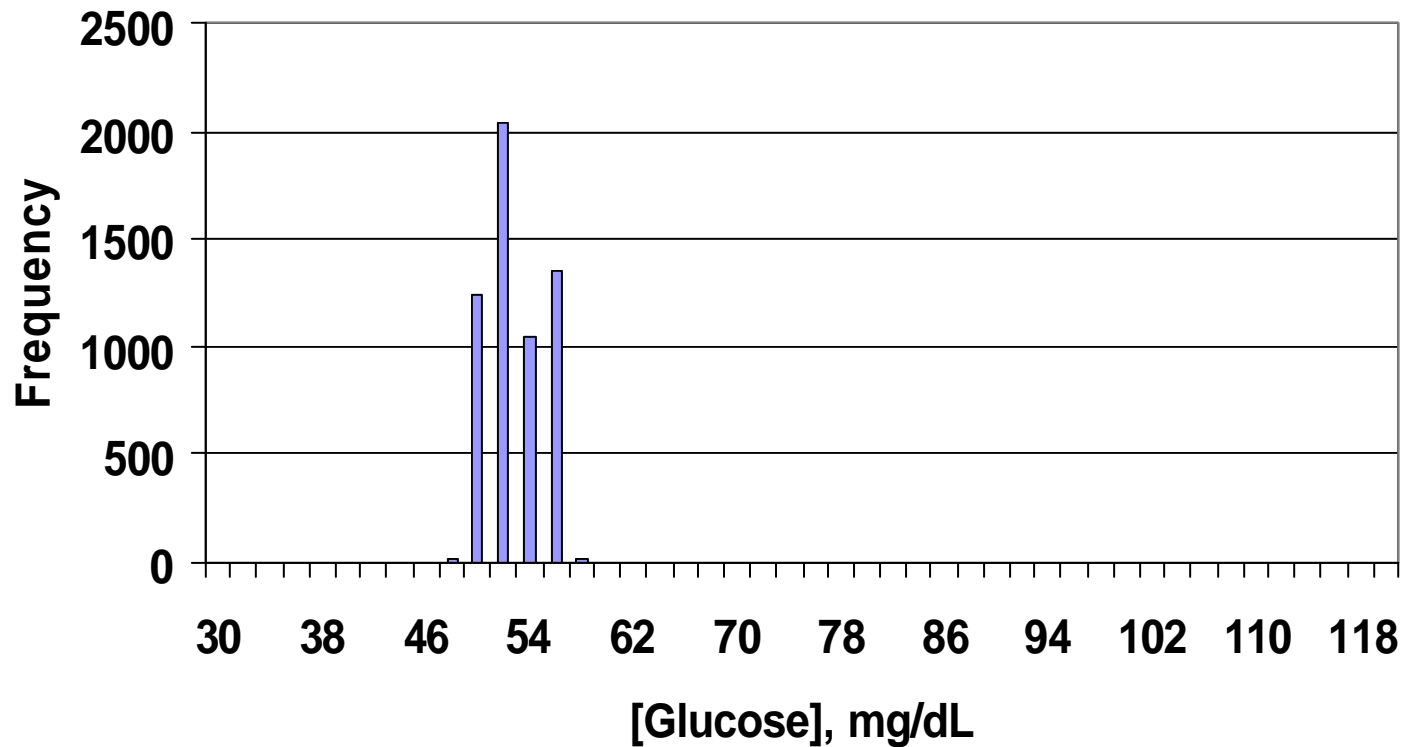
# 1947 Glucose PT Results

(Belk and Sunderman. *Am J Clin Pathol* 1947;17:853-61)



