

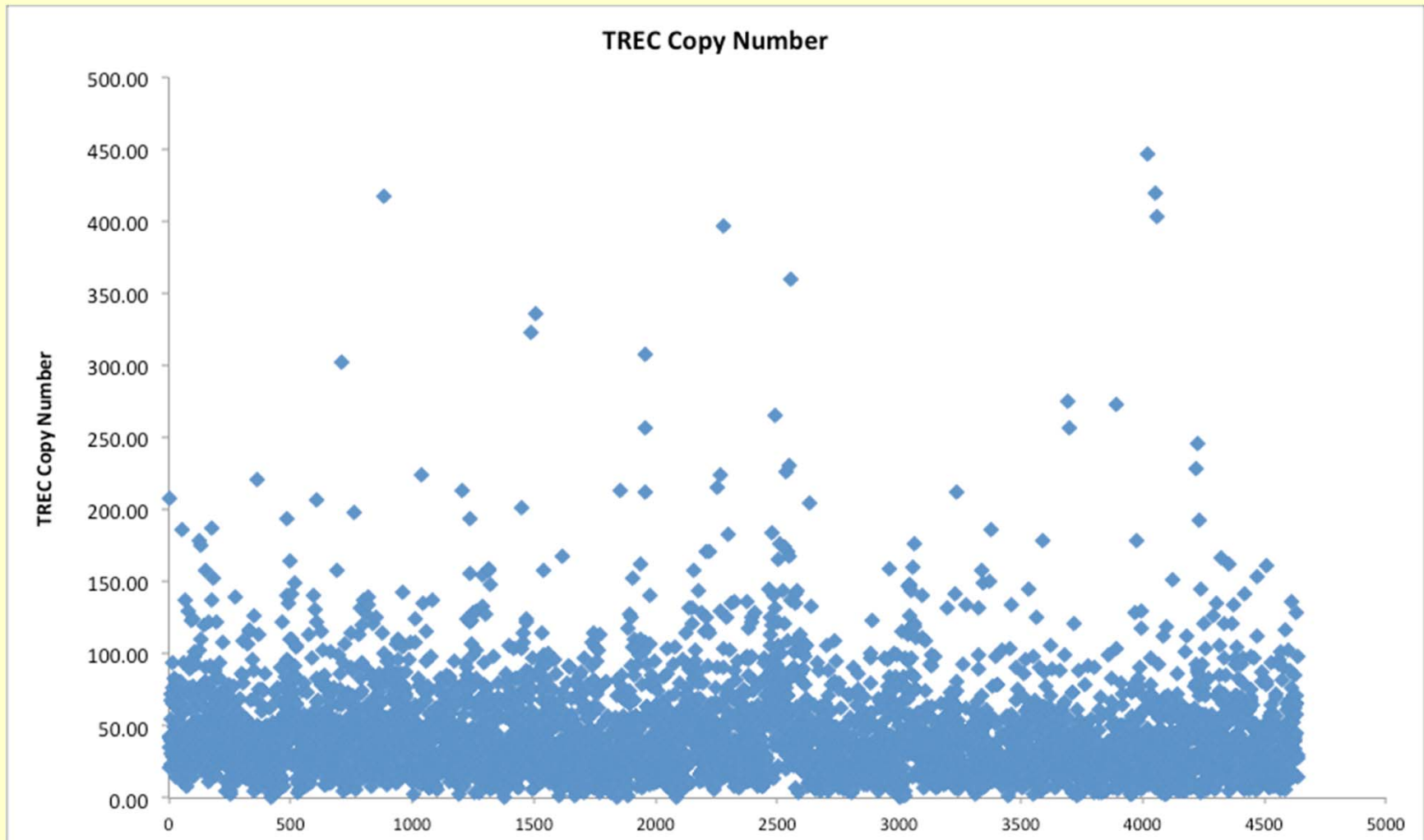


# Using Multiples of the Median (MoM) for Normalization of TREC Results Meets the Need for Standardized SCID Reporting

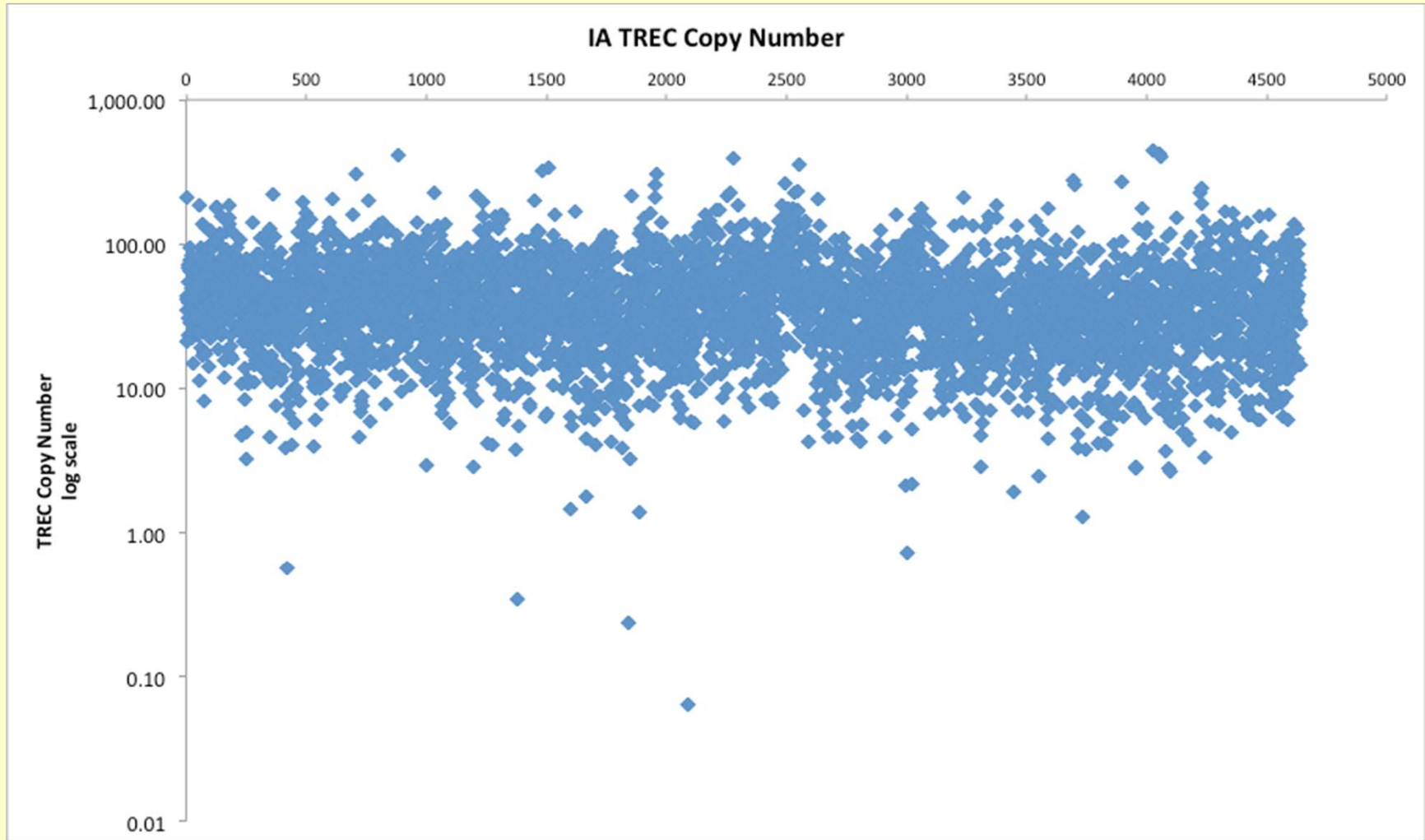
2013 Joint Meeting of the  
Newborn Screening and Genetic Testing Symposium  
and the  
International Society for Neonatal Screening  
May 5-10, 2013  
Atlanta, GA

