



Assay-specific control reagents and statistics

for effective performance monitoring of blood safety testing

21 May 2026 – Sven Kerst

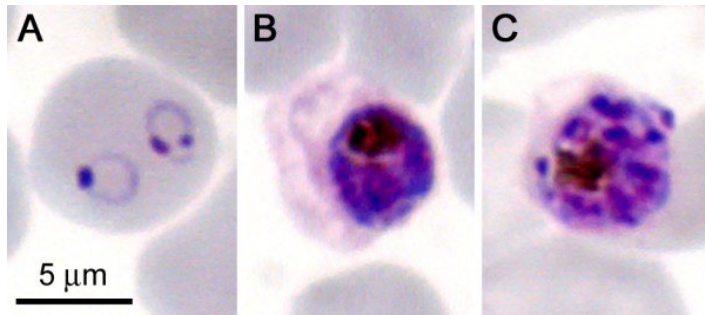
IPFA/PEI 32nd International Workshop
on Surveillance and Screening of Blood-borne Pathogens

Outline

- Establishment of *Plasmodium falciparum* standard
- New statistical report for run control reproducibility

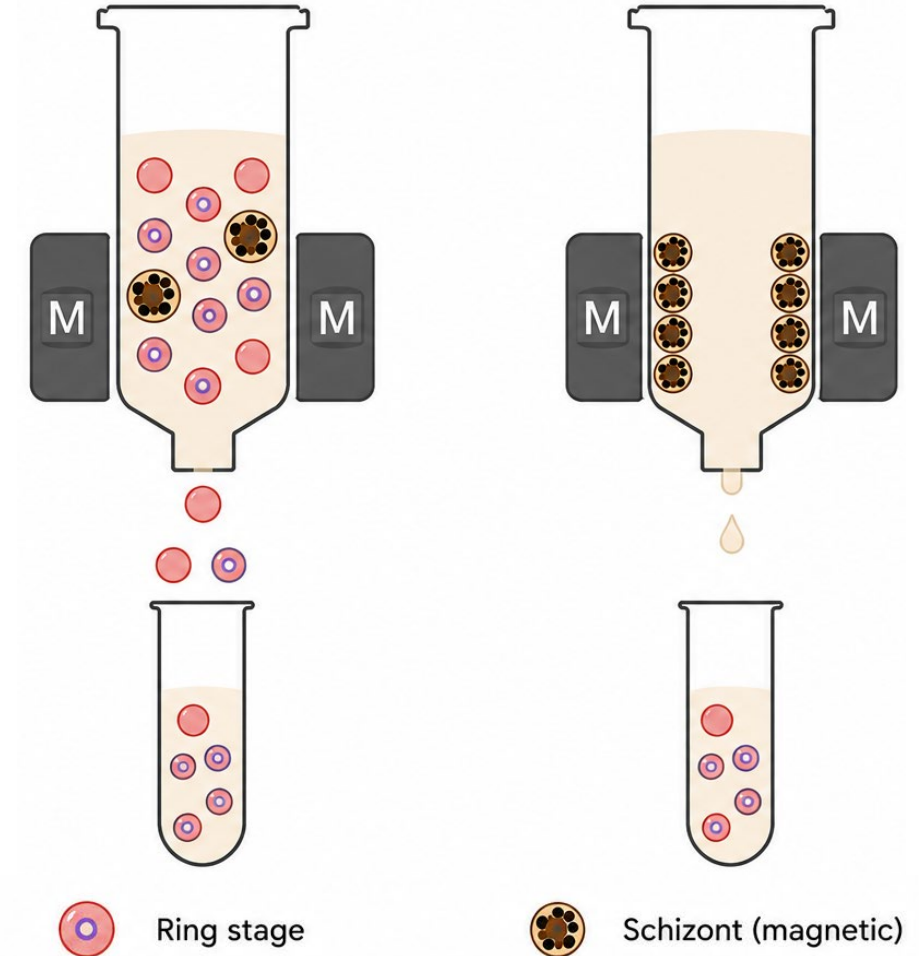
Development of *Plasmodium falciparum* source standard