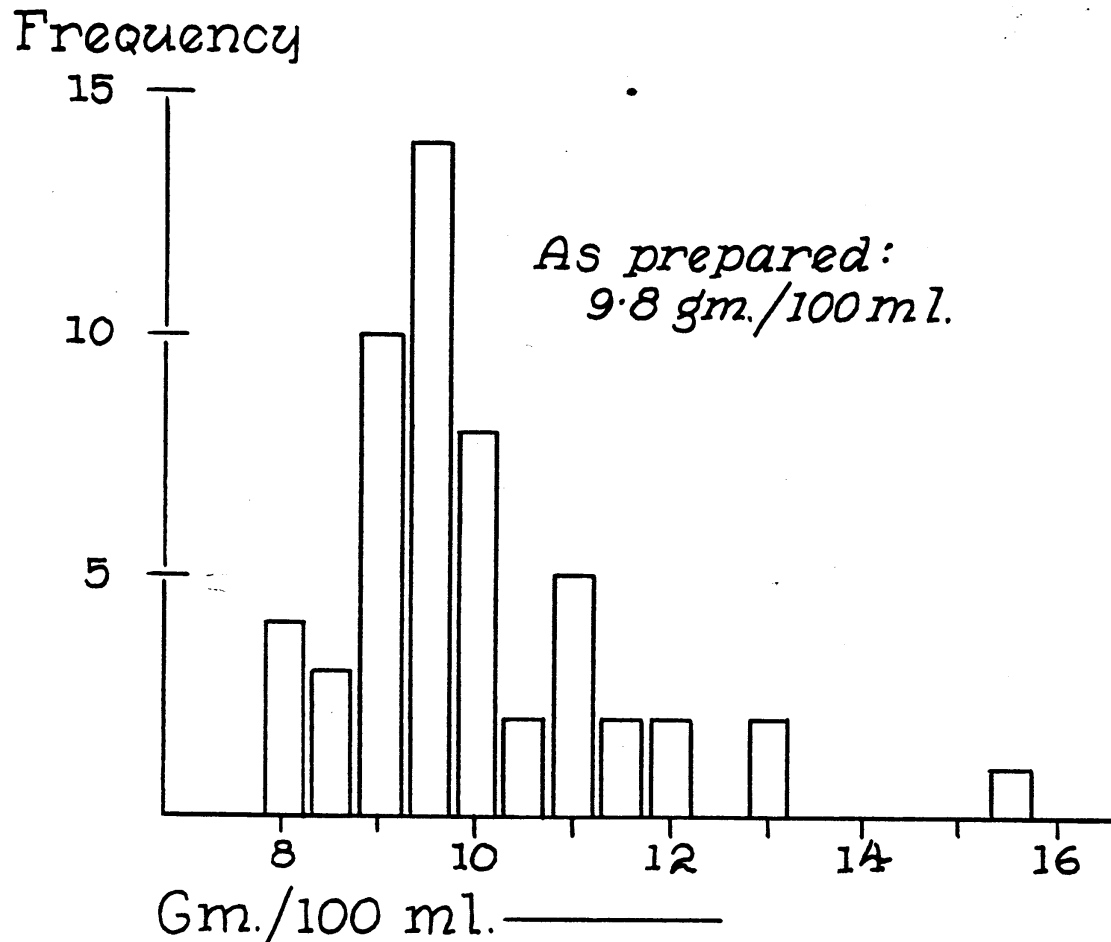
# 2000 Glucose PT Results

CAP Survey C-03 2000 Glucose



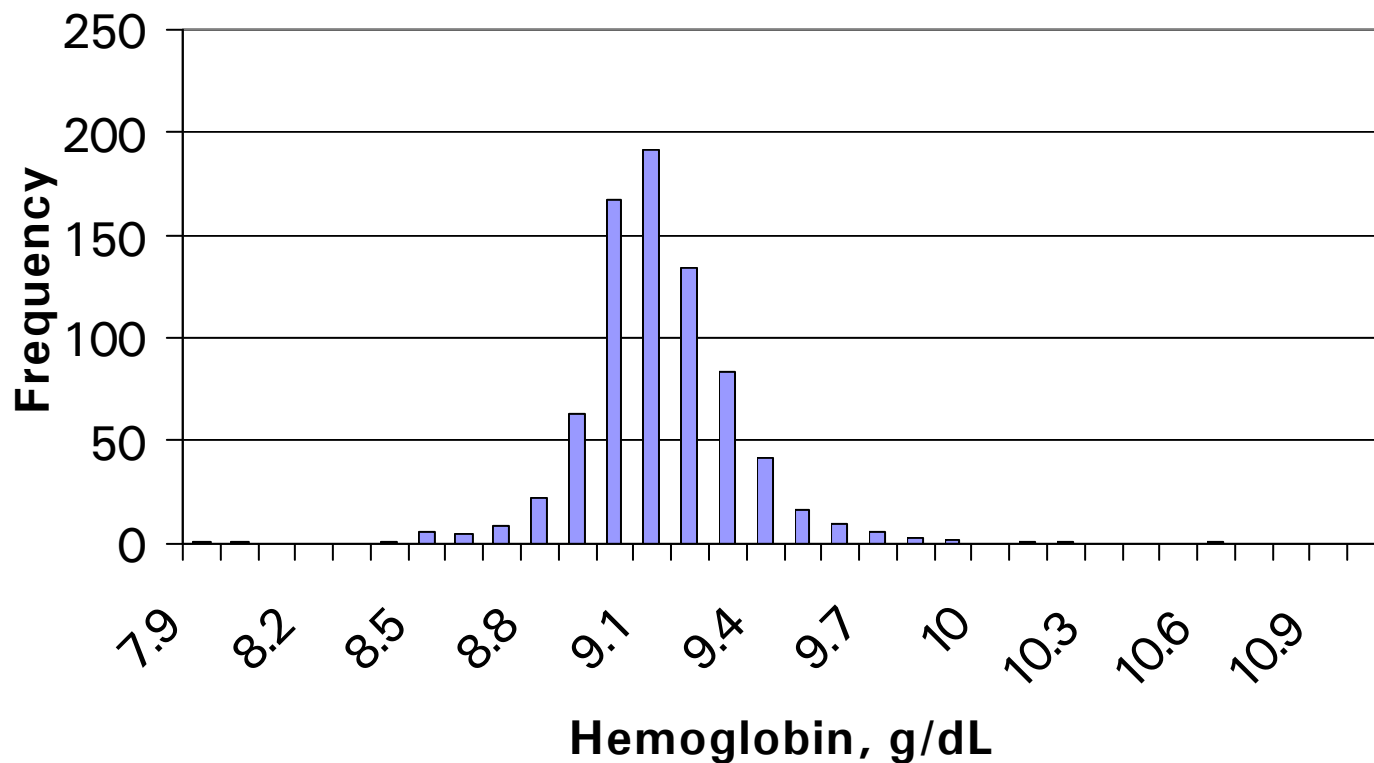
# Hemoglobin Proficiency Testing Results

(Belk and Sunderman. *Am J Clin Pathol* 1947;17:853-61)



# 1999 Hemoglobin PT Results

1999 CAP HE-03 Survey





# **CAP Surveys PT/EQAS Program**

- Evolved from Belk and Sunderman's 59 labs with 24 samples testing performance for 7 measurands distributed in 1947 to >25,000 labs with >250,000 samples testing >500 measurands in 2001
- Liquid, lyophilized, frozen serum, plasma, whole blood, urine, CSF samples sent from 2 to 4 times/yr
- Strengths:
  - Largest clinical laboratory performance data base in the world,
  - Largest variety of measurands of any PT program,
- Weaknesses:
  - Largely uses “peer group” target assignment.

# Evils of “Peer Group” Comparisons

Criticism of the CAP grading approach is not new:

“By encouraging continuation of peer group comparison, we signal an implicit endorsement of methodologies that fail to satisfy fundamental accuracy goals and of laboratories that use them.”

Tietz NW, Rodgerson DO, Laessig RH. *Clin Chem* 1992;38:473-5.