Stanton L. Berberich, PhD  
State Hygienic Laboratory at the University of Iowa

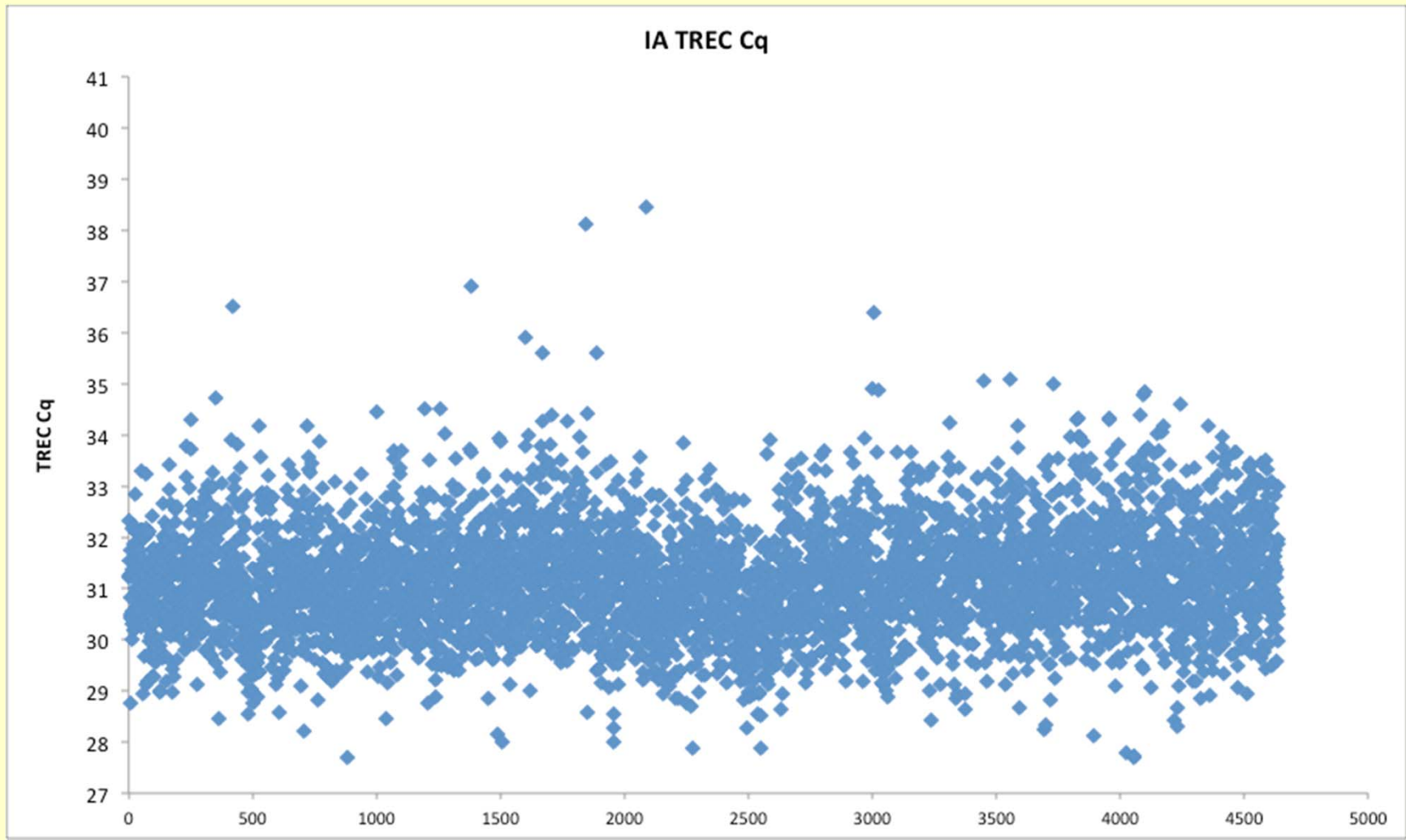
# Distribution by TREC Copy #



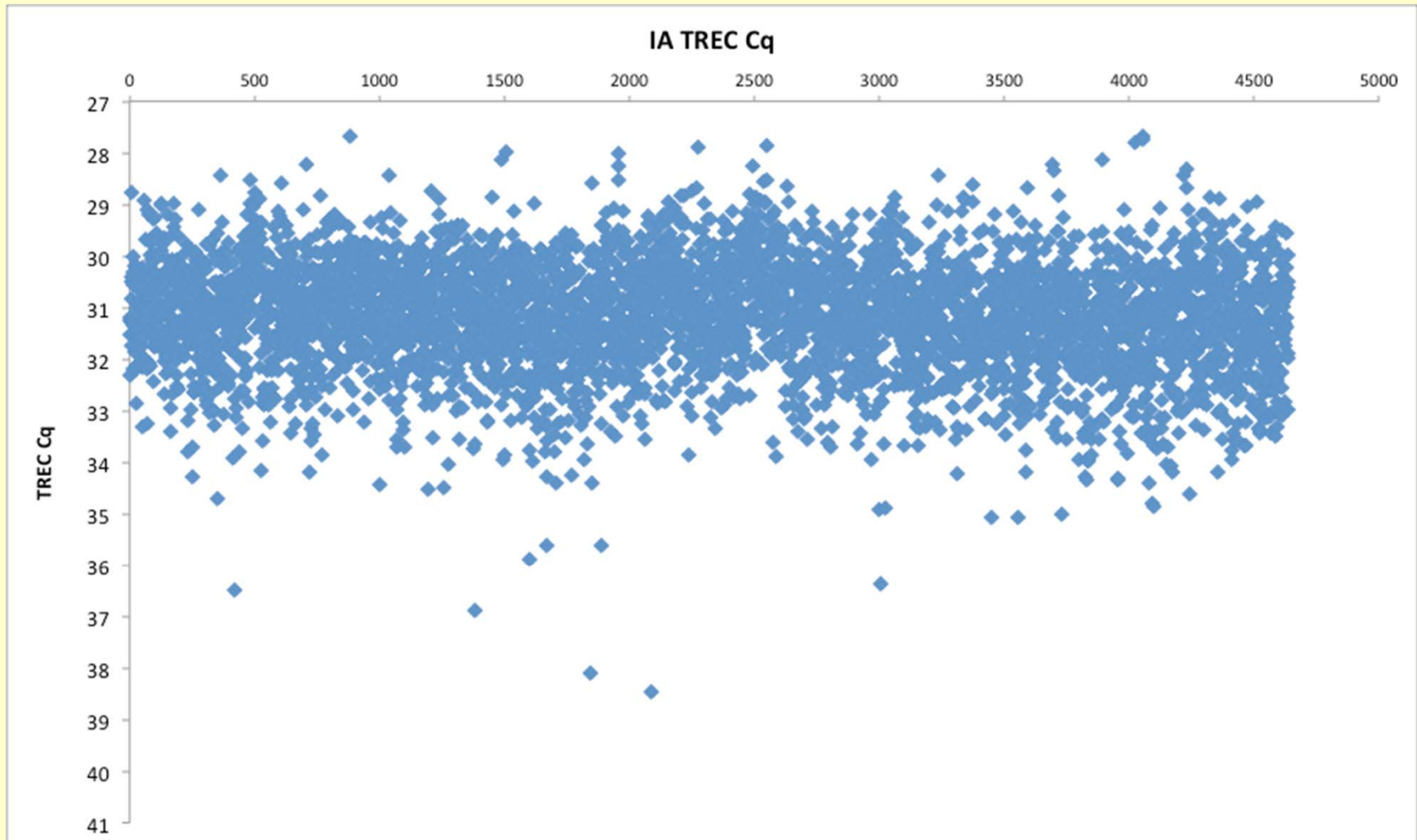
# Distribution by TREC Copy # (log scale)