- P. falciparum* forms during blood-stage infection

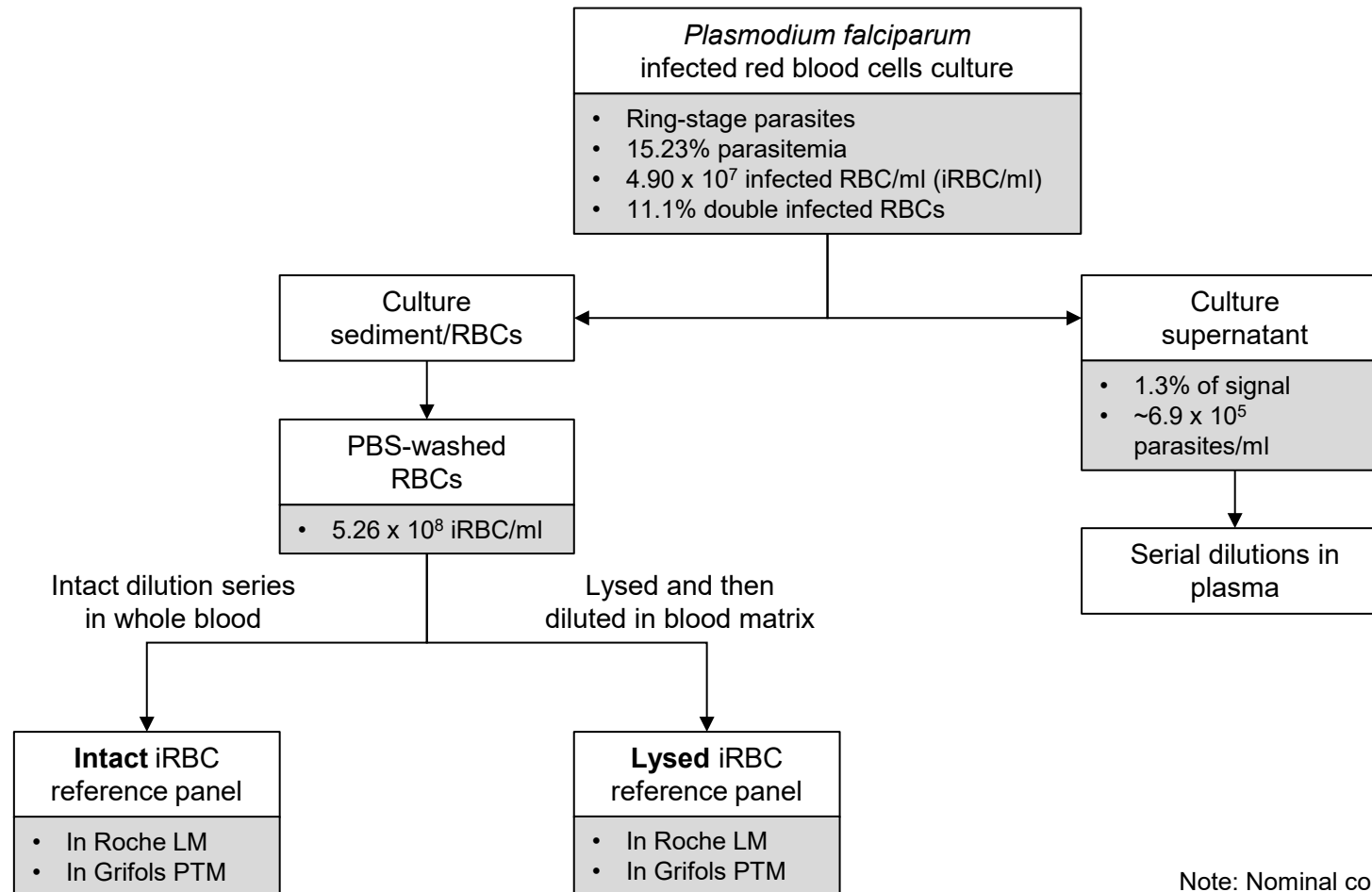


Urbán et al. (Nanoscale Res Lett. 2011)

- Ring stage parasites (A) circulate in the blood stream
- Isolation with magnetic columns
- After 2 days parasitemia was counted twice: 15.23%



Preparation of *Plasmodium falciparum* reference panels



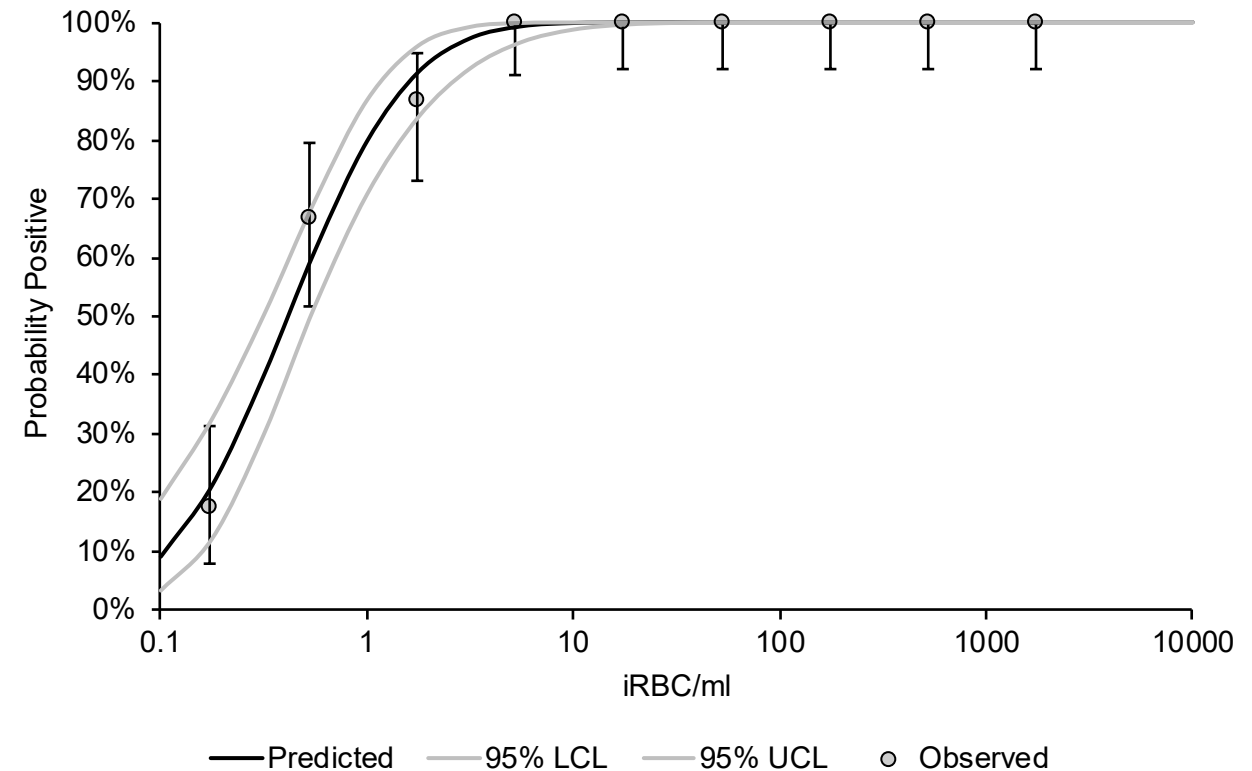
Note: Nominal concentration is based on histological examination (Giemsa staining) at Radboudumc, Nijmegen (NL).

Intact iRBC panel in Procleix Plasmodium Assay

iRBC/ml	Total nr. tested	Observed % positive
1754.66	45	100%
526.40	45	100%
175.47	45	100%
52.64	46	100%
17.55	45	100%
5.26	40	100%
1.75	45	87%
0.53	48	67%
0.18	46	17%

LOD	iRBC/ml (95% CI)
50%	0.42 (0.31 – 0.53)
63%	0.59 (0.46 – 0.78)
95%	2.36 (1.60 – 4.33)