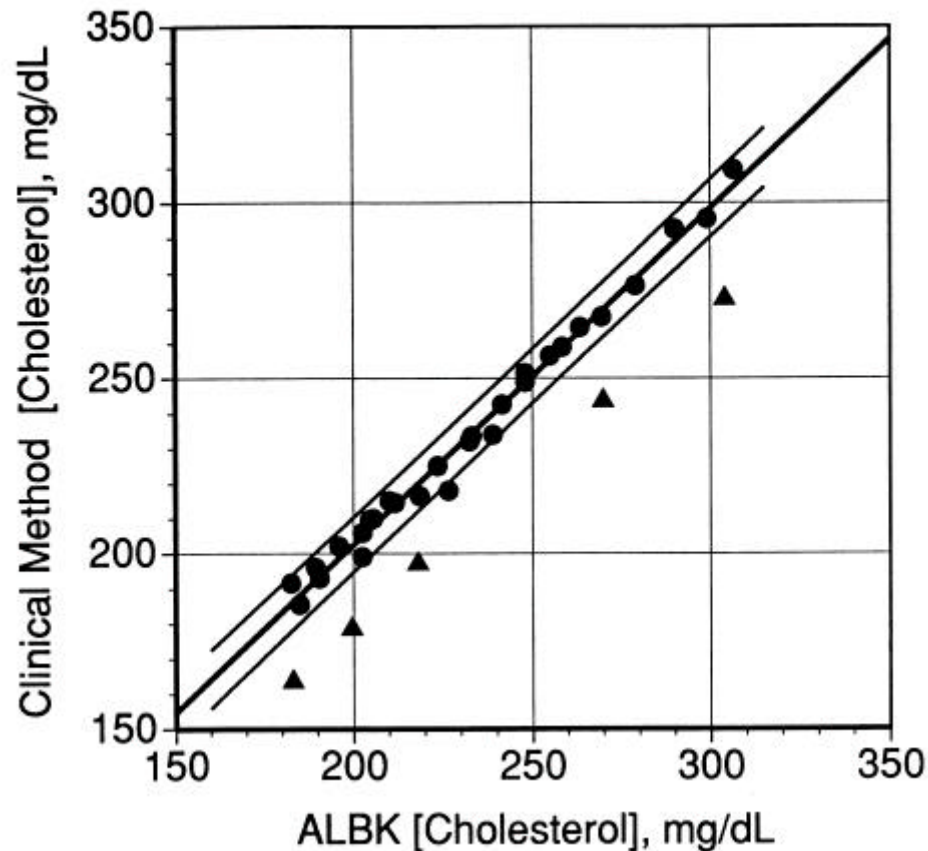
# **Decisions on CAP Grading Policies**

- CAP membership includes >16,000 pathologists, mostly from the USA,
- Governed by a 12-member Board who are mostly anatomic pathologists,
- 24 discipline-specific scientific resource committees (e.g., Chemistry RC, TDM/Endocrinology RC, etc.) which report through the Council for Scientific Affairs to the CAP Board,
- Commission on Laboratory Accreditation oversees the Laboratory Accreditation Program (LAP),
- CAP LAP has “deeming authority” from the US federal government CMS (formerly HCFA) as a provider of laboratory accreditation.

# **Limitations of Stabilized, Processed Reference Materials as “Trueness Controls” and Calibrators**

- **Non-commutable “trueness controls” can lead to erroneous conclusions as to accuracy of a method in a PT/EQAS situation (concern about assigning “failing” grade to labs inappropriately),**
- **Adjustment of instrument calibration to make PT/EQAS materials fall within acceptable ranges has led to poorer, not better, accuracy of patient clinical test results**

Clinical Method vs. Comparative Method Showing  
Linear Regression Line and 95% Confidence Limits



