

# Quantum Blue® Adalimumab: Development of the first point of care rapid test for therapeutic drug monitoring of serum adalimumab levels

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## BACKGROUND

Adalimumab is a human monoclonal antibody directed against tumor necrosis factor alpha (TNF $\alpha$ ) used for the treatment of inflammatory diseases like Crohn's Disease (CD) and Ulcerative Colitis (UC). For efficient treatment trough levels of adalimumab need to be adjusted within a therapeutic window, which is 5 to 10  $\mu\text{g/mL}$  (Moss et al., 2015). A rapid test allows a much faster reporting of trough levels, providing a great advantage over test formats that need samples to be send to a central lab. Here we report current results of the completed Quantum Blue® Adalimumab test optimization. The test is now under validation.

## METHODS

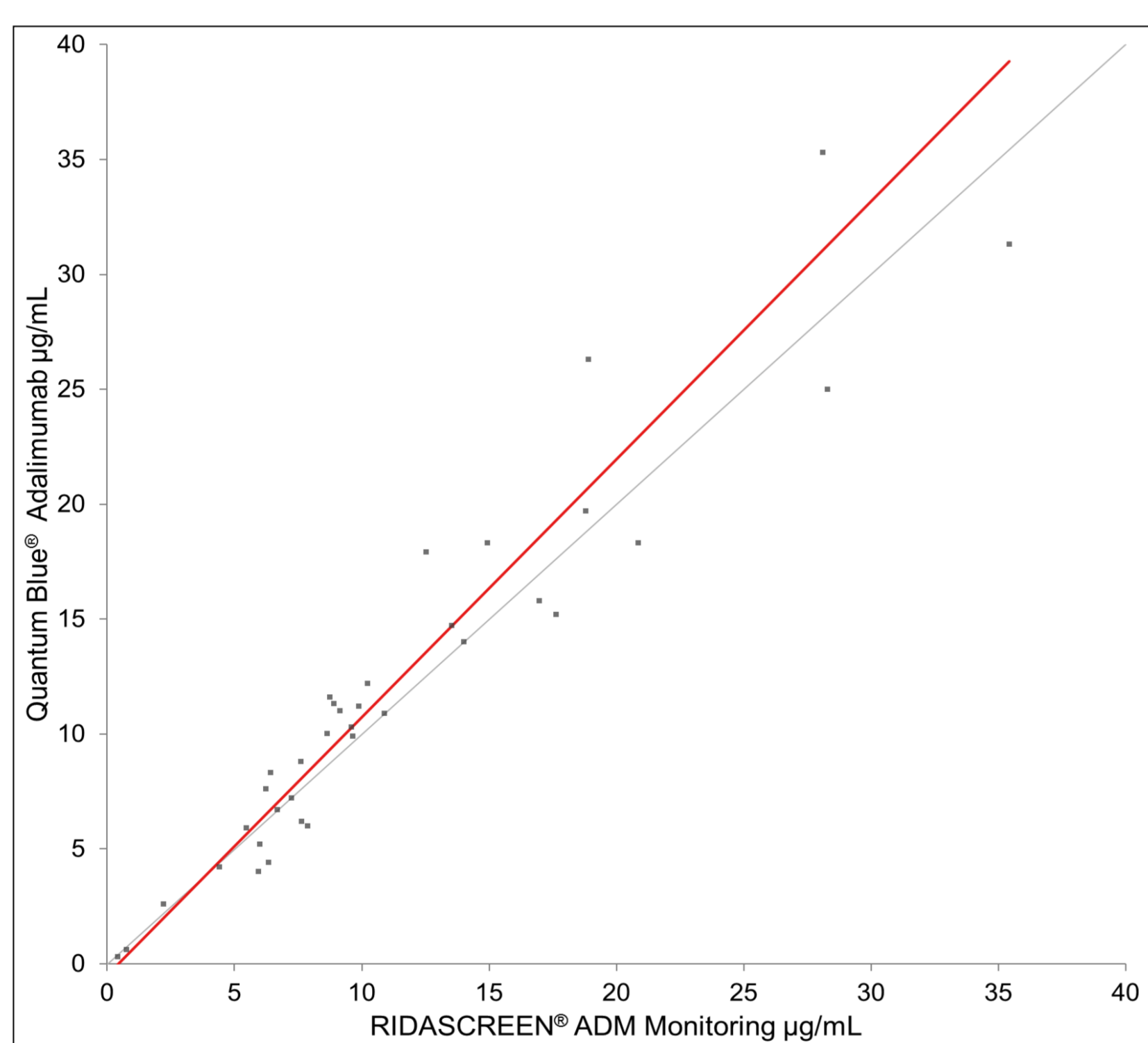
The sandwich lateral flow immunoassay uses a TNF $\alpha$  coated gold label and a highly specific monoclonal antibody to detect adalimumab in a diluted human serum sample. Sensitivity of the assay was estimated via Limit of Detection (LoD) and Limit of Quantification (LoQ) according to CLSI EP17-A2. Moreover the assay was evaluated regarding cross-reactivity with other therapeutic antibodies targeting TNF $\alpha$ , influence of rheumatoid factors (RFs) and high dose hook effect. A method comparison was performed using a commercially available ELISA (RIDASCREEN® ADM Monitoring, Art. No. G09043, R-Biopharm, Darmstadt, Germany) to compare the serum level results of 40 adalimumab treated patients.