Theoretical 63% LOD = 1.11 iRBC/ml

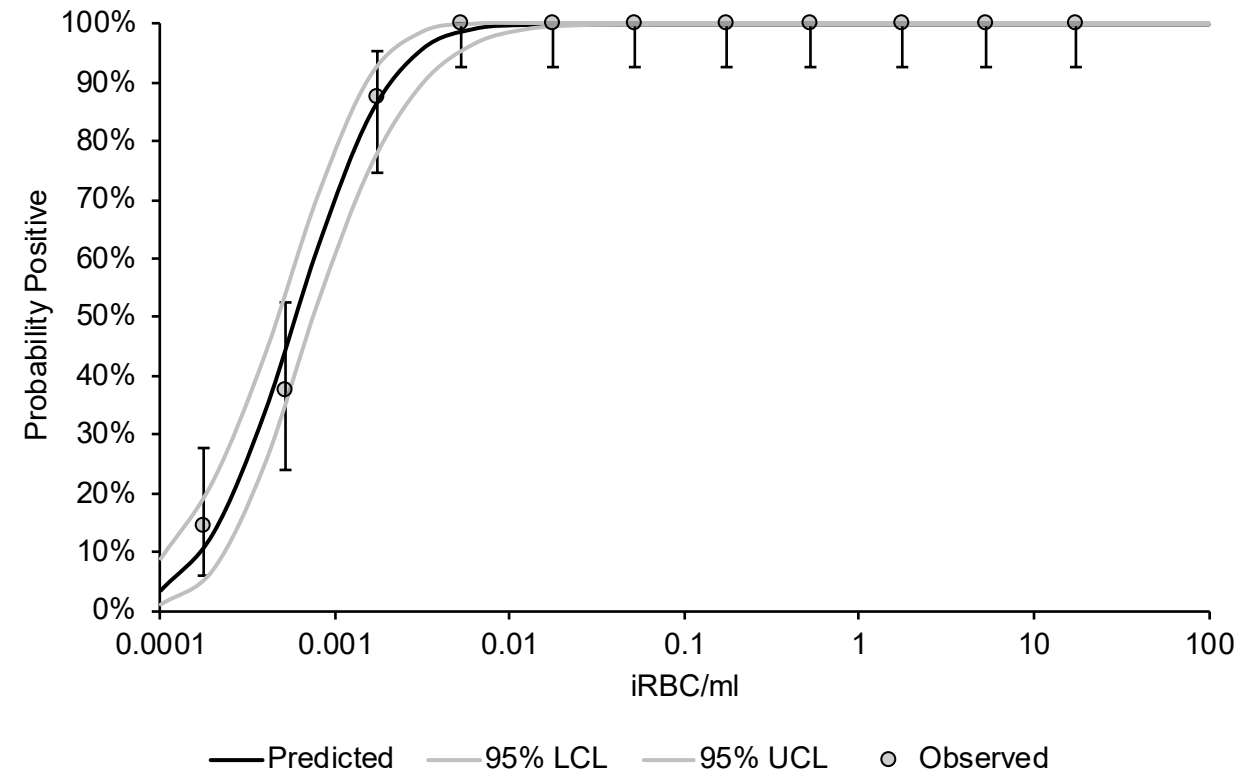


Testing is performed by Grifols Diagnostic Solutions (San Diego, CA).

Lysed iRBC panel in Procleix Plasmodium Assay

iRBC/ml	Total nr. tested	Observed % positive
17.5466	48	100%
5.2640	48	100%
1.7547	48	100%
0.5264	48	100%
0.1755	48	100%
0.0526	48	100%
0.0175	48	100%
0.0053	48	100%
0.0018	48	88%
0.0005	48	38%
0.0002	48	15%

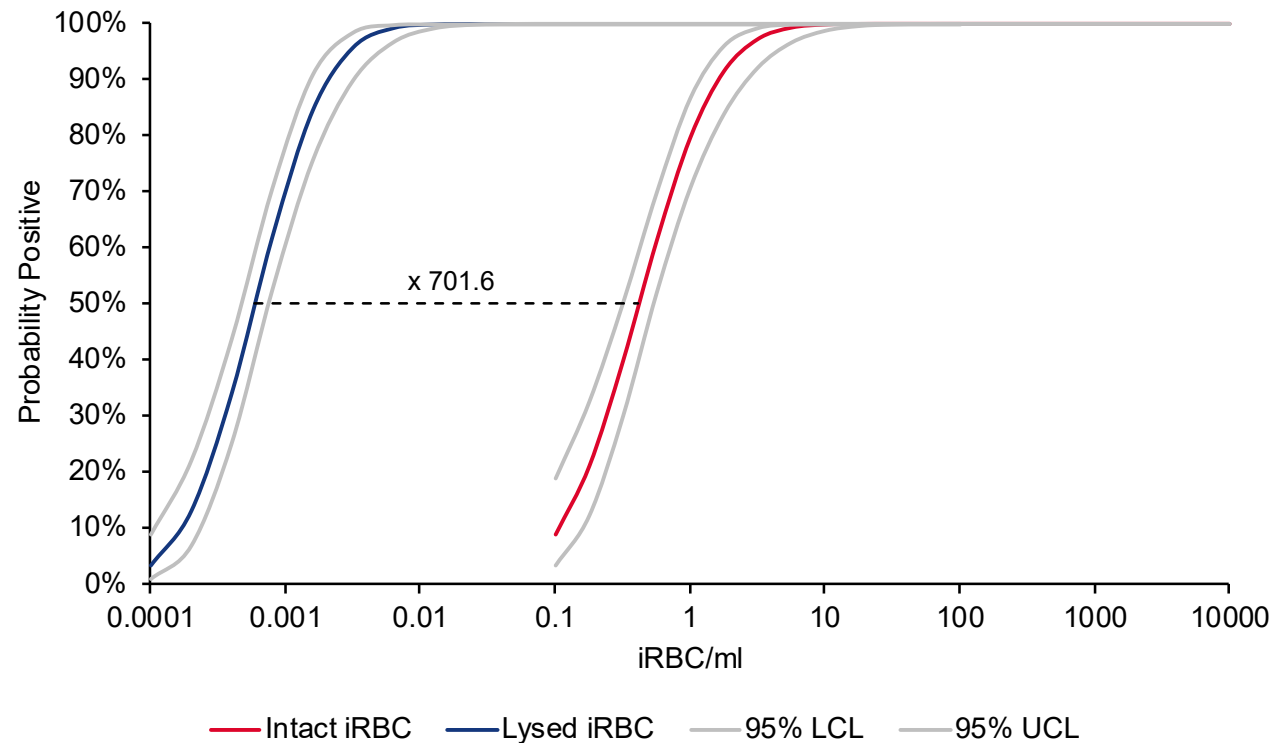
LOD	iRBC/ml (95% CI)
50%	5.9 (4.7 – 7.4) x 10 ⁻⁴
63%	8.2 (6.5 – 10.1) x 10 ⁻⁴
95%	29.1 (20.4 – 49.4) x 10 ⁻⁴



Testing is performed by Grifols Diagnostic Solutions (San Diego, CA).

