

P1014 PERFORMANCE OF THE BÜHLMANN QUANTUM BLUE® ADALIMUMAB RAPID TEST DEDICATED FOR THERAPEUTIC DRUG MONITORING OF SERUM ADALIMUMAB TROUGH LEVELS

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INTRODUCTION

Adalimumab is a human monoclonal antibody 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 of 5 to 12 $\mu\text{g/mL}$ ¹. A rapid test allows a fast analysis of trough levels, providing a great advantage over test formats that need samples to be sent to a central laboratory. Here, we present the analytical performance characteristics as part of the validation of the Quantum Blue® Adalimumab lateral flow test from BÜHLMANN.

METHODS

The sandwich lateral flow immunoassay uses a tumor necrosis factor alpha coated label and a highly specific monoclonal antibody to detect adalimumab in a diluted human serum sample. Evaluation was performed according to CLSI guidelines. For **linearity**, two sample pools, low and high, were blended to obtain 16 concentration levels covering and exceeding the expected measuring range. The blends were assayed in 10 replicates on two test cassette lots. Five pools of clinical adalimumab serum samples were tested over 20 days, in two independent runs with two replicates per run to establish total **precision**. **Method comparison** was performed with RIDASCREEN® ADM Monitoring ELISA, (G09043, R-Biopharm, Darmstadt, Germany), based on 130 clinical and contrived (3.1% of total) serum samples, tested in triplicates. For **recovery** six clinical samples over the measuring range were spiked with 5.4 $\mu\text{g/mL}$ adalimumab in negative serum and compared with the expected values. Samples were measured in 10 replicates with one reagent lot. The **high dose hook effect** was evaluated with spiked pooled human serum in two runs, the second run with an additional 1:20 dilution of the samples into the measuring interval of the test.