# Distribution by TREC Cq

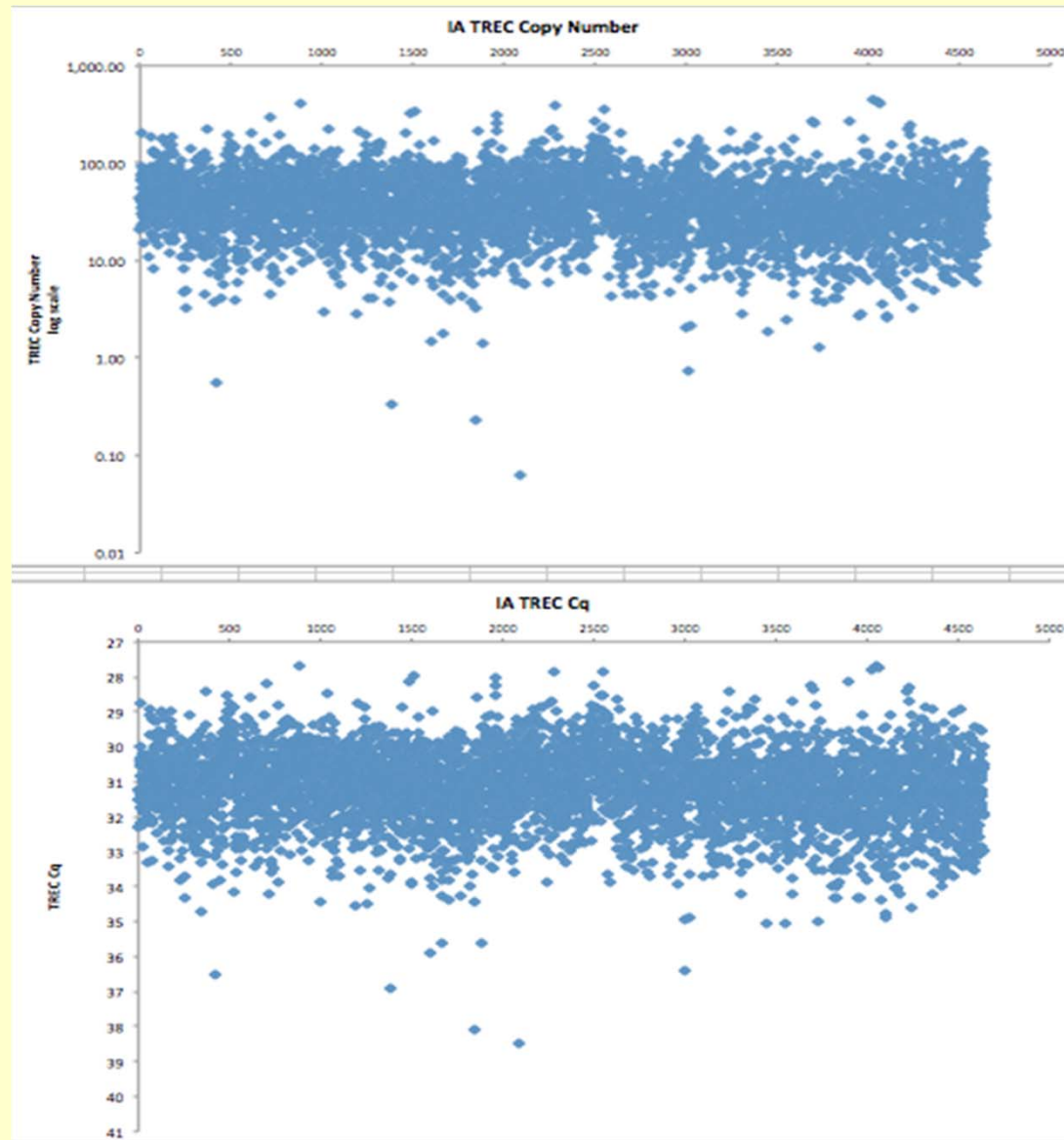


# Distribution by TREC Cq (Reverse Order)



# TREC Copy # (log scale)

## TREC Cq (reverse order)



# What is Public Health Medical Screening?

Screening is the **systematic** application of a test or **inquiry**, to identify individuals at sufficient risk of a **specific disorder** to **benefit** from further investigation or direct preventive action, among persons **who have not sought medical attention on account of symptoms of that disorder.**

*J Med Screen 1994 1:1*

# What is Public Health Medical Screening?

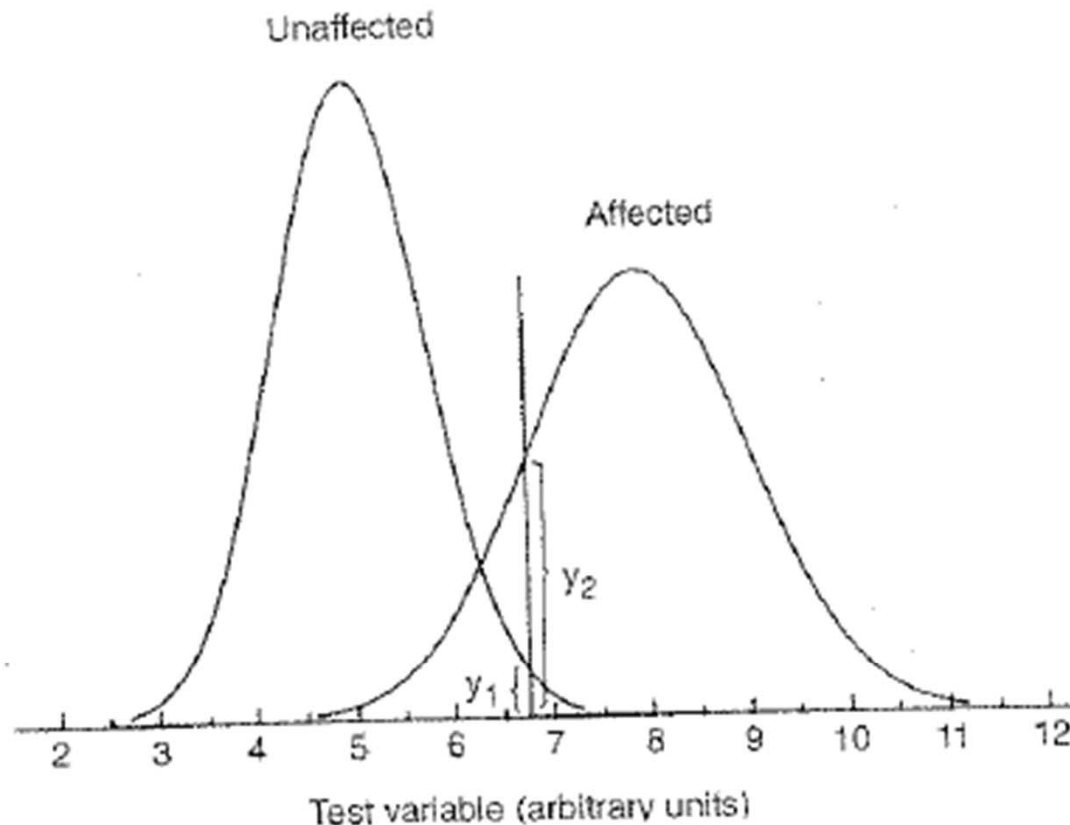
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*J Med Screen* 1994 1:1

- Screening is to assess risk.
- Screening differs from diagnostic testing in that, there is no intention to make a diagnosis of a medical disorder.



# Odds of Being Affected given a Specific Result



**Fig. 1.3** Hypothetical relative frequency distribution of a screening test variable in affected and unaffected individuals. The likelihood ratio ( $y_2/y_1$ ) for being affected at exactly 6.75 units is 5.4.

# Multiples of the [Normal] Median

“Multiples of the [normal population] Median” (MoM) was first proposed for the reporting of serum AFP levels by N. J. Wald and H. Cuckle in the “Report of U. K. Collaborative Study on Alpha-fetoprotein in Relation to Neural-tube Defects” published in Lancet in 1977.

Measurements of AFP can be affected by laboratory technique, resulting in difficulty comparing absolute results between laboratories; therefore, Multiples of the Median (MoM) was used as a method to normalize data from participating laboratories so that individual test results could be compared.

35 years later it is the established standard for reporting maternal serum screening results.

# Multiples of the [Normal] Median

The MEDIAN is the MIDDLE value when the values are arranged in order; therefore the median is not influenced by outlying values.