● = patient  
serum  
samples

▲ = CAP  
Survey  
samples

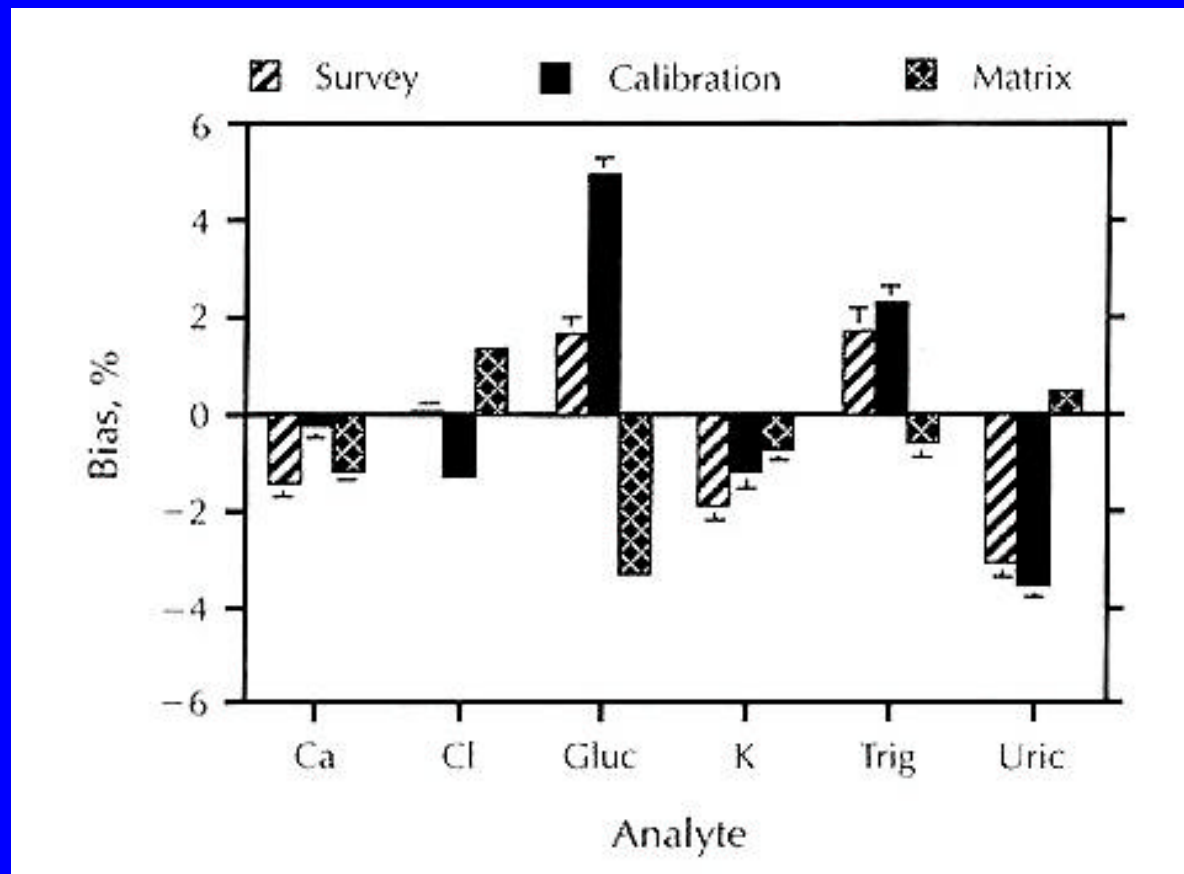
Eckfeldt and Copeland. *Arch Pathol Lab Med* 1993;117:381-6.