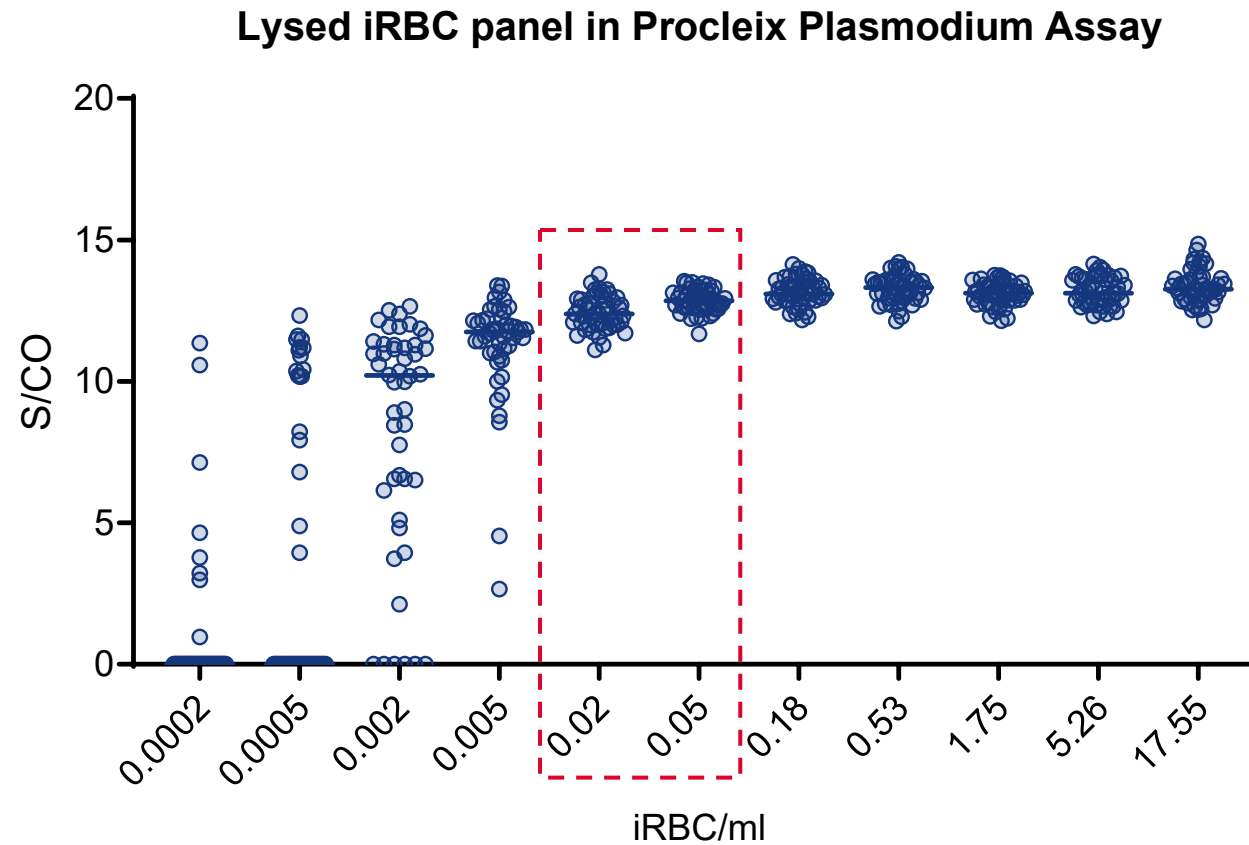
Lysis of iRBCs increases Procleix Plasmodium Assay sensitivity 702-fold

- 50% LOD differs a factor ~ 702 between the intact iRBC panel and the lysed iRBC panel
- One ring stage parasite contains ~ 4548 ribosomal RNA (18S rRNA) copies



Positioning of *Plasmodium falciparum* run control

- Concentration of run control is assay-specific (~10x 95% LOD)

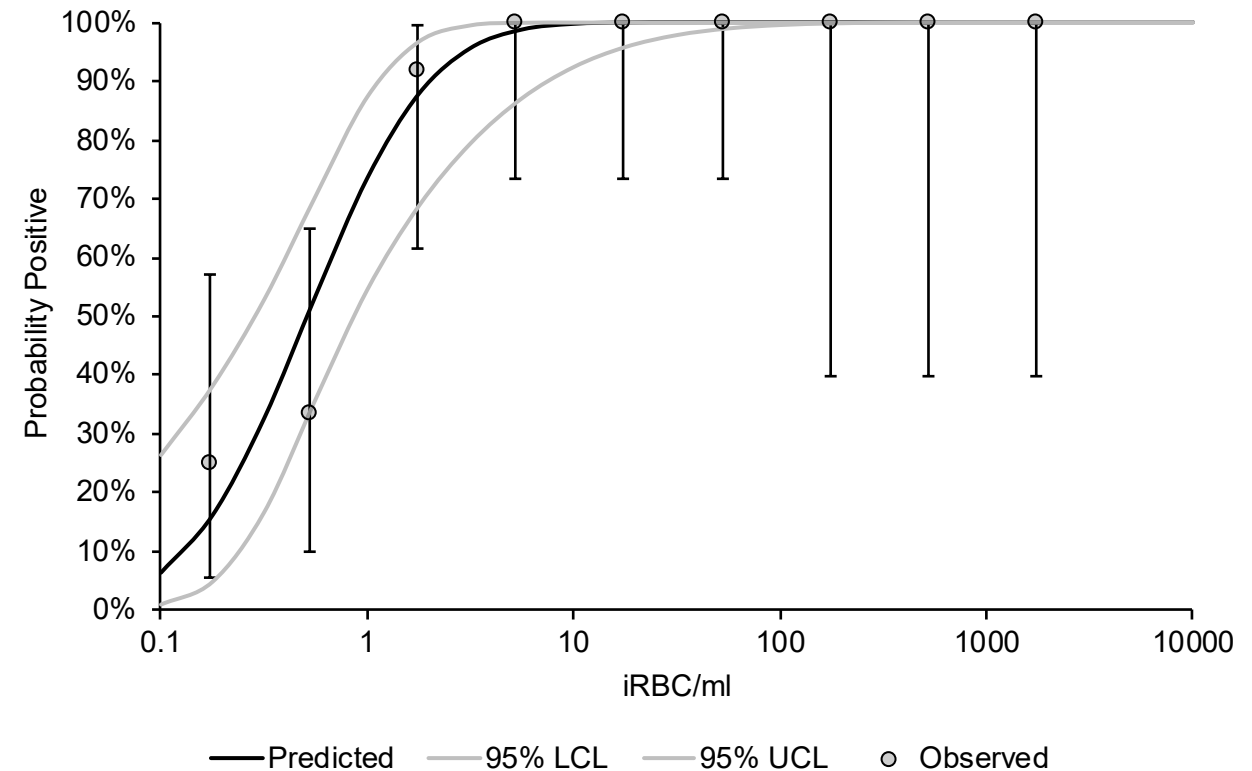


Intact iRBC panel in cobas Malaria (preliminary results)

iRBC/ml	Total nr. tested	Observed % positive
1754.66	4	100%
526.40	4	100%
175.47	4	100%
52.64	12	100%
17.55	12	100%
5.26	12	100%
1.75	12	92%
0.53	12	33%
0.18	12	25%