1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 [6 is the median]

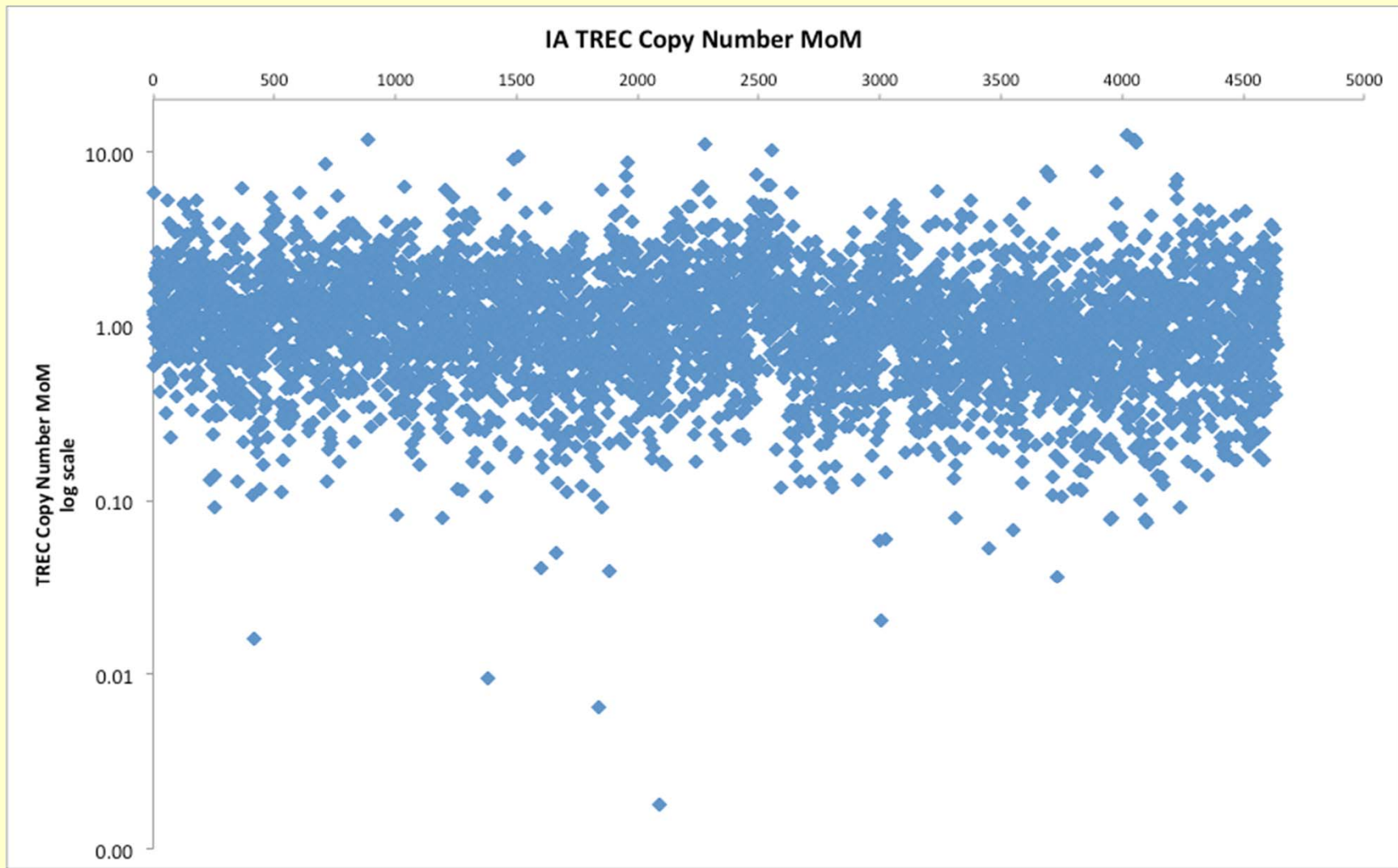
1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 5000 [6 is still the median]

Patient MoM = Patient result / Population Median

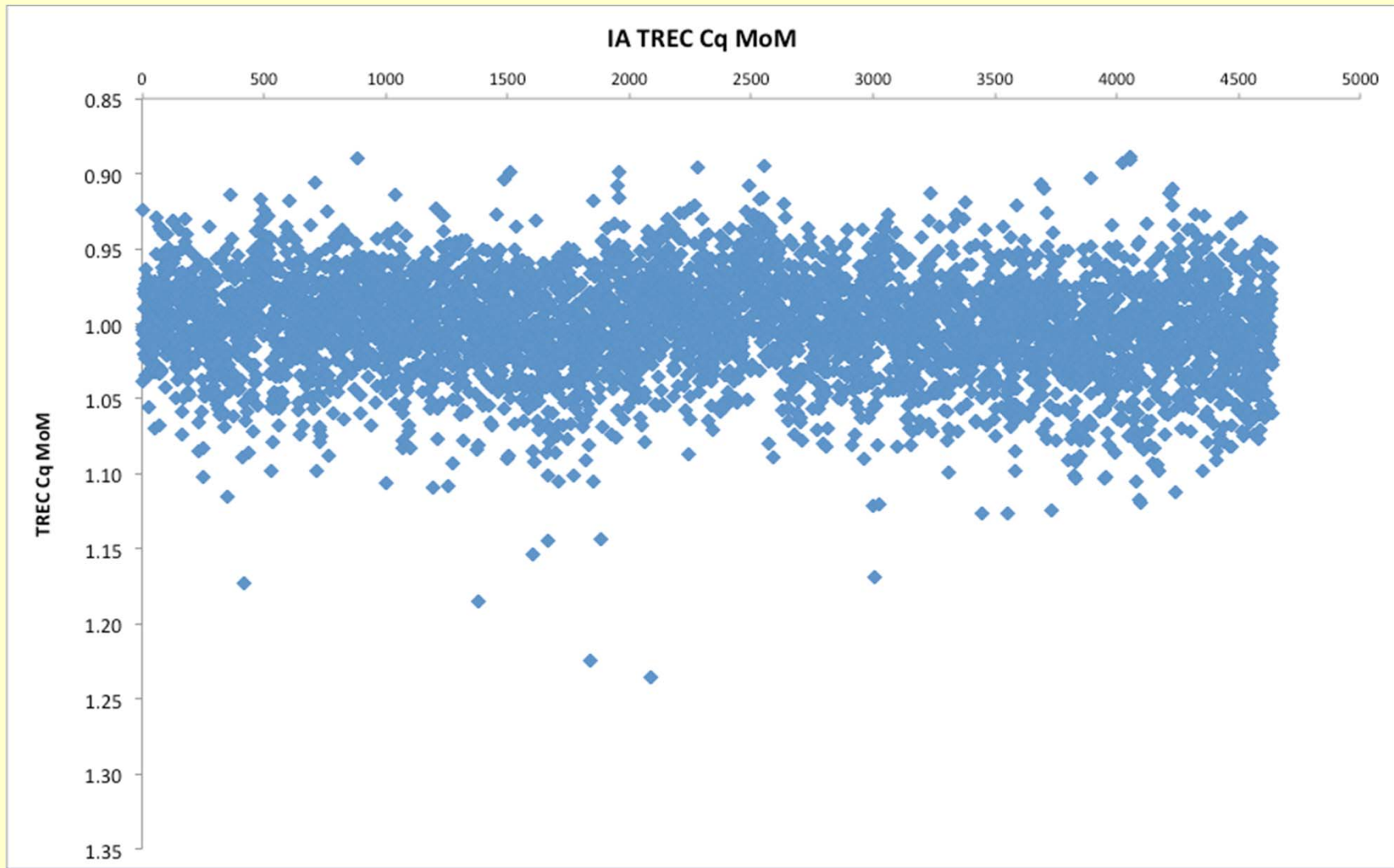
Multiples of the Median are more convenient to use than percentiles; they are easier to derive and more stable.

Each laboratory must establish its own reference data, and determine the median value for its population.

