Validation of Quantitative Biomarker Assays to Meet FDA Regulatory Expectations

Marie Rock, PhD
laboratory developed biomarker assays

Russell Weiner, PhD
commercial / FDA diagnostic biomarker assays kits

Bill Nowatzke, PhD
Moderator
The figure shows the number of submissions of new molecular entities (NMEs) — drugs with a novel chemical structure — and the number of biologics license application (BLA) submissions to FDA over a 10-year period. Similar trends have been observed at regulatory agencies worldwide.
“...the two most important areas for improving medical product development are biomarker development (Topic 1) and streamlining clinical trials (Topic 2).”
No Standardization → Inconsistent Data

![Graph showing concentration vs. fraction with Luminex and ELISA data](image-url)
No Standardization → Inconsistent Data

- Identical Samples
- Same lab
- Same kit vendor
- Two ‘validated’ methods

![Graph showing concentration vs. fraction with a 200% increase between Luminex and ELISA](image)
The Alzheimer’s Association external quality control program for cerebrospinal fluid biomarkers

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\begin{align*}
&\text{Aβ1-42 (pg/mL)} \\
&D \\
&\begin{array}{c}
\text{2009:1A} \\
\text{2009:1B} \\
\text{2010:2A} \\
\text{2010:2B}
\end{array}
\end{align*}

\begin{tabular}{|c|c|c|c|}
\hline
Mean/(pg/mL) & 266 & 175 & 286 & 280 \\
\hline
CV\% & 33 & 36 & 29 & 25 \\
\hline
\end{tabular}

\textbf{400\%}
Method Comparison (CLIA Kits)

Equivalent Results

3.6 Year Assay Maintenance (RUO Kit)

%CV ~ 6%

Wang J et al., The AAPS Journal, Vol. 11, No. 2, June 2009
Marie Rock, PhD
Validation of laboratory developed biomarker assays to meet FDA guidelines when supporting regulated drug development studies

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Validation of commercial / FDA diagnostic assay kits to meet FDA guidelines when supporting regulated drug development studies