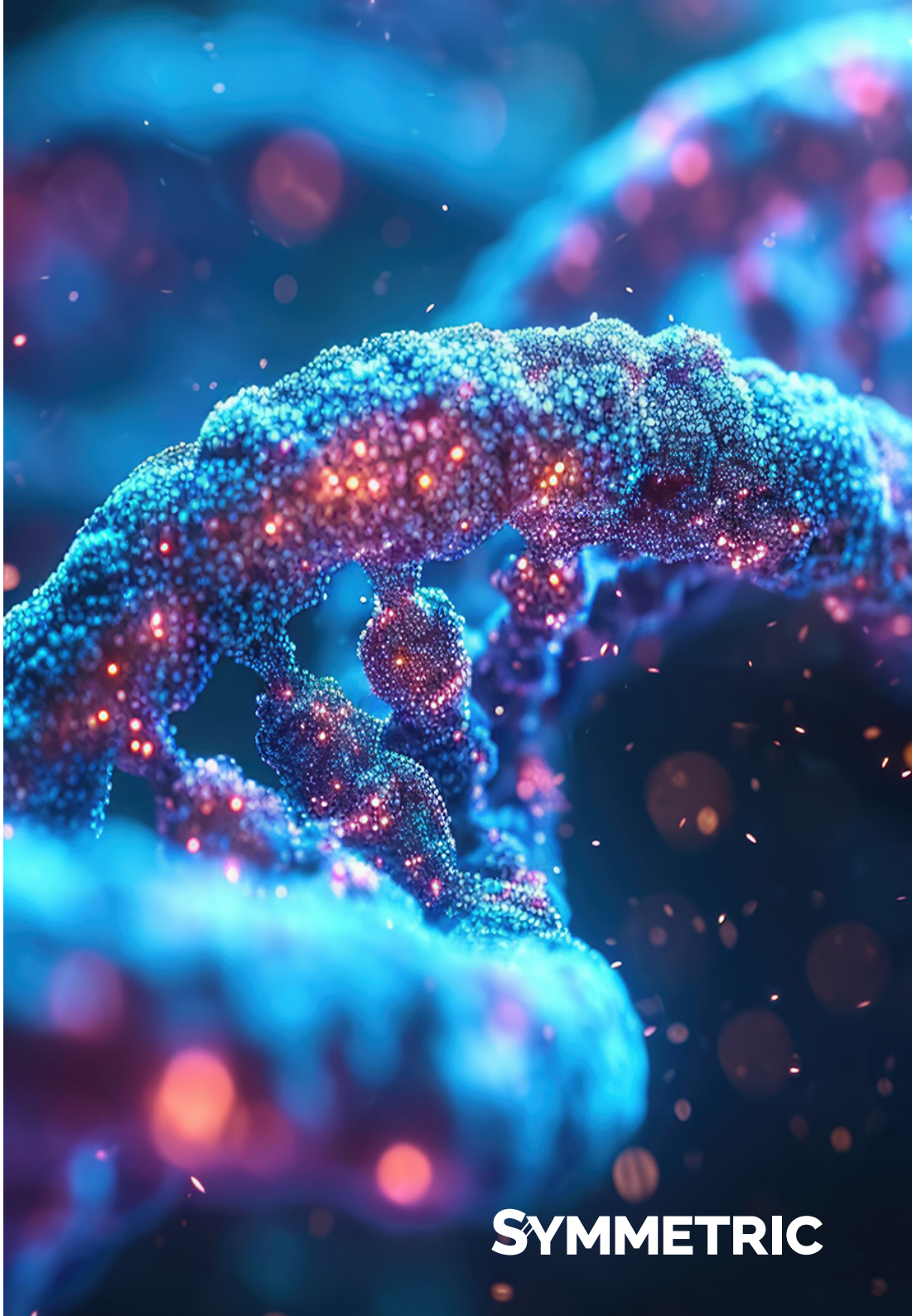
Sneak Peek

PK and ADA Assays for Biologics

Dr. Gwen Wise-Blackman
BioData Solutions, USA,
Senior Consultant

ONLINE
TRAINING



Regulatory Guidance – Phase 1 vs. Phase 2 vs. Phase 3

01

Phase 1

- Healthy volunteers
- Small number of subjects
- Shorter timeline, limited dosing
- Validated PK, ADA Ready

Phase 2

- Disease subjects
- Enrollment issues
- Validated PK, Validated ADA

Phase 3

- Large clinical trial
- Preparing post market strategy
- Validated PK and Validated ADA + NAb