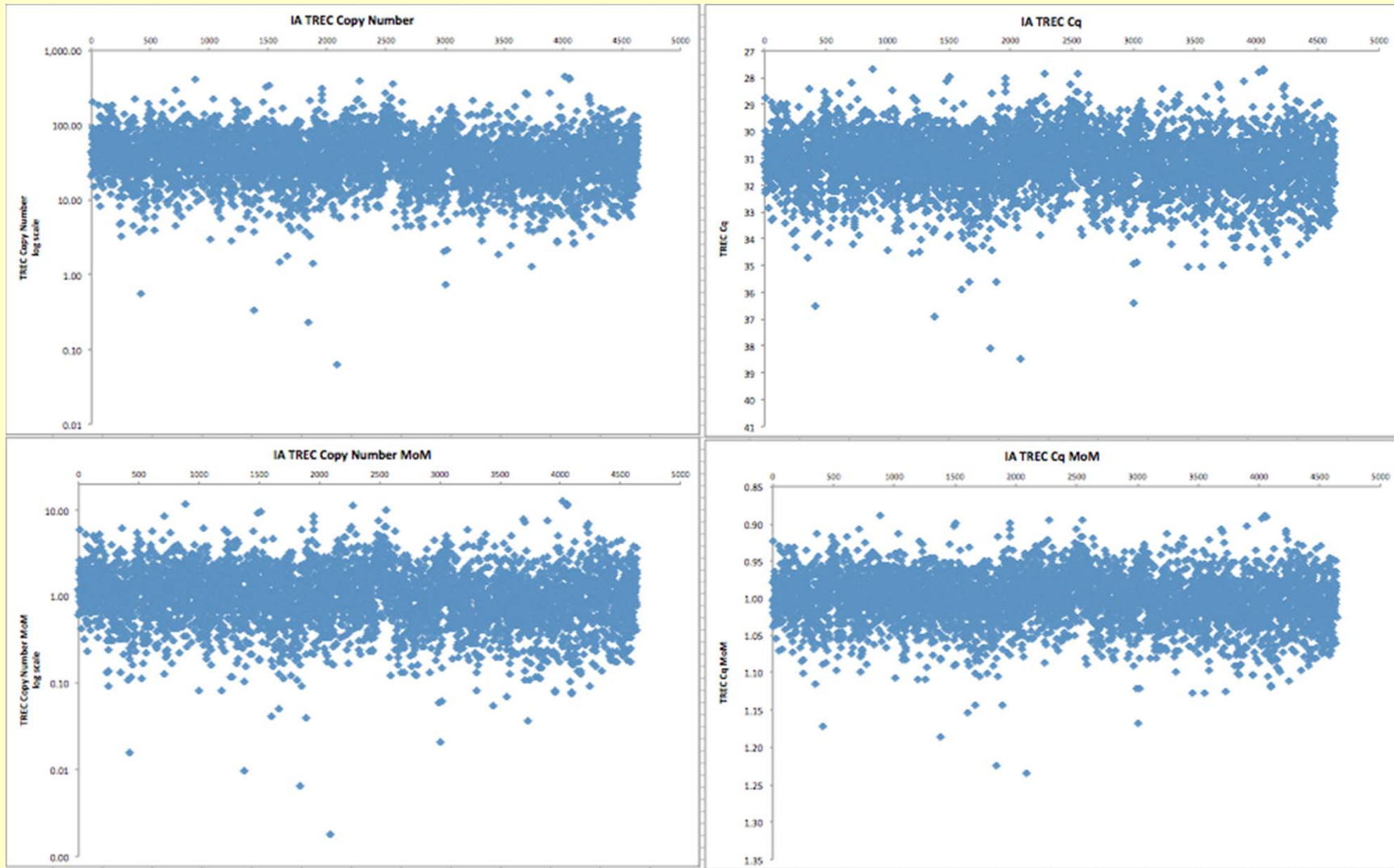
# Distribution by MoM TREC Copy # (log scale)



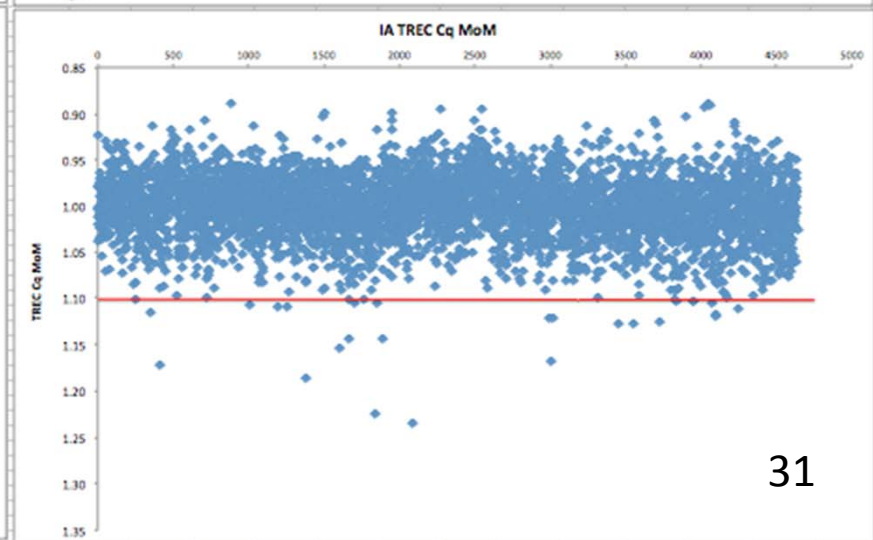
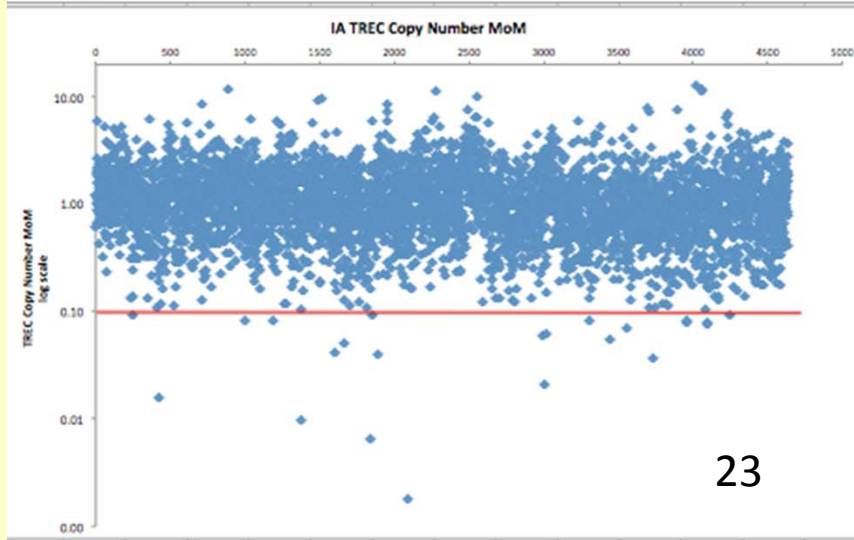
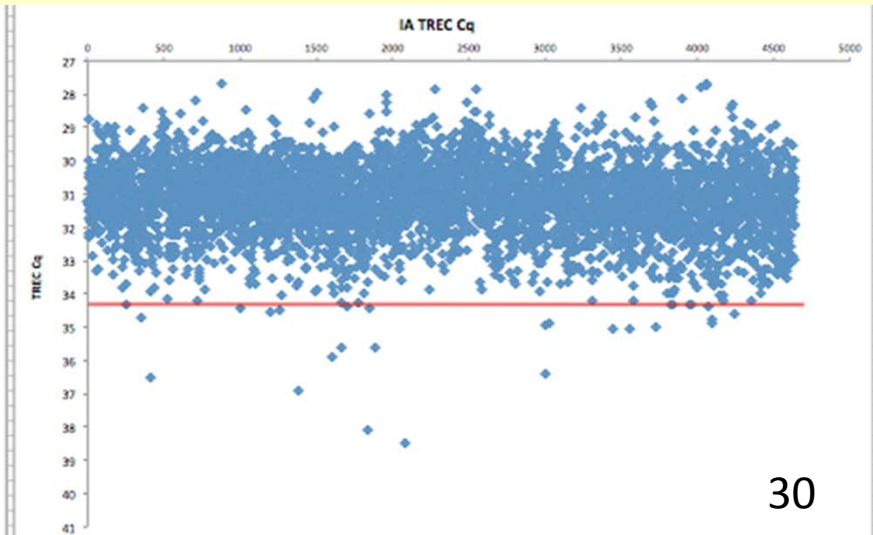
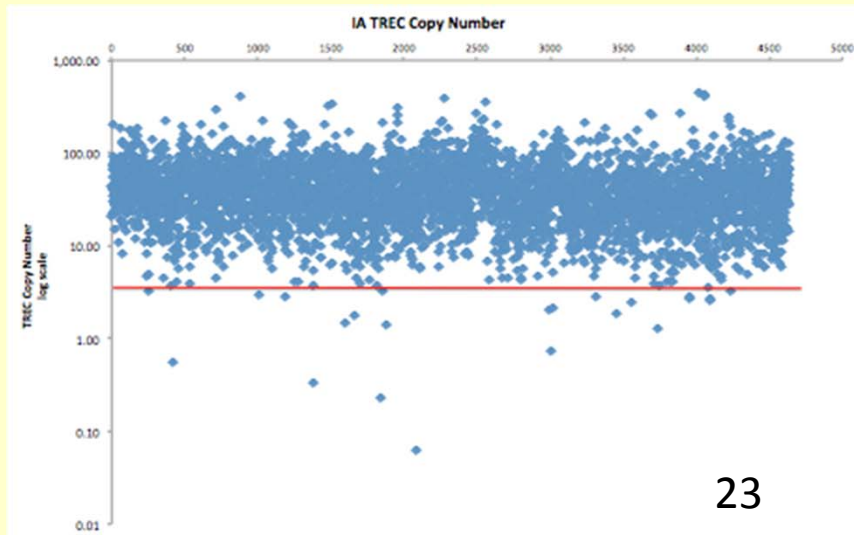
# Distribution by MoM TREC Cq (Reverse order)