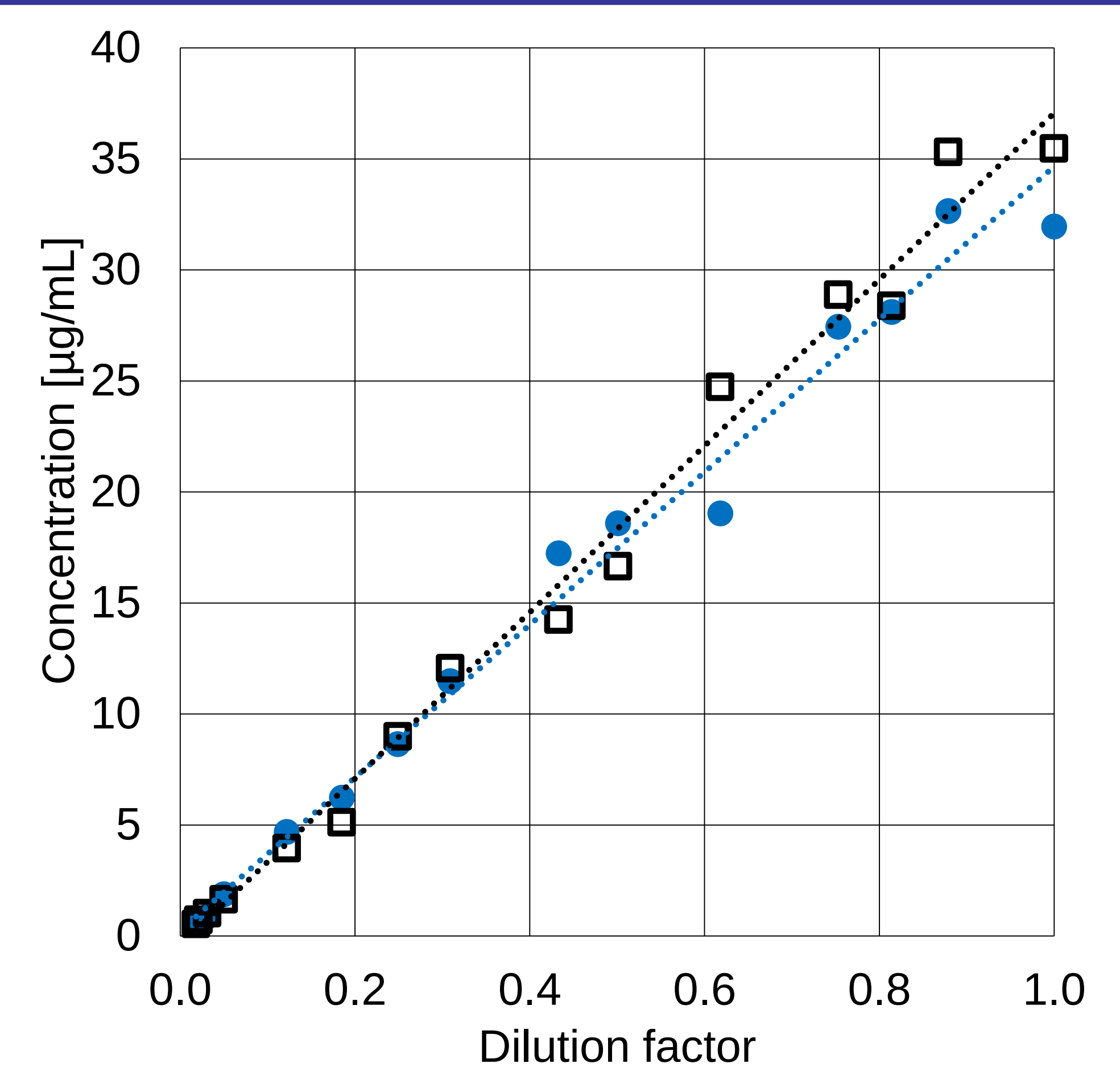


Fig. 1. Linearity testing of two Lots: L45AA (●) and L03BA (□).