Source: Dr. Gwen Wise-Blackman

M10 - Critical Reagents

02

Category	M10		2018 FDA Guidance
Required Information	• The data sheet for the critical reagent should include at a minimum identity, source, batch/lot number, purity (if applicable), concentration (if applicable), and stability/ retest date/storage conditions		• Appropriately characterize and document (i.e., determine the identity, purity and stability).
Validation	• Defines minor changes as those not expected to influence the method performance (e.g., the source of one reagent is changed) and a single comparative accuracy and precision assessment is sufficient for characterization. • Defines major changes as those that may significantly impact the performance (e.g., a change in production method of antibodies, additional blood collection from animals for polyclonal antibodies, and new clones or new supplier for monoclonal antibody production) and additional validation experiments are recommended. • Ideally, the assessment of changes should compare the method with the new reagents to the method with the old reagents directly.		• Assay validation is important when there are changes to the critical reagents, such as lot-to-lot changes or switches to another reagent. • If there are changes to the labeled analytes, detector reagents, or antibodies, the sponsor should: evaluate binding and re-optimize assays; verify performance with a standard curve and QCs; and evaluate cross-reactivities.

Source: Dr. Gwen Wise-Blackman

Data Trending

03

Run Failures

- QC set 1 and 2 (in column 5/6) passes
- QC set 3 and 4 (in column 9/10) fails
- Looking at each QC observe a clear %bias shift

%Bias	Set 1	Set 2	Set 3	Set 4
HQC	-6.00	-10.2	-19.2	-24.1
MQC	-13.1	-20.6	-20.5	-24.8
LQC	-12.7	-17.5	-24.1	-23.8

Source: Dr. Gwen Wise-Blackman

PK Assays

Matrix interference – hemolysis/lipemia/disease matrix

- Preclinical animal studies
  - No lipemic matrix
  - Test hemolyzed (2-5%, usually 2%)

- Clinical studies
  - Lipemic (usually purchased from a vendor)
  - Hemolyzed (usually 2-5%, purchased form a vendor)

- Acceptance criteria for %CV and %RE is the standard for QCs

Source: Dr. Gwen Wise-Blackman

Overcoming Interference of the Drug

05

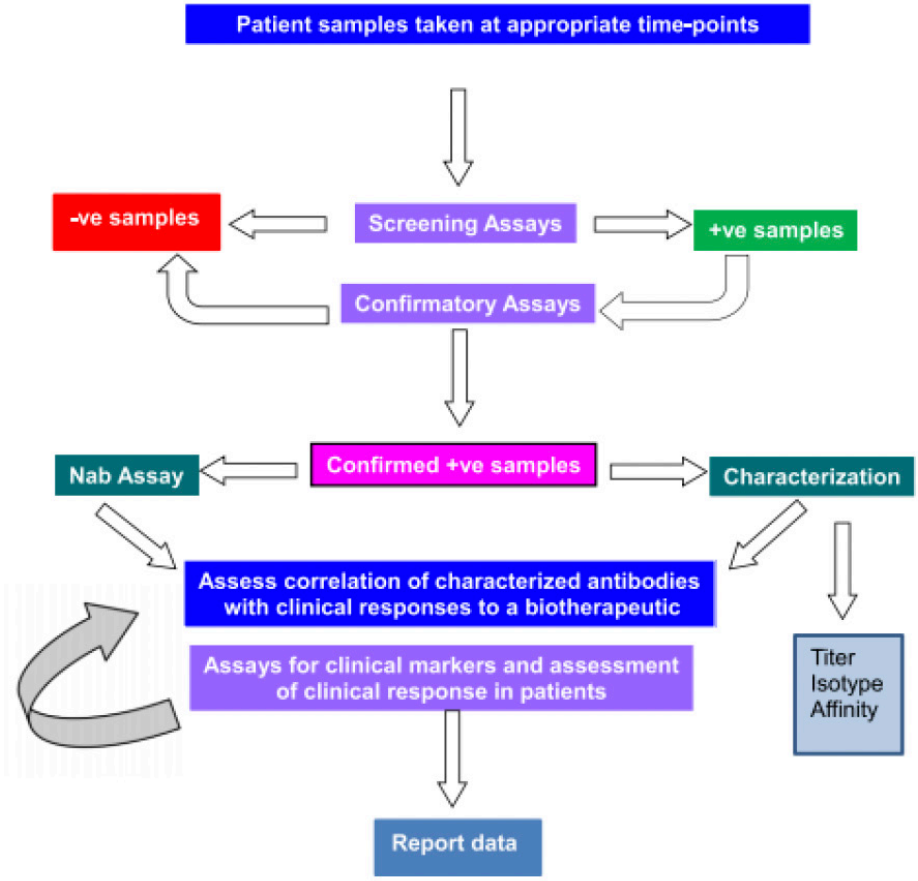
Tier approach for detection of ADA in biological matrices (usually serum)