LOD	iRBC/ml (95% CI)
50%	0.51 (0.29 – 0.86)
63%	0.73 (0.45 – 1.40)
95%	2.96 (1.51 – 15.2)

Theoretical 63% LOD = 0.91 iRBC/ml

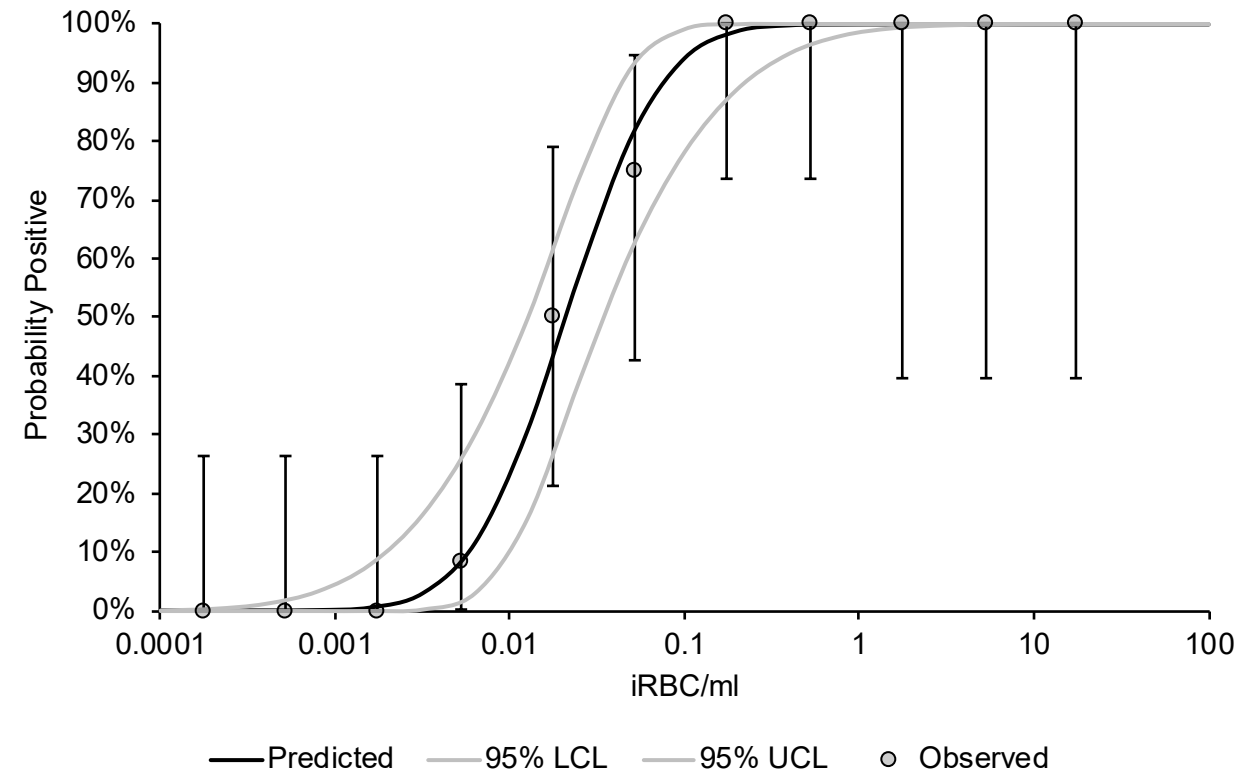


Note: study to increase to 48 replicates is ongoing in collaboration with Roche Molecular Systems (Pleasanton, CA).

Lysed iRBC panel in cobas Malaria (preliminary results)

iRBC/ml	Total nr. tested	Observed % positive
17.5466	4	100%
5.2640	4	100%
1.7547	4	100%
0.5264	12	100%
0.1755	12	100%
0.0526	12	75%
0.0175	12	50%
0.0053	12	8%
0.0018	12	0%
0.0005	12	0%
0.0002	12	0%

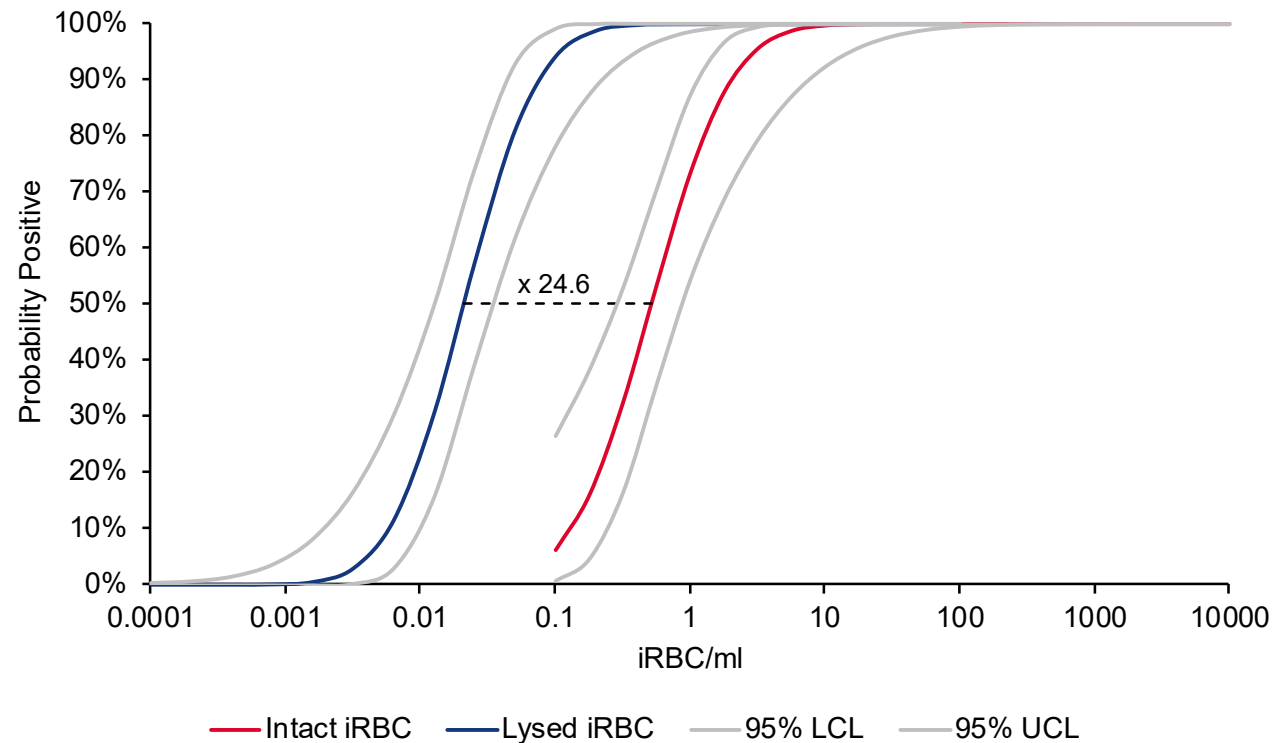
LOD	iRBC/ml (95% CI)
50%	$2.1 (1.3 - 3.4) \times 10^{-2}$
63%	$2.9 (1.9 - 5.3) \times 10^{-2}$
95%	$10.7 (5.8 - 39.7) \times 10^{-2}$