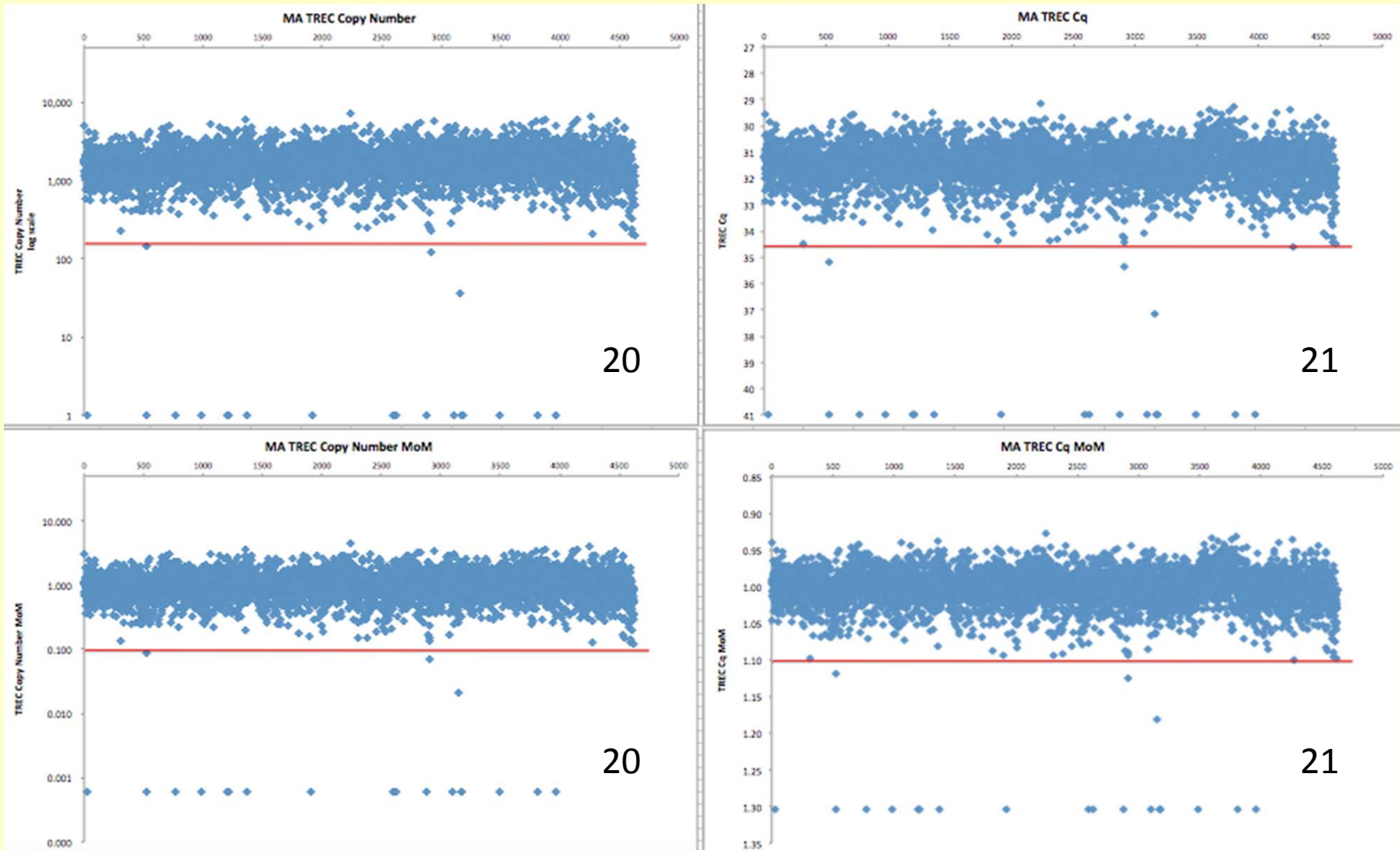
Copy # (log scale) | Cq (Reverse order)  
MoM Copy # (log) | MoM Cq (Reverse)