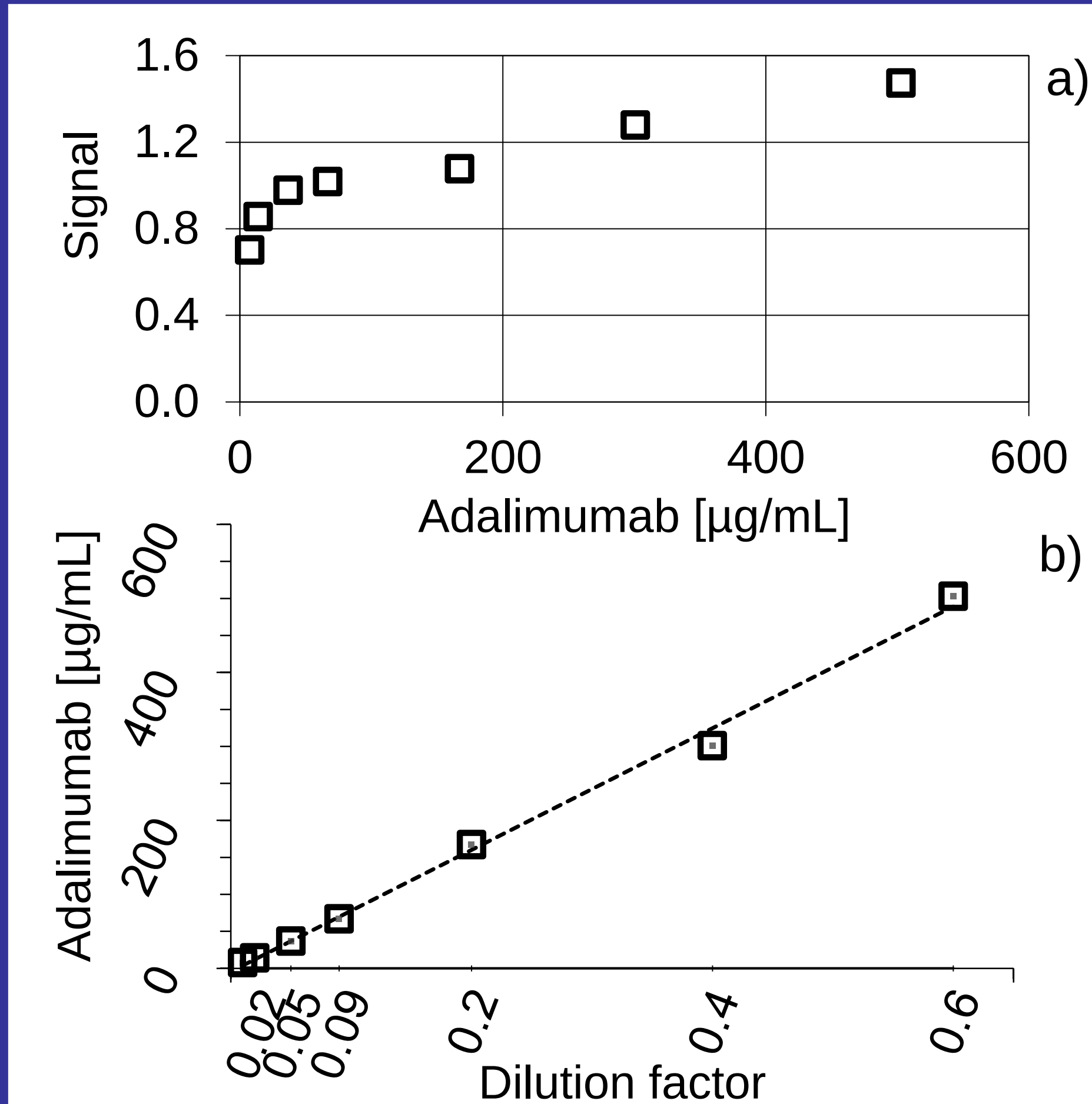


Fig. 2. a) Antigen excess testing b) Sample dilution linearity with an additional 1:20 dilution.