## RESULTS

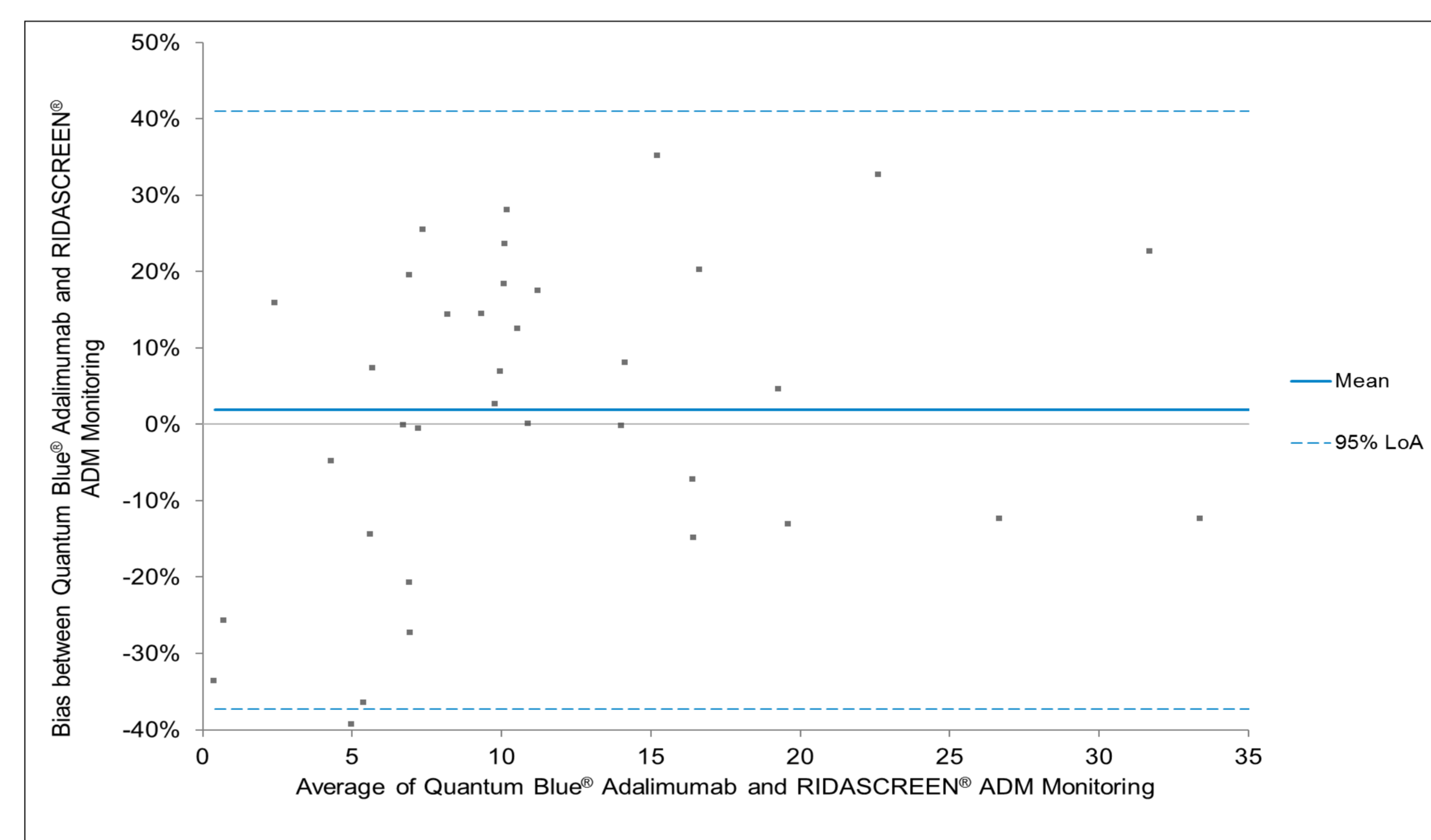
The current Quantum Blue® Adalimumab test allows analysis of serum samples within 15 minutes. The samples are diluted 1:20 in chase buffer before application on a test cassette (volume 80  $\mu\text{L}$ ). The readout is performed with the Quantum Blue® Reader resulting in concentration levels of adalimumab in  $\mu\text{g/mL}$  (Tab. 1).