# **CAP Chemistry Resource Committee**

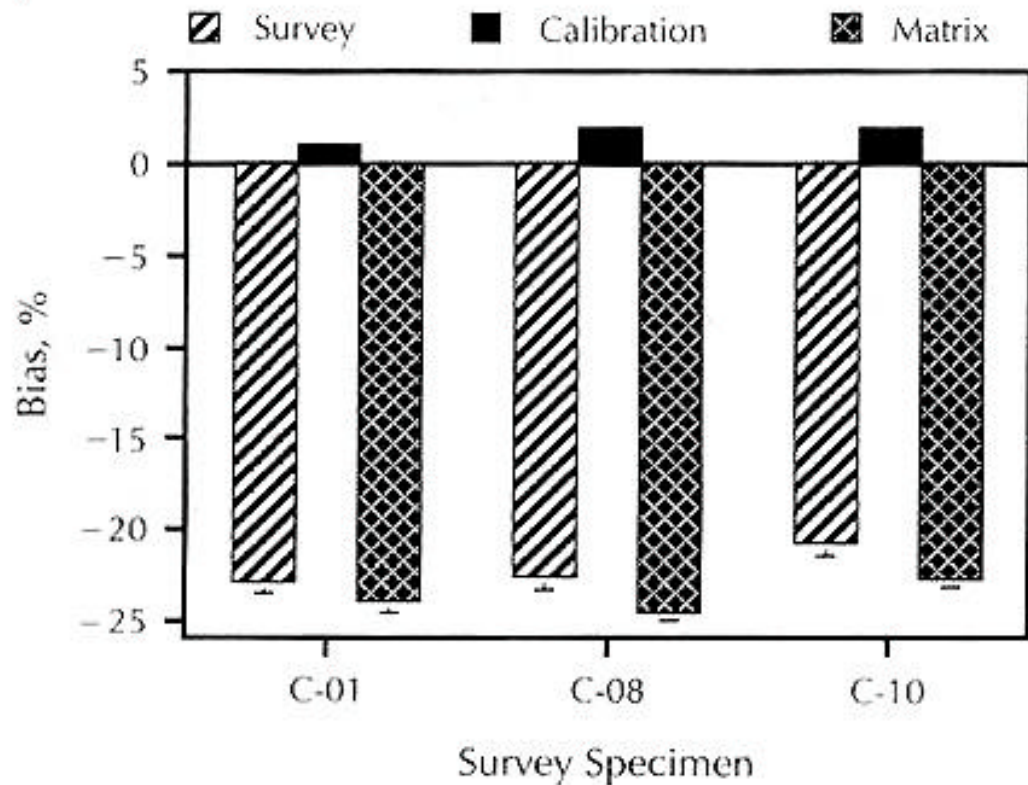
## **Fresh Frozen Serum (FFS) Survey**

- Fresh frozen serum (FFS) pool sent to 700 clinical labs selected to be using one of 14 “methods” at the same time they were testing CAP Survey samples on two different occasions during 1994,
- Eleven measurands analyzed in triplicate in the FFS sample and in the ten regular CAP Survey samples,
- For each measurand and each method, a “calibration bias” computed from the FFS mean, a “Survey bias” from each Survey sample’s mean, and by difference a “matrix bias.”

(Ross JW, et al. *Arch Pathol Lab Med* 1998;122:587-608.)