Semi-quantitative assays that use cut points (threshold) rather than concentrations

Tier 1: Screening Assay

Tier 2: Confirmatory Assay

Tier 3: Characterization using Titer Assay, nAb assay and Isotpying



Source: Dr. Gwen Wise-Blackman

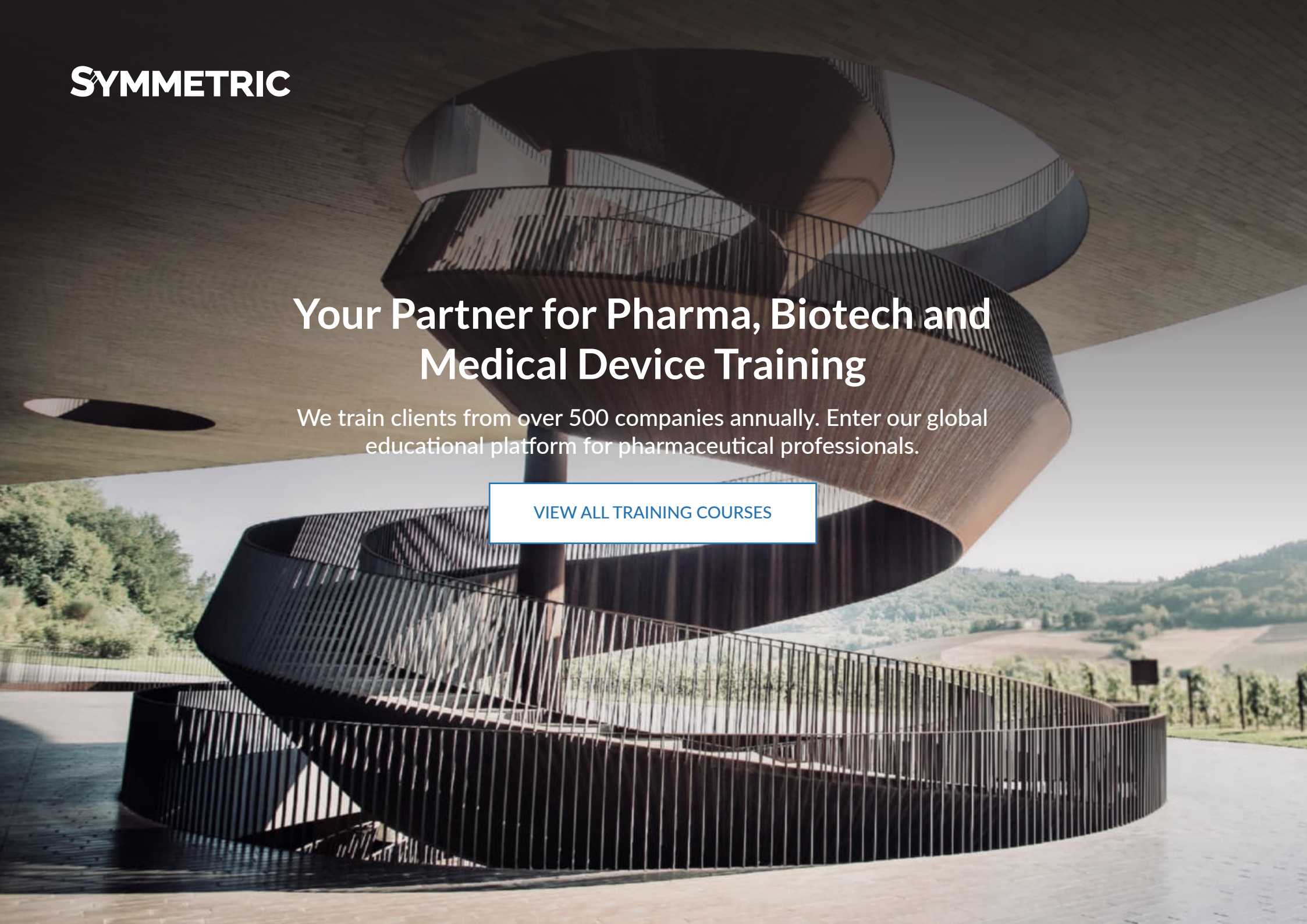
Registration

06

Sneak Peek

PK and ADA Assays for Biologics

Mliekarenská 9, 821 09
Bratislava, Slovak Republic
ID: 47 068 124
VAT no: SK2023741973
Office: +421 948 262 346


SYMMETRIC
Your Partner for Pharma, Biotech and Medical Device Training
We train clients from over 500 companies annually. Enter our global educational platform for pharmaceutical professionals.
VIEW ALL TRAINING COURSES