



Integration of reference materials into the production process of A β 1-42 assays.

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The goals

- From a 'Relative' quantitative assay to a 'Definitive' quantitative assay.
- Generation of Universal cut-off values

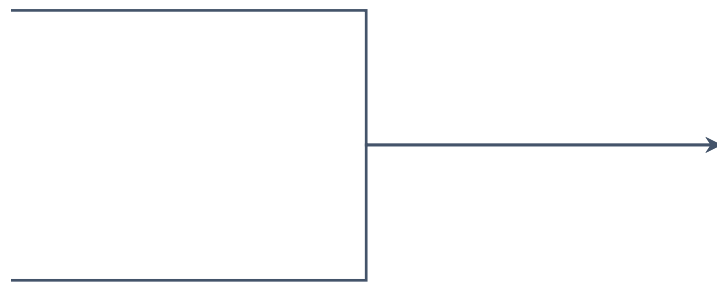


The presence

- Approved reference methods (*Mass Spec*)
- New generation of immunoassays

The future

- Supply of reference materials (*neat CSF*)



The need
Re-calibration of assays



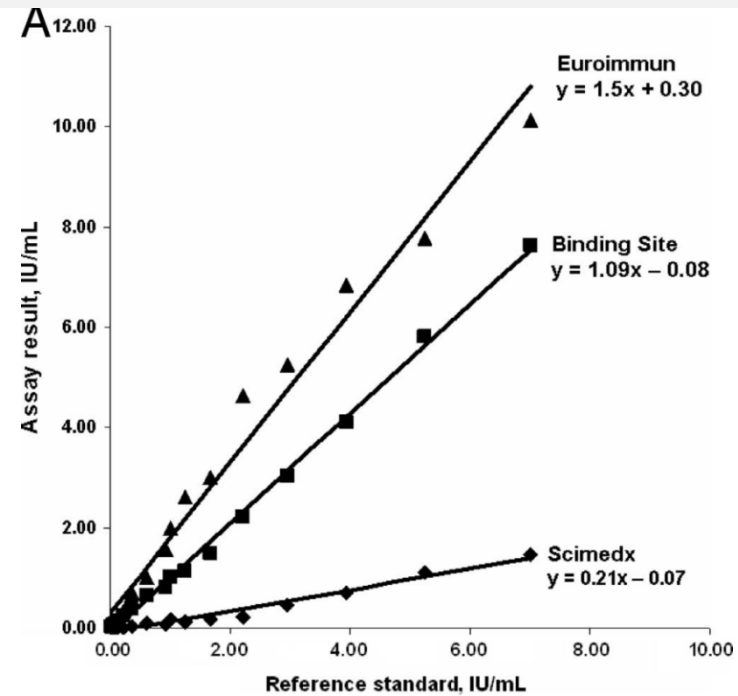


IRM (International Reference Material)

Examples of other biomarker proteins

Biomarker Examples
Parathormone
Vitamine D
Calcitonine
Tetanus toxine
TSH
Diphtherie
...

? Do you have the Reference for this figure



Availability of IRM does not always result in identical values using different assays.
Better approach for integration needed?



From IRM to re-calibrated assays: the approach for Aβ(1-42)

Fact: approved reference method



IRM
Certified reference standard(s)
Sample type Neat CSF (<i>n=3; H/M/L</i>)
Risks adsorption to recipients homogeneity stability
To be controlled Temperature, freeze/thaw

Assay
Technology
Antibodies
Calibrator
Buffer
Test protocol
Performance (analytical)

The process
Direct
Indirect



From IRM to re-calibrated assays: the approach for Aβ(1-42)

Fact: approved reference method → Robustness ? Precision ?

Release time ?

IRM
Certified reference standard(s)
Sample type Neat CSF (n=3; H/M/L)
Risks adsorption to recipients homogeneity stability
To be controlled Temperature, freeze/thaw

Revised SOP
Collection & Storage

Assay
Technology
Antibodies
Calibrator
Buffer
Test protocol
Performance (analytical)

New Generation

The process
Direct
Indirect

SOP
IRM integration



External
Quality Control

AA QC
Instand
Other ?



**Sample
preparation**

**Value
assignment**



Certified Reference Materials

CSF
(H, M, L)

**Sample
preparation**

**Value
assignment**



Certified Reference Materials

More **(CRM)** samples
(proportional linearity)

CSF
(H, M, L)

**Sample
preparation**

Lob tubes

Reference CSF
Calibrator series

**Value
assignment**





Certified Reference Materials

Prepare internal **CSF series**
(*neat*, > 30)



Aliquotation & Freezing



CSF Series
(Internal)

CSF
(H, M, L)

**Sample
preparation**

**Value
assignment**



Certified Reference Materials

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Aliquotation & Freezing



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Reference CSF



CSF
(H, M, L)

