Measurement quality a route to improved patient outcome

Hanna Ritzén
Product Development Manager
Mercodia AB



Measurement quality a route to improved patient outcome

- Biomarker research has been a great interest in the past years.
- Biomarkers are used in research, diagnosis, screening and predictions of a disease, monitoring treatment response and complications.

How does measurement quality improved patient outcome?

- Researchers and clinicians need to make sound decisions about the acceptability of method performance.

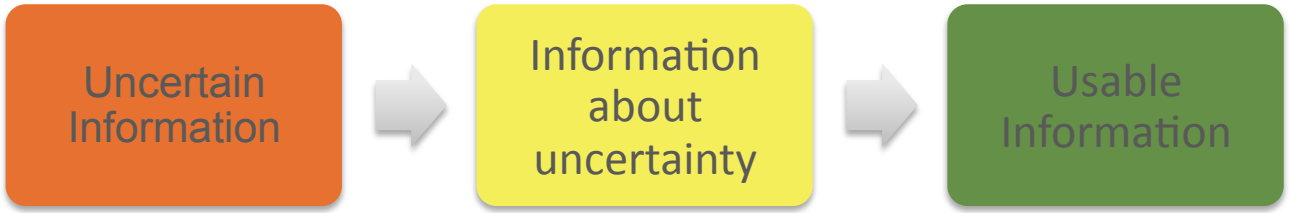
- The decisions are based on comparison of the analytical errors of a method with the medically allowable error for the analyte being evaluated.

- Making the right interpretation of collected data ultimately rely on the expertise of the scientist and the quality of the measurement methods used.



Mercodia
Developing diagnostics

Measurement Uncertainty



Measurement Uncertainty

- The uncertainty is often given as an interval around an estimate of a quantity, difference or effect.
- If the decision would be the same for all values within the interval we have sufficient information.





Mercodia
Developing diagnostics

Measurement Errors

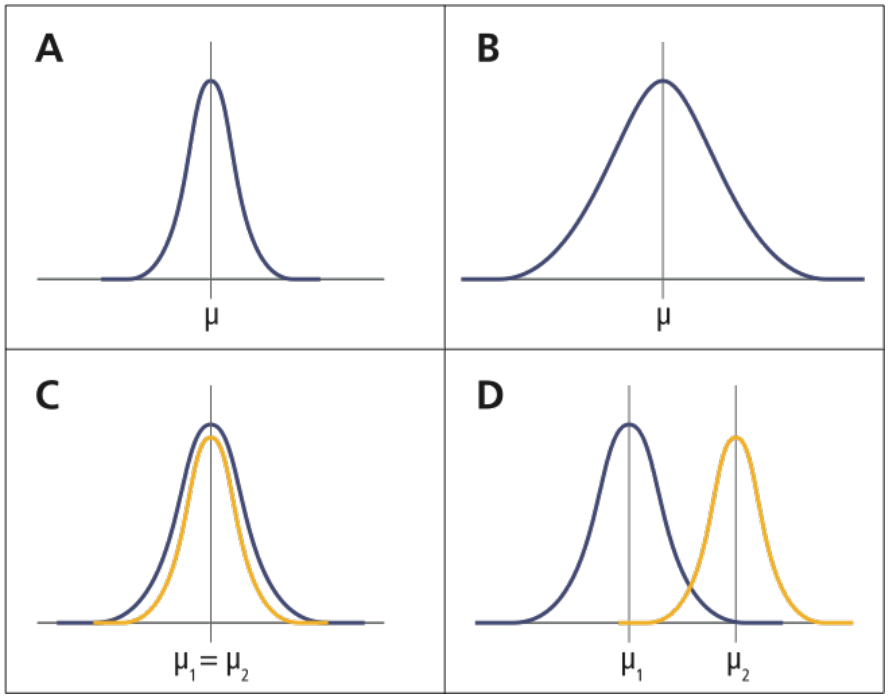
In planning, conducting and conclusion of studies

- An example: Monitoring the growth of an unborn baby.
- This is done by measuring the mothers belly with a measuring tape and compare the results with expected values and ranges.
  - The midwifes technique
  - The baby's position
  - The form of the uterus
  - Expected value and ranges