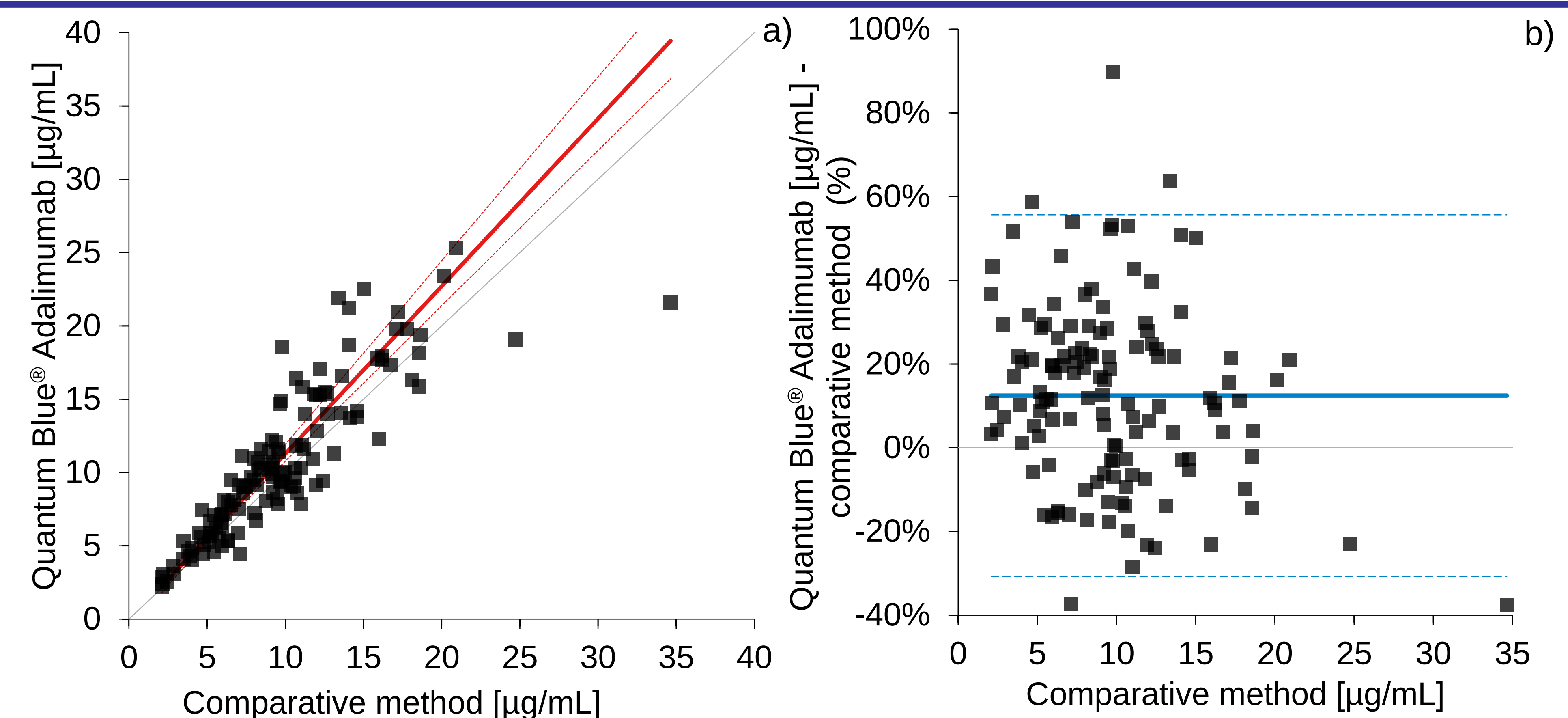


Fig. 3. Passing-Bablok (a) and Bland-Altman (b) plot of Quantum Blue® Adalimumab vs. comparative method.

Table 1: Within-laboratory precision of lot L03BA.

Mean conc. [µg/mL]	Within-run (repeatability)	Between-day	Within-laboratory
1.26	26.7%	8.5%	28.0%
2.03	18.7%	1.6%	19.1%
6.63	16.6%	0.0%	20.9%
9.40	17.8%	1.1%	19.3%
22.70	28.6%	8.0%	29.9%

Table 2: Spiking-recovery result of six clinical samples with a spike of 5.4 $\mu\text{g/mL}$.

Base value [µg/mL]	Expected base + Spike [µg/mL]	Observed base + Spike [µg/mL]	Recovery [%]
2.6	8.0	6.7	83
4.6	10.1	9.0	89
5.2	10.7	8.6	80
8.1	13.5	11.1	82
8.5	13.9	12.5	90
12.2	17.6	15.2	86

RESULTS

The Quantum Blue® Adalimumab test exhibits a linear range of 0.5 - 35.5 $\mu\text{g/mL}$ (Fig. 1). No high dose hook effect was observed up to 800 $\mu\text{g/mL}$ of adalimumab. Sample dilution linearity was demonstrated to be in the range of 7.6 to 502.8 $\mu\text{g/mL}$ (Fig. 2). The method comparison (Passing Bablok) revealed a slope of 1.14 and a Pearson's r of 0.87 and is suggesting that the new Quantum Blue® Adalimumab test showed an excellent correlation compared to the ELISA method (Fig. 3). A mean bias of 12.5% was determined using Bland-Altman analysis, while the bias at cut-off 5.0 and 12.0 $\mu\text{g/mL}$ was 0.3% and 13.8%, respectively. The total within-laboratory precision of the device was between 19.1 and 29.9% with a within-run precision of 16.6 to 28.6% (Table 1). Recovery was between 80 and 90% (Table 2).

CONCLUSION

The Quantum Blue® Adalimumab test enables the quantitative determination of adalimumab levels from 1 to 35 $\mu\text{g/mL}$ in serum with a time to result of only 15 minutes. The developed test allows to measure adalimumab over a wide range, well beyond the therapeutic window. Hence, it represents a valuable tool for the clinician to assess adalimumab trough levels.

REFERENCE

1. Mitrev, N. *et al.* Review article: consensus statements on therapeutic drug monitoring of anti-tumor necrosis factor therapy in inflammatory bowel diseases. *Aliment. Pharmacol. Ther.* (2017). doi:10.1111/apt.14368