**Sample
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CSF Series
(Internal)

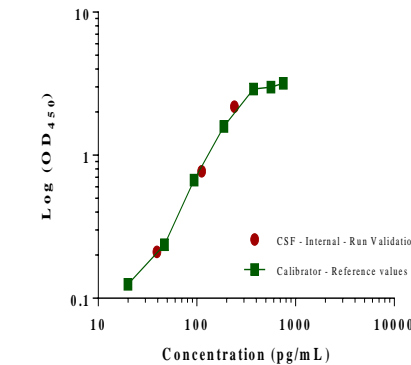
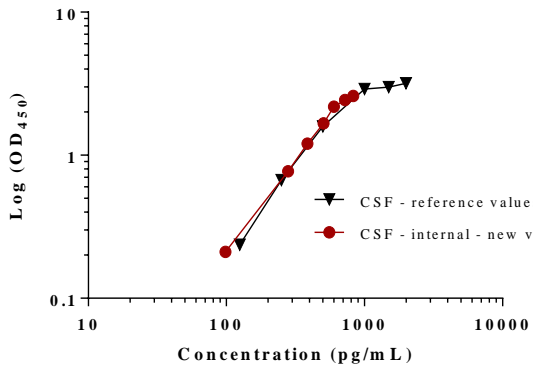
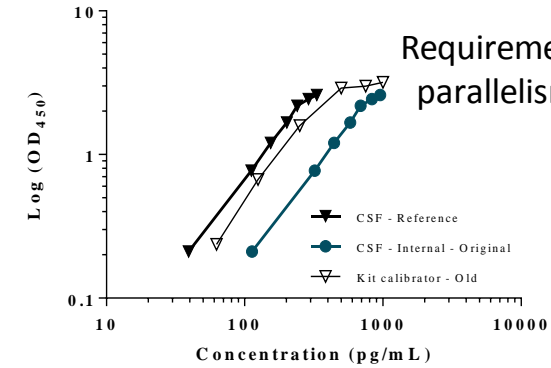
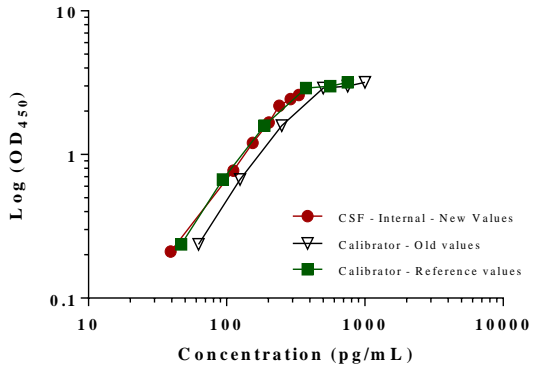
Reference CSF

Requirement
parallelism

**Value
assignment**

Internal
Calibrators

CSF
New values





Certified Reference Materials

CSF
(H, M, L)

**Sample
preparation**

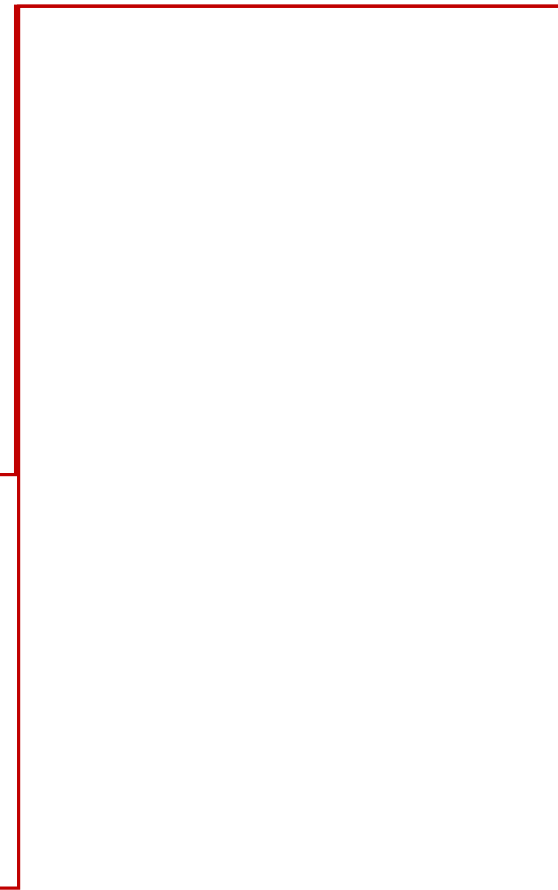
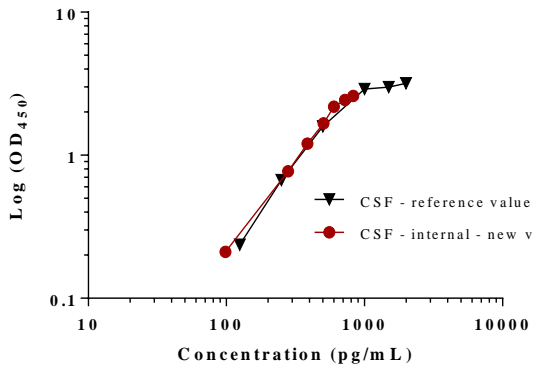
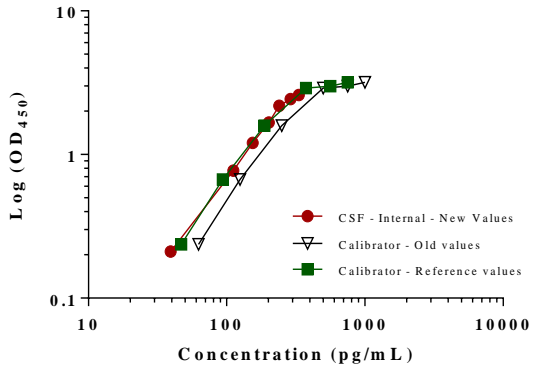
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Aliquotation & Freezing

CSF Series
(Internal)

Internal
Calibrators

**Value
assignment**





From **IRM** to **re-calibrated** assays: the approach for A β (1-42)

Fact: approved reference method



IRM
Certified reference standard(s)

Assay

The process



External
Quality Control

AA QC
Instand
Other ?