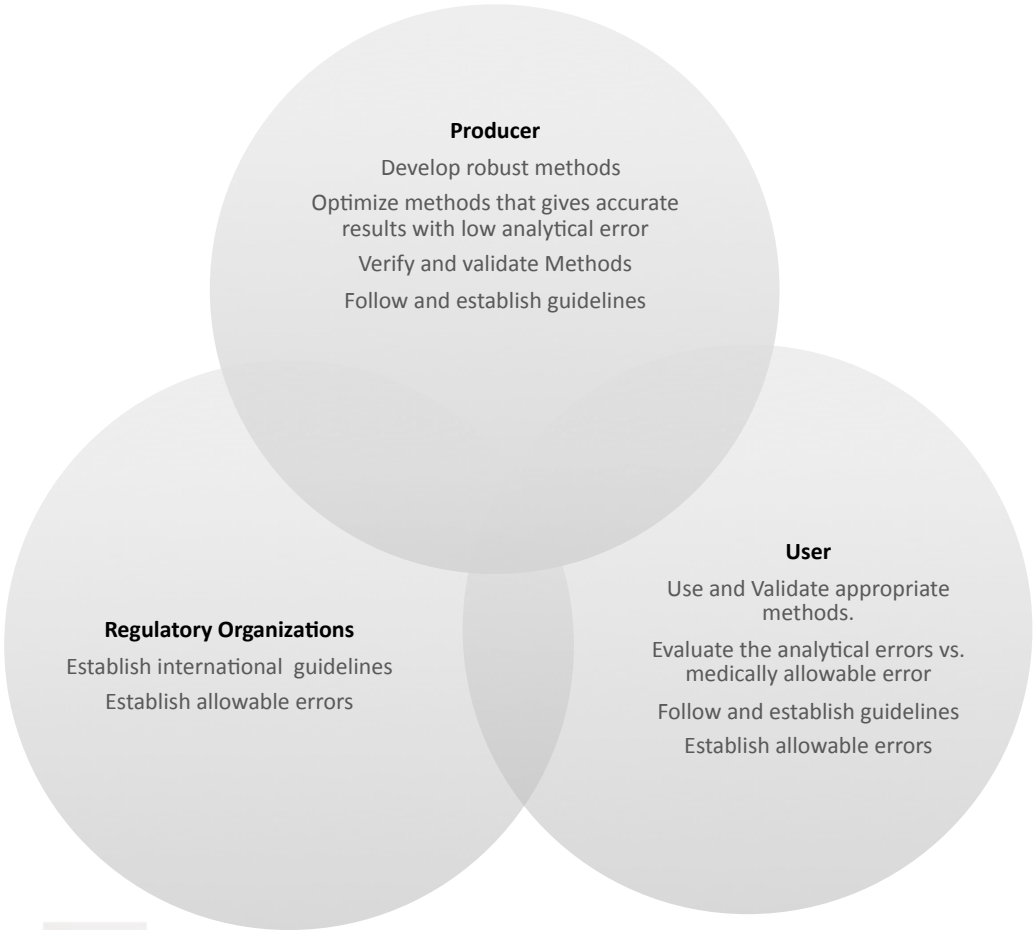
Measurement Errors

In planning, conducting and conclusion of studies



Measurement Quality

-Joint responsibilities



Measurement Quality

-Establish Guidelines

Mercodia
Developing diagnostics

FDA U.S. Food and Drug Administration
Protecting and Promoting *Your* Health



CLINICAL AND LABORATORY STANDARDS INSTITUTE

ISO



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

gsk

novo nordisk

SANOFI

AstraZeneca

Measurement Quality

-Determine Allowable Errors

Mercodia
Developing diagnostics

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

- Congress passed the Clinical Laboratory Improvement Amendments (CLIA) in 1988 establishing quality standards for all laboratory testing to ensure the accuracy, reliability and timeliness of patient test results regardless of where the test was performed.

- CLIA 88 has published acceptable performance criteria for analytes that are graded in proficiency surveys.