Note: study to increase to 48 replicates is ongoing in collaboration with Roche Molecular Systems (Pleasanton, CA).

Lysis of iRBCs increases cobas Malaria sensitivity 25-fold

- 50% LOD differs a factor ~25 between the intact iRBC panel and the lysed iRBC panel



Conclusions

- *Plasmodium falciparum* standards established
- Analytical sensitivity of Malaria NAT assays determined
- Run controls and panels can be prepared in assay-compatible blood matrix
- Characterized culture supernatant can be used for reference materials in plasma

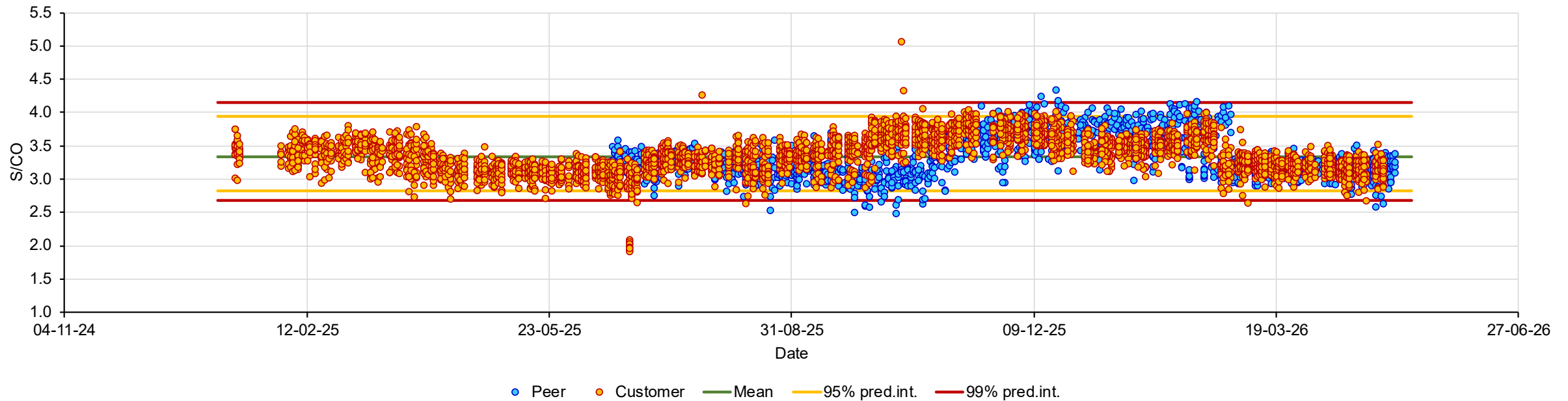
Key features of new run control reproducibility report

- Transparent comparisons between laboratories, instruments, assay reagent lots and run control batches
- Quality control alerts when proportion of weak reactivity is too high
- Limits in QC charts calculated based on assay-specific distribution of response values
 - TMA NAT: distribution-free statistics
 - PCR NAT: normal distribution
 - Serology: lognormal distribution

Assay-specific statistical analysis on run control results

- Example: Abbott Alinity s HBsAg results on our multi-marker run control for this assay

Figure 1. Levey-Jennings chart



Customer results are grouped to identify the source of variability

- A historically established alert limit (dashed line) is used for the assessment
 - Based on large amount of data on our standardized run controls

Figure 2. Scatter plot of customer results by Product Batch / Test Reagent Lot combination