# IA: Line at 10% of Population Median

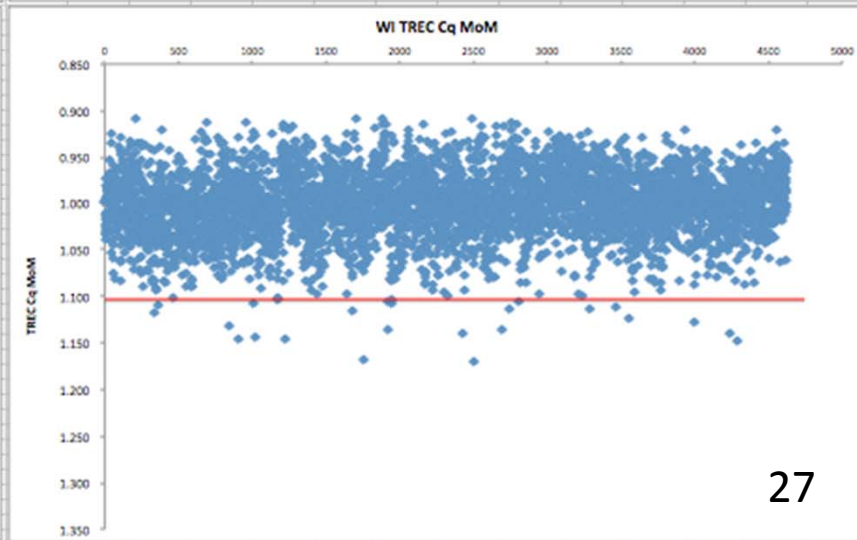
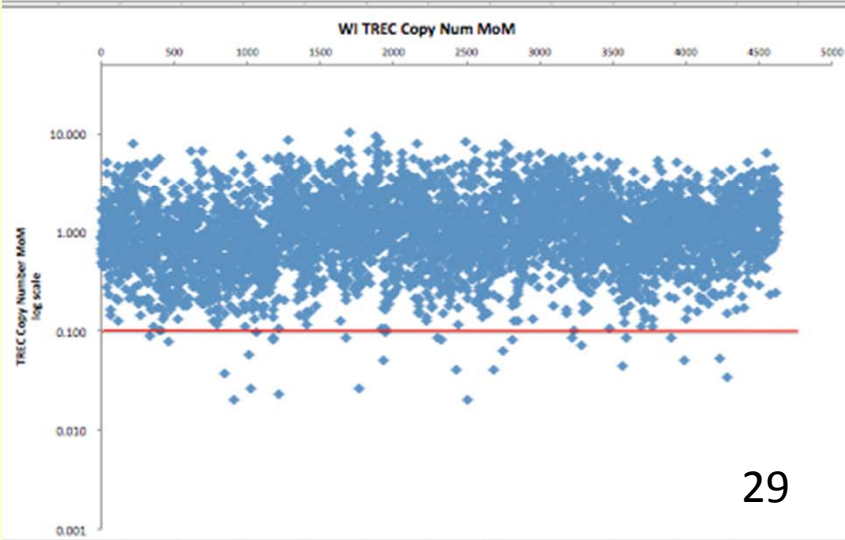
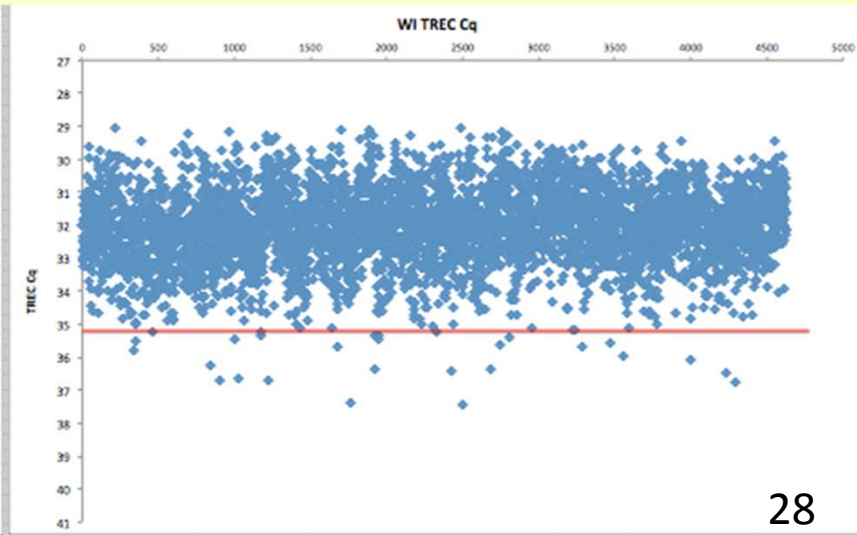
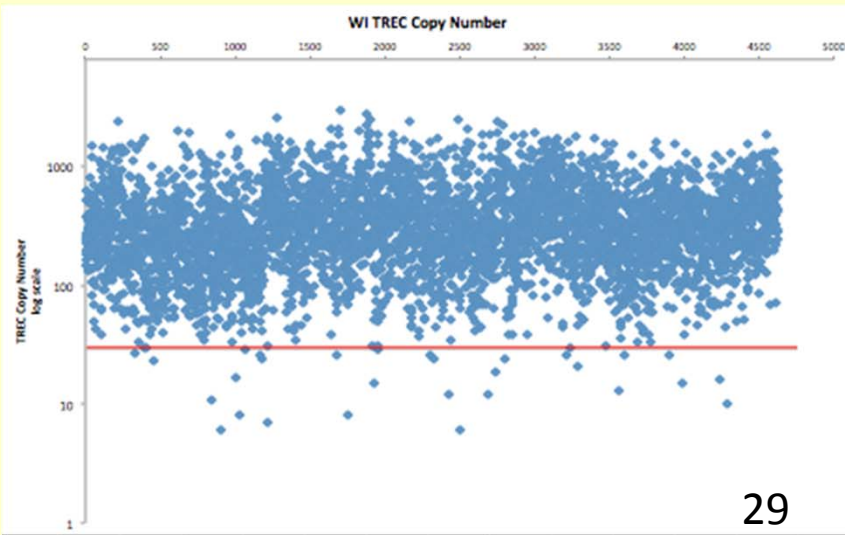