Routine Chemistry	CLIA Acceptable Performance	Medical Decision Level	CLIA Allowable Error	Medically Allowable Error
Albumin	+/-10%	3.5 g/dL	0.35 g/dL	0.24 g/dL
Bilirubin	+/-20% or 0.4 mg/dL	1.0 mg/dL	0.40 mg/dL	0.54 mg/dL
		20 mg/dL	4.00 mg/dL	10.8 mg/dL
Calcium	+/-1.0 mg/dL	7.0 mg/dL	1.00 mg/dL	0.37 mg/dL
		10.8 mg/dL	1.00 mg/dL	0.48 mg/dL

Mercodia
Developing diagnostics

Measurement Quality

-Determine Allowable Errors



ELSEVIER

Journal of Immunological Methods 289 (2004) 1–16

JIM Journal of Immunological Methods

www.elsevier.com/locate/jim

Standardization

Recommendations for the design and optimization of immunoassays used in the detection of host antibodies against biotechnology products

Anthony R. Mire-Sluis[a,*], Yu Chen Barrett[b], Viswanath Devanarayan[c], Eugen Koren[d], Hank Liu[e], Mauricio Maia[f], Thomas Parish[g], George Scott[h], Gopi Shankar[i], Elizabeth Shores[j], Steven J. Swanson[d], Gary Taniguchi[k,†], Daniel Wierda[l], Linda A. Zuckerman[m]

[a] Office of Biotechnology Products, Center for Drug Evaluation and Research, FDA, 5515 Security Lane, HFD-3, Rm 1011, Rockville, MD 20852, USA
[b] Bristol-Myers Squibb Company, PO Box 5400 Princeton, NJ 08543, USA
[c] Global Statistical Sciences, Lilly Research Labs, DC 2233, Eli Lilly & Co., Indianapolis, IN 46285, USA
[d] Clinical Immunology, Amgen Inc., Thousand Oaks, CA 91320, USA
[e] Wyeth Pharmaceuticals, 401 N. Middletown Road, Pearl River, NY 10965, USA
[f] Preclinical and Clinical Development Sciences, PDL Inc., 34801 Campus Drive Fremont, CA 94555, USA
[g] Procter and Gamble Pharmaceuticals, Route 320 Woods Corners, Norwich NY 13346, USA
[h] Ligand Binding Services, MDS Pharma Services, 2350 Cohen Street, St. Laurent, Quebec, Canada H4R 2N6
[i] Department of Clinical Pharmacology, CENTOCOR, Inc., 200 Great Valley Parkway, Malvern, PA 19355, USA
[j] Division of Therapeutic Proteins, CDER, FDA, N29A RM2A01 HFM-538, 8800 Rockville Pike, Bathesda MD 20892, USA
[k] Clinical Laboratory Operations, Biomarin Pharmaceutical Inc., 371 Bel Marin Keys Blvd., Novato, CA 94949, USA
[l] Department of Immunotoxicology, Eli Lilly & Company, 2001 W Main Street, Greenfield, IN 46140, USA
[m] BioAnalytical Research and Development, ZymoGenetics, Inc., Seattle, WA 98102, USA

Received 14 March 2004; accepted 14 June 2004

Abstract

Most biopharmaceutical therapeutics elicit some level of antibody response against the product. This antibody response can, in some cases, lead to potentially serious side effects and/or loss of efficacy. Therefore, the immunogenicity of therapeutic proteins is a concern for clinicians, manufacturers and regulatory agencies. In order to assess immunogenicity of these molecules, appropriate detection, quantitation and characterization of antibody responses are necessary. Inadequately designed antibody assays have led to the hampering of product development or, during licensure, post-marketing commitments. This document provides scientific recommendations based on the experience of the authors for the development of anti-product antibody immunoassays intended for preclinical or clinical studies. While the main focus of this document is assay design considerations, we provide scientific focus and background to the various assay performance

* Corresponding author.
† Formerly at Genentech Inc., South San Francisco.
E-mail address: mire-sluisa@cder.fda.gov (A.R. Mire-Sluis).

0022-1759/$ - see front matter © 2004 Elsevier B.V. All rights reserved.
doi:10.1016/j.jim.2004.06.002

In Summary

When performing biomarker research some sort of measurements are needed. In all measurement methods there are a variety of components that are affecting the test results.

- The producer of an measurement methods has a great responsibility to ensure that the product gives accurate results.

- The user should be well educated, validate methods and evaluate the analytical error in comparison with the medically allowable error.

- Regulatory organizations have a great responsibility to drive the international guidelines, standardization and harmonization programs forward



Mercodia
Developing diagnostics

Absolute certainty is a privilege of uneducated minds- and fanatics

Keyser





Thank you for your attention!