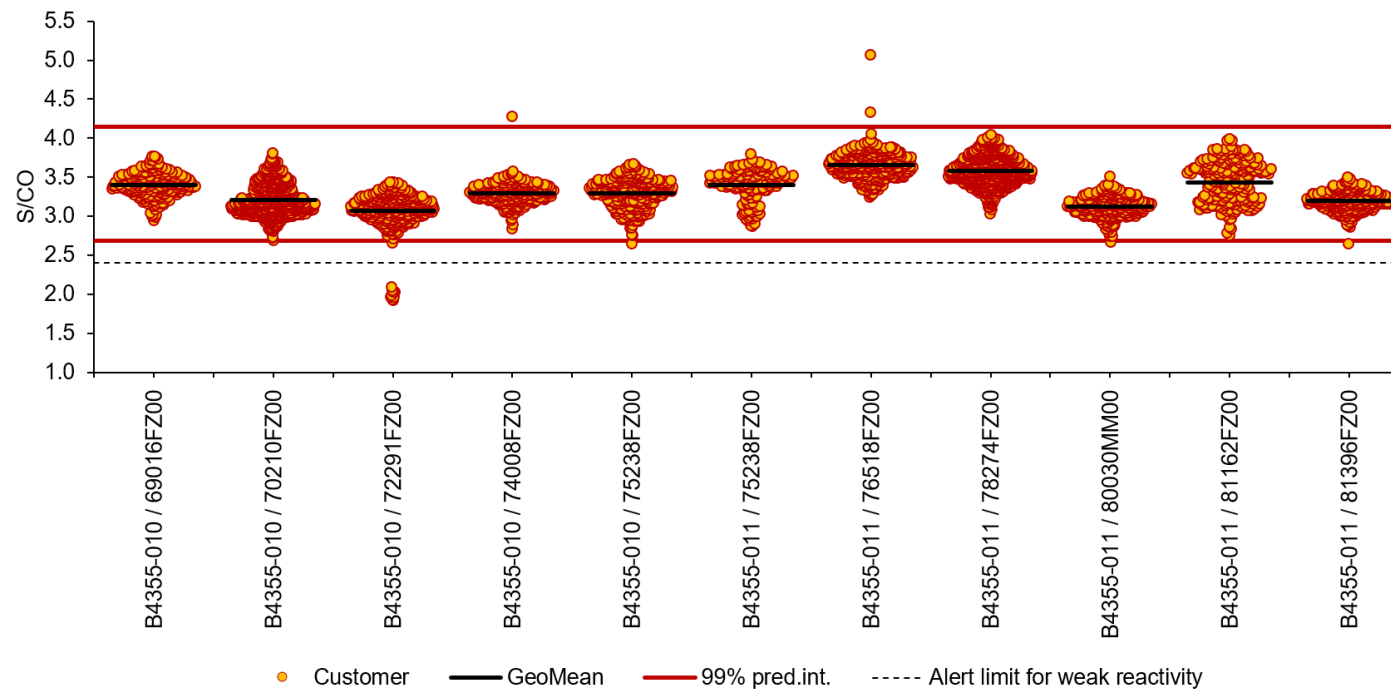
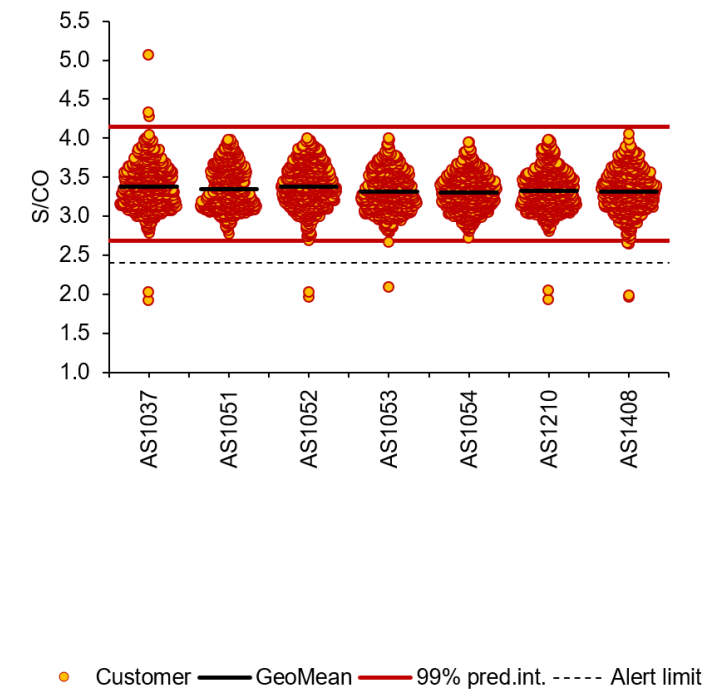


Figure 3. Scatter plot of customer results by equipment



Deviating combinations trigger a quality control alert

- Combinations are flagged when >1.5% of results is beyond the alert limit

Quality control assessment of the test system

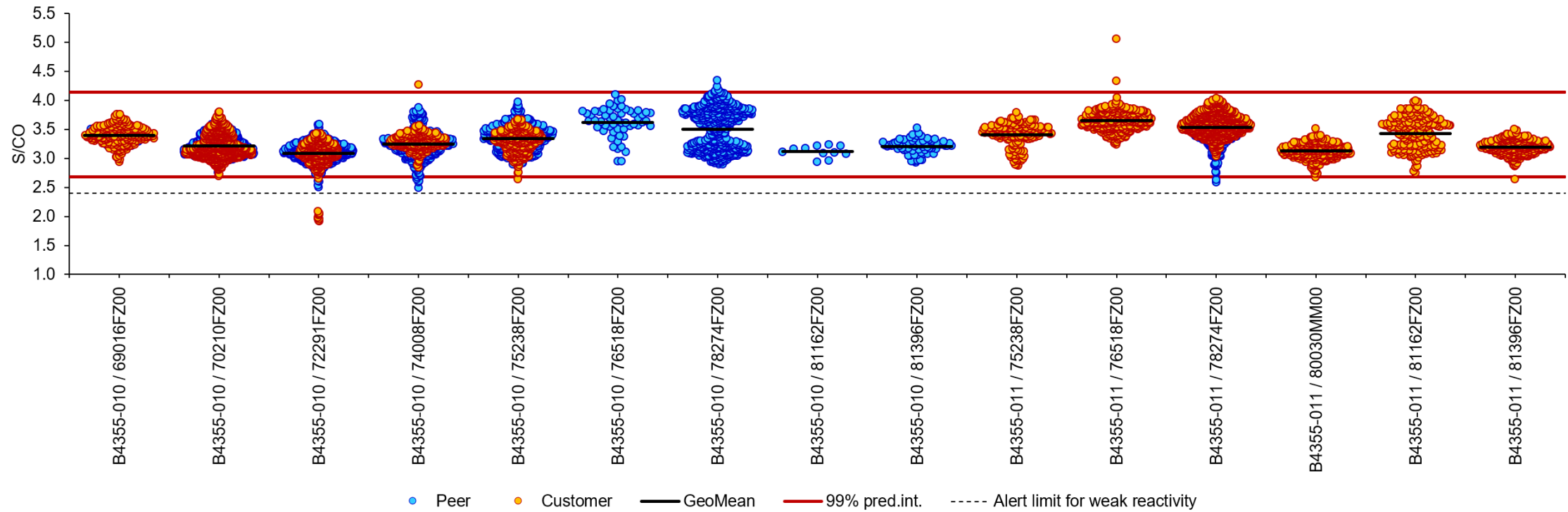
QUALITY CONTROL ALERT: One Product Batch / Test Reagent Lot combination in this report exceeds the acceptance criterion¹ (see highlighted row in Table 4). Root cause analysis is recommended.