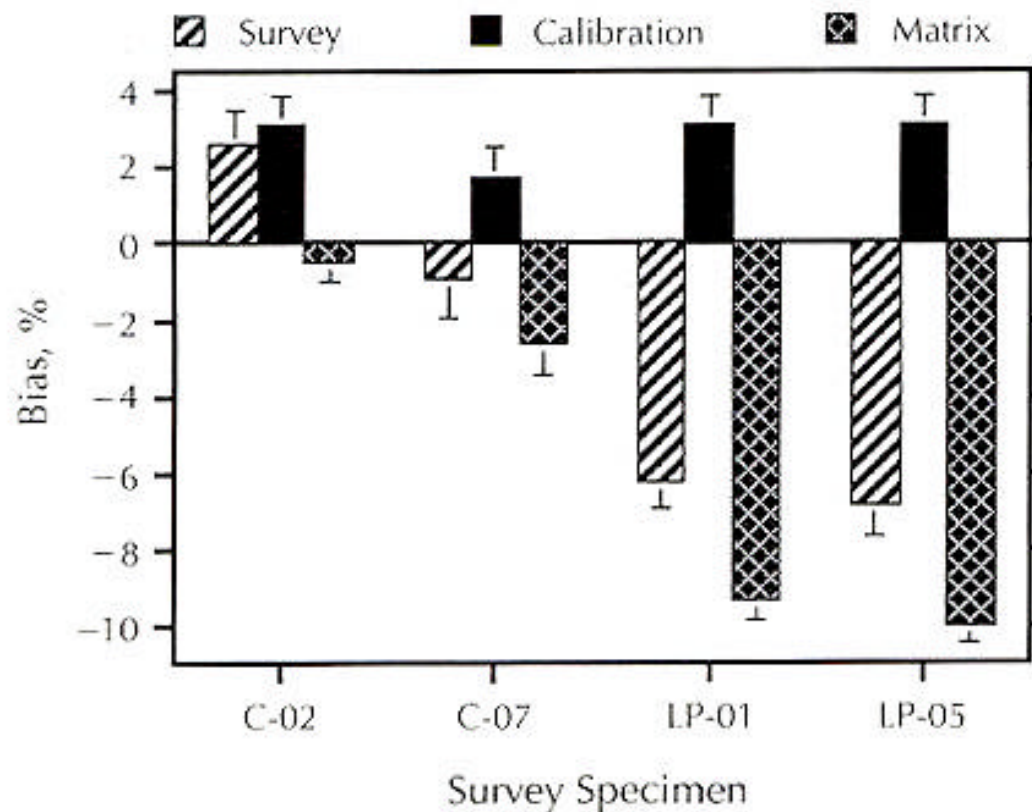


**Figure 2. Kodak Ektachem 400/700 analyzers' Survey, calibration and matrix biases for C-01 from Ross JW, et al. *Arch Pathol Lab Med* 1998; 122:587-608.**



**Figure 6. Beckman CX 4, 5, 7 analyzers' uric acid Survey, calibration, and matrix biases from Ross JW, et al. *Arch Pathol Lab Med* 1998; 122:587-608.**





**Figure 5. Beckman CX4, 5, 7 analyzers' cholesterol Survey, calibration, and matrix biases from Ross JW, et al. *Arch Pathol Lab Med* 1998; 122:587-608.**

## **CAP FFS Study Limitations**

- **Matrix biases only apply to material used in 1994 (lyophilized processed human plasma),**
- **Only 11 HCFA-regulated measurands examined,**
- **CAP Chemistry Survey material changed to a liquid-based processed human plasma in 1998, eliminating any ability to predict matrix biases,**
- **The study cost ~US\$150,000 making CAP's Board very hesitant to approve any new matrix study,**
- **CAP's participating labs, IVD manufacturers and many others have trouble understanding matrix effect and full implications of the FFS Study.**

# **NHLBI/CDC NCEP Lipid Standardization Program (LSP)**

- **Early recognition of the shortcomings of lyophilized materials as calibrator and PT/EQAS materials,**
- **Frozen serum pools and fresh patient sample comparisons used for accuracy transfer,**
- **Manufacturers and clinical laboratory certification based on sound statistical principles,**
- **Shortcoming--expensive and time consuming,**
- **Led to development of a NCCLS/CAP/NIST frozen-serum reference material for lipids (chol, triglyceride, HDL-chol, LDL-chol) for IVD manufacturers to calibrate their methods better.**

# **Reference Method Target Value Grading--Unintended Consequences**

- Chemistry Resource Committee elected to grade glucose based on a single target value in ~ 1993,
- Glucose CLIA limits are “target value” +/- 10%,
- One major IVD manufacturer marketing executive felt their method was being unfairly penalized and urged all US customers to drop use of CAP Surveys,
- This in turn led to a letter from the President of CAP to the company’s CEO suggesting a more constructive approach to accuracy improvement,
- Nevertheless, most CMS-regulated measurand grading was changed to “peer-group” targets by CAP resource committees in ~ 1998

# **Further Developments in CAP Grading Criteria**

- **Chemistry Resource Committee elected to produce two grades ~ 2000,**
  - **“Regulatory grade” based on peer group target values**
  - **“Educational grade” based on reference method target values**
- **Only the regulatory grade sent to regulatory bodies (federal and/or state)**
- **Educational grades were dropped by most CAP resource committees in early 2002 because some regulators began penalizing labs for “out of limit” educational grades.**

# Summary

- There has been a huge improvement in laboratory test accuracy over the past half century,
- CAP through the expertise in clinical laboratory testing of its scientific resource committees (e.g., Chemistry, TDM/Endocrinology, and many other committees) made up of pathologists and other highly knowledgeable laboratory scientists has been a leader in these efforts,
- Though costly and time consuming, reference method-established target values have been tried on several occasions by CAP only to be abandoned,

## **Summary (continued)**

- **Most of CAP's scientific resource committee members believe that use of reference method-established target values on processed, stabilized plasma products do not assess accuracy on patient samples for many measurands and are thereby inherently unfair and inappropriate,**
- **Matrix effects need to be understood for any PT/EQAS materials before using reference method-established target value for clinical laboratory performance grading,**
- **A new CAP FFS project is planned for spring 2003 and will include all routine chemistry, TDM, and endocrinology measurands (CAP's C, K and Y Surveys) and all participants (2,000 to 7,000 labs).**