# MA: Line at 10% of Population Median

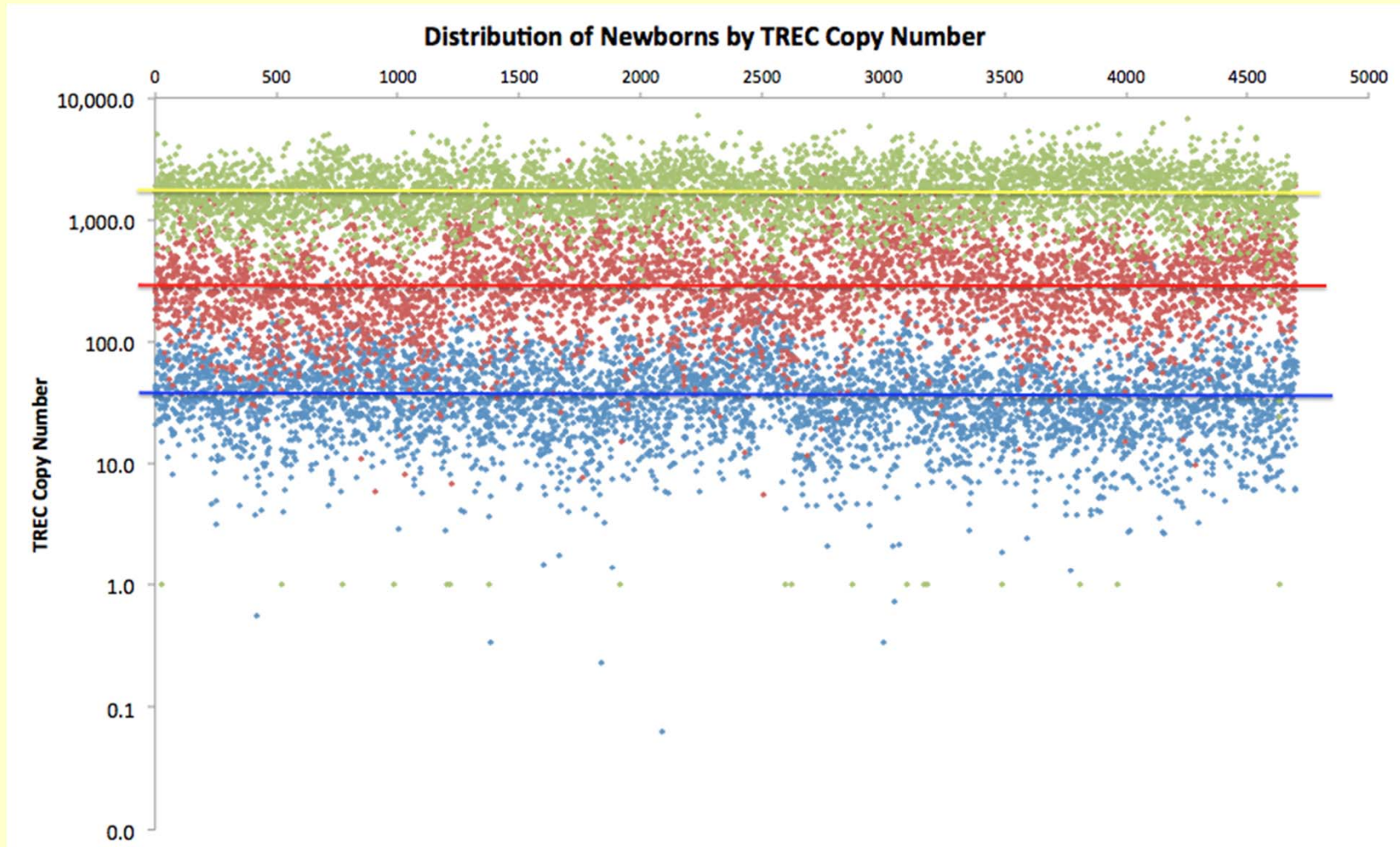




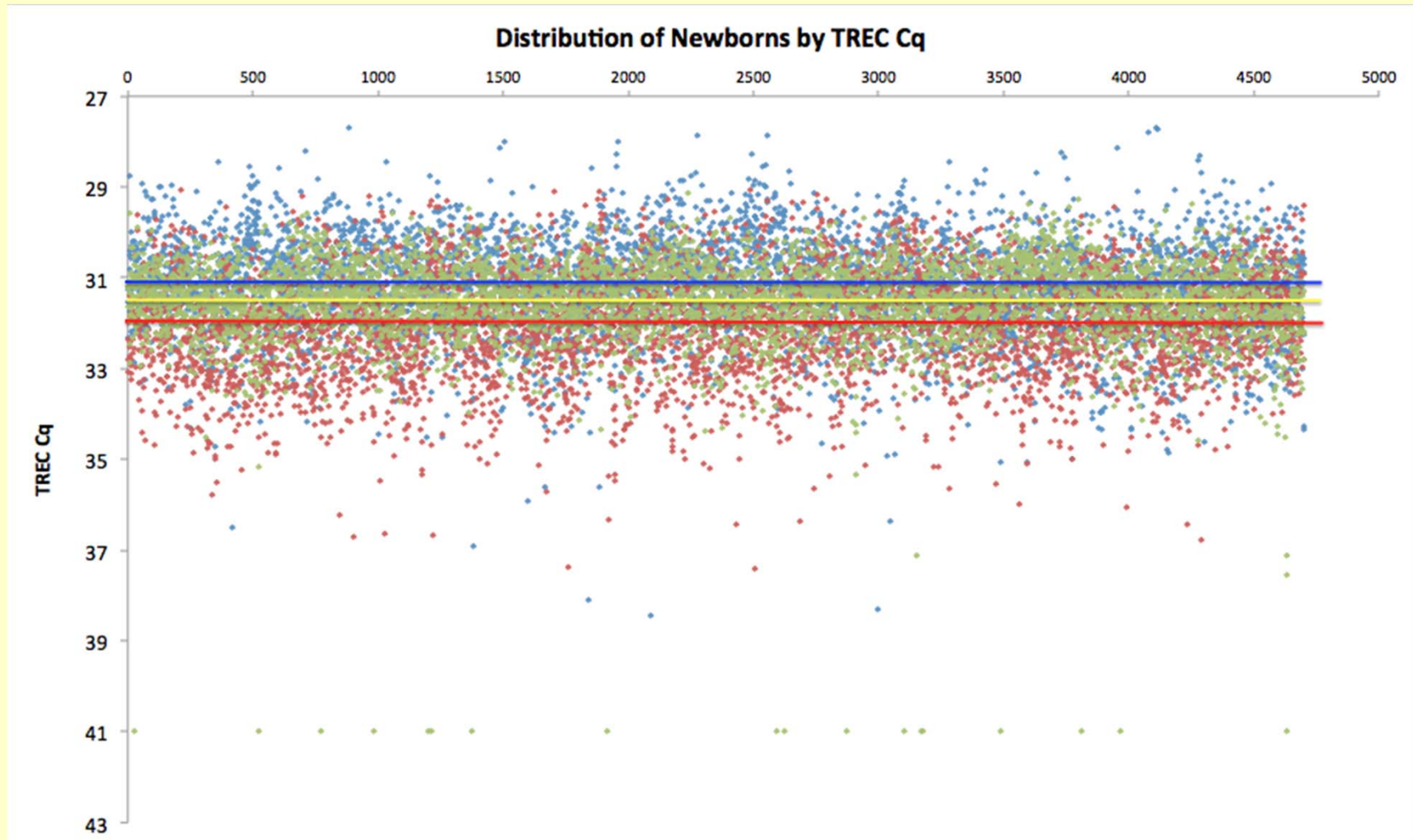
# WI: Line at 10% of Population Median



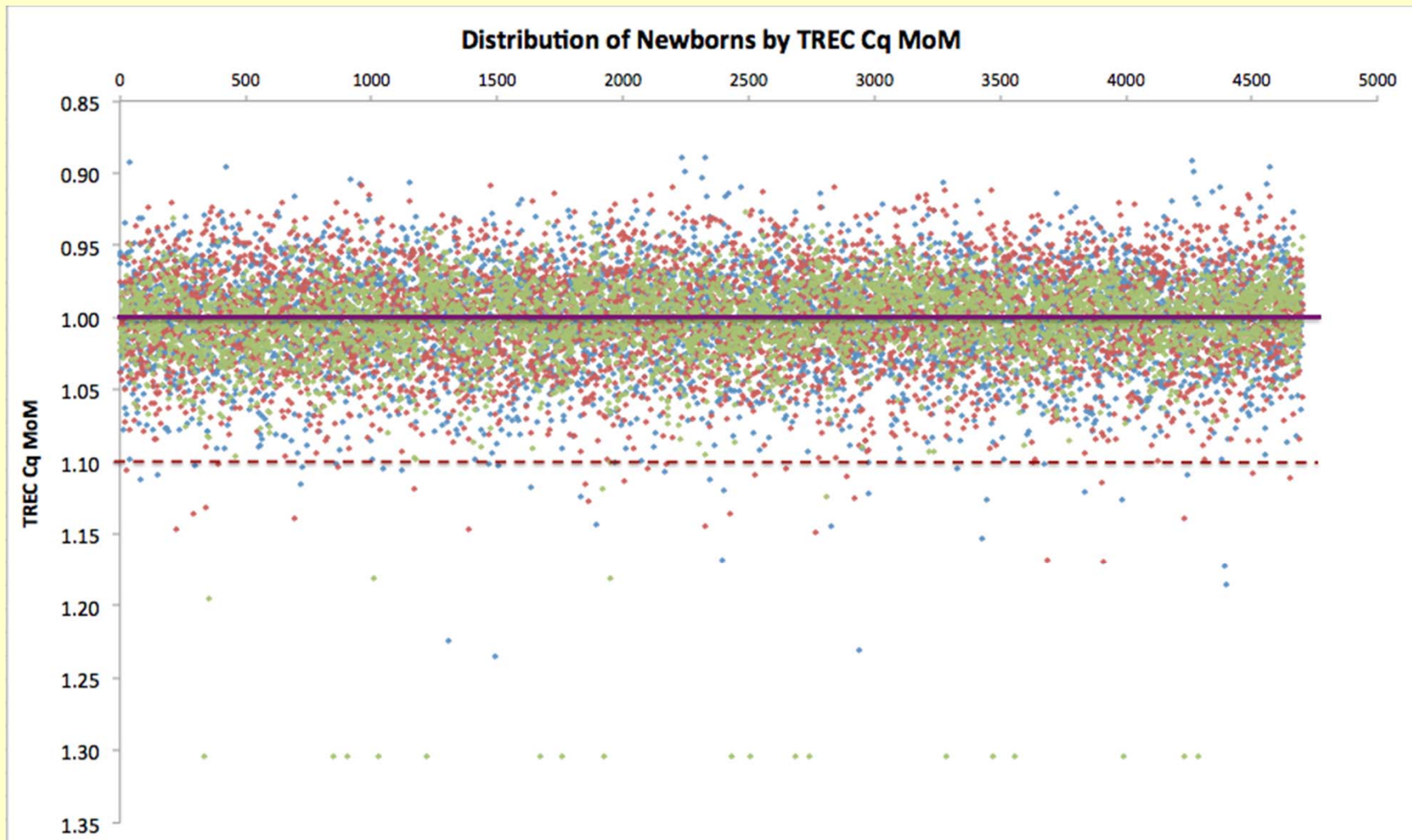
# 3 States by TREC Copy #



# 3 States by TREC Cq



# 3 States by MoM TREC Cq



IA: 31 (0.7%)

WI: 27 (0.6%)

MA: 21 (0.5%)

# Conclusions

- Individual TREC results expressed as Multiples of the TREC Cq Median (TREC Cq MoM) can be used as the screening variable for SCID screening.
- Multiples of the Median (MoM) can be used as a method to normalize TREC assay data from different laboratories so that individual test results can be compared.
- Multiples of the Median (MoM) may be a method to normalize test results for other NBS assays so that individual test results from different laboratories can be compared.

# Acknowledgements

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2005



2008





2010



2012