Table 4. Summary of customer results by Product Batch / Test Reagent Lot combination

Product Batch	Test Reagent Lot	GeoMean	n	Results < Alert limit	Start	End
B4355-010	69016FZ00	3.40	225	0 (0.00%)	13-01-25	04-03-25
B4355-010	70210FZ00	3.20	734	0 (0.00%)	28-02-25	06-06-25
B4355-010	72291FZ00	3.07	348	9 (2.59%)	27-05-25	11-07-25
B4355-010	74008FZ00	3.29	243	0 (0.00%)	08-07-25	13-08-25
B4355-010	75238FZ00	3.29	300	0 (0.00%)	08-08-25	15-09-25
B4355-011	75238FZ00	3.40	161	0 (0.00%)	16-09-25	04-10-25
B4355-011	76518FZ00	3.65	338	0 (0.00%)	03-10-25	13-11-25
B4355-011	78274FZ00	3.58	780	0 (0.00%)	08-11-25	13-02-26
B4355-011	80030MM00	3.13	288	0 (0.00%)	04-04-26	02-05-26
B4355-011	81162FZ00	3.43	209	0 (0.00%)	10-02-26	06-03-26
B4355-011	81396FZ00	3.20	297	0 (0.00%)	04-03-26	11-04-26

Results are compared with data on reagent lots used by peers

Figure 4. Scatter plot of results by Product Batch / Test Reagent Lot combination across all customers



Customers can compare their overall performance to peers

Figure 5. Scatter plot of results by customer (customer vs individual peers)

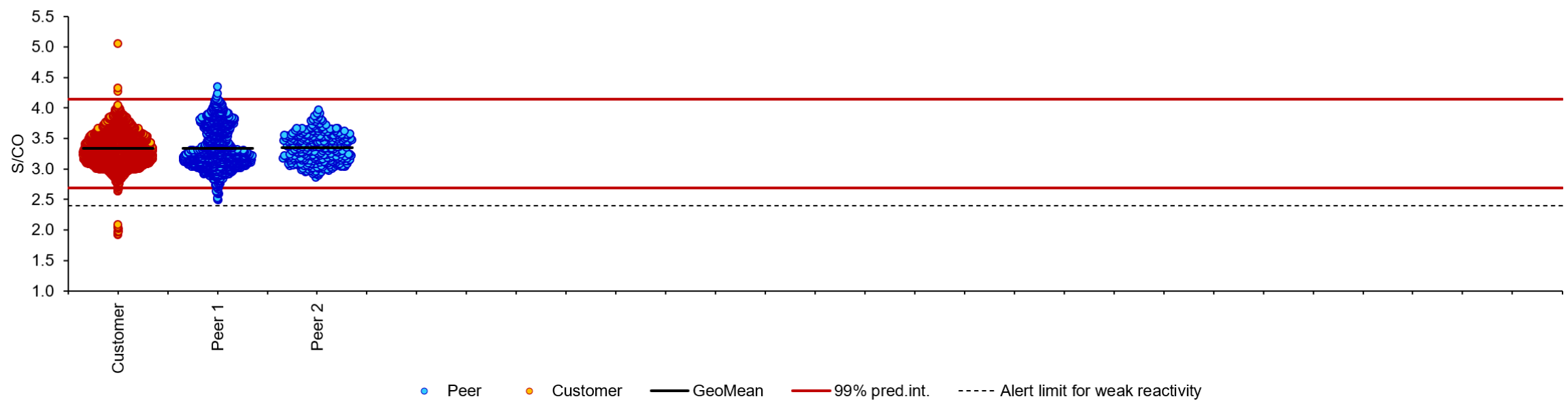


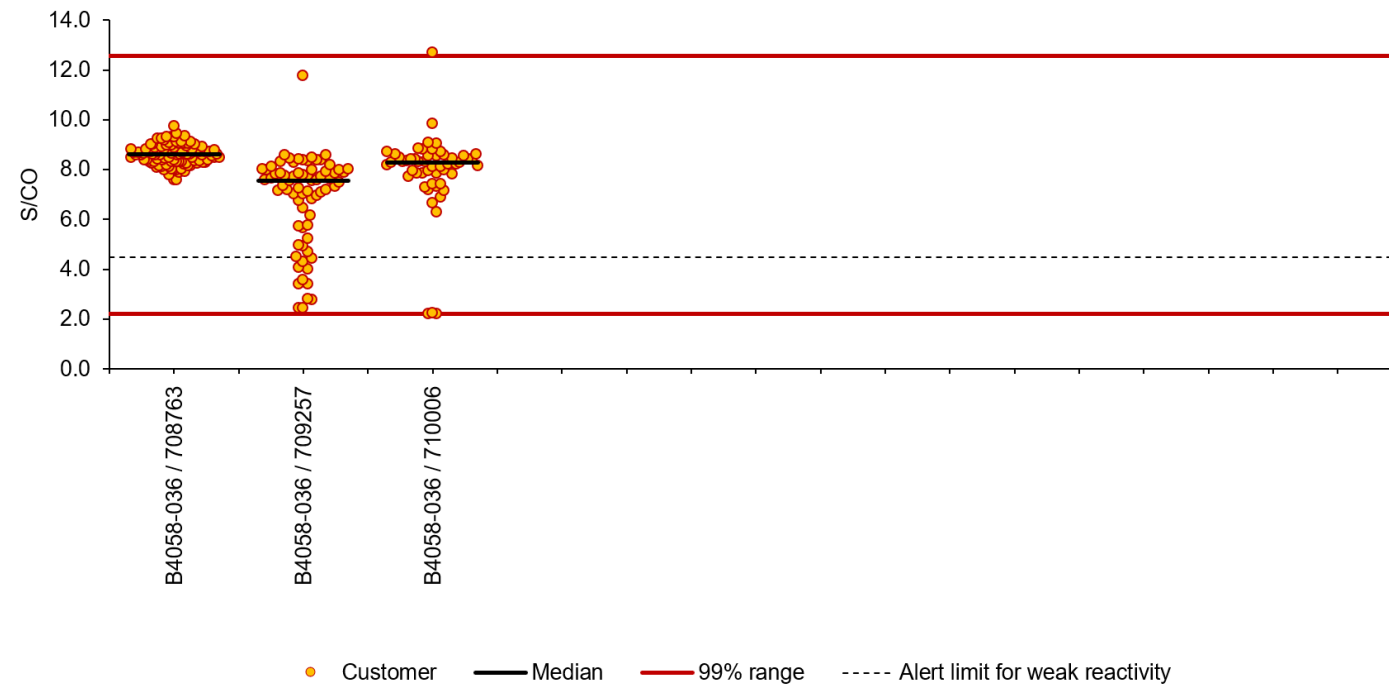
Table 7. Summary of results by customer (customer vs individual peers)

Laboratory	GeoMean	n	Results < Alert limit	Start	End
Customer	3.34	3923	9 (0.23%)	13-01-25	02-05-26
Peer 1	3.33	1194	0 (0.00%)	18-06-25	07-05-26
Peer 2	3.34	315	0 (0.00%)	30-07-25	05-05-26

Reagent lots with reduced analytical sensitivity