The test exhibits a LoD of 0.2  $\mu\text{g/mL}$ , which was calculated on the basis of the Limit of Blank (LoB). A LoQ of 0.69  $\mu\text{g/mL}$  was determined according to the relevant CLSI-guideline. The obtained data ensure a measuring range of 1 to 35  $\mu\text{g/mL}$  of adalimumab in patient samples. No high dose hook effect was detected for spiked serum samples containing up to 1000  $\mu\text{g/mL}$  adalimumab. Other therapeutic TNF $\alpha$  blockers, like infliximab and golimumab, showed no cross-reactivity with the Quantum Blue® Adalimumab test, furthermore RFs showed no influence on correct measurement of adalimumab at the tested concentrations.

The performed method comparison revealed a slope of 1.12 and a regression coefficient ( $r^2$ ) of 0.90 (Passing-Bablok, Fig. 1). A Bland-Altman analysis showed a bias of 1.88% confirming the overall excellent correlation of the two methods (Fig. 2). Moreover a comparison of both assays revealed an excellent agreement of 82.5% (Fig. 3).



**Fig. 1:** Passing-Bablok regression analysis of the two assays.



**Fig. 2:** Bland-Altman analysis revealed a bias of 1.88% in the method comparison.

		RIDASCREEN® ADM MONITORING		
		low	optimal	high
Quantum Blue® Adalimumab	low	20.0%	5.0%	0.0%
	optimal	0.0%	27.5%	0.0%
	high	0.0%	12.5%	35.0%

82.5%

**Fig. 3:** Diagnostic agreement revealed high comparability between the assays.

**Tab. 1:** Quantum Blue® Adalimumab test key specifications.

Quantum Blue® Adalimumab	
Measuring Range	1 - 35 $\mu\text{g/mL}$
Sample Specimen	Serum
Application Volume	80 $\mu\text{L}$
Sample Dilution	1:20
Time to Result	15 minutes
Assay Read-out	Quantum Blue® Reader

## CONCLUSIONS

The BÜHLMANN Quantum Blue® Adalimumab assay enables the quantitative determination of adalimumab trough level in serum with a time to result of only 15 minutes. The developed assay allows to measure adalimumab over a wide range. Hence, it represents a valuable tool for the clinician to assess the adalimumab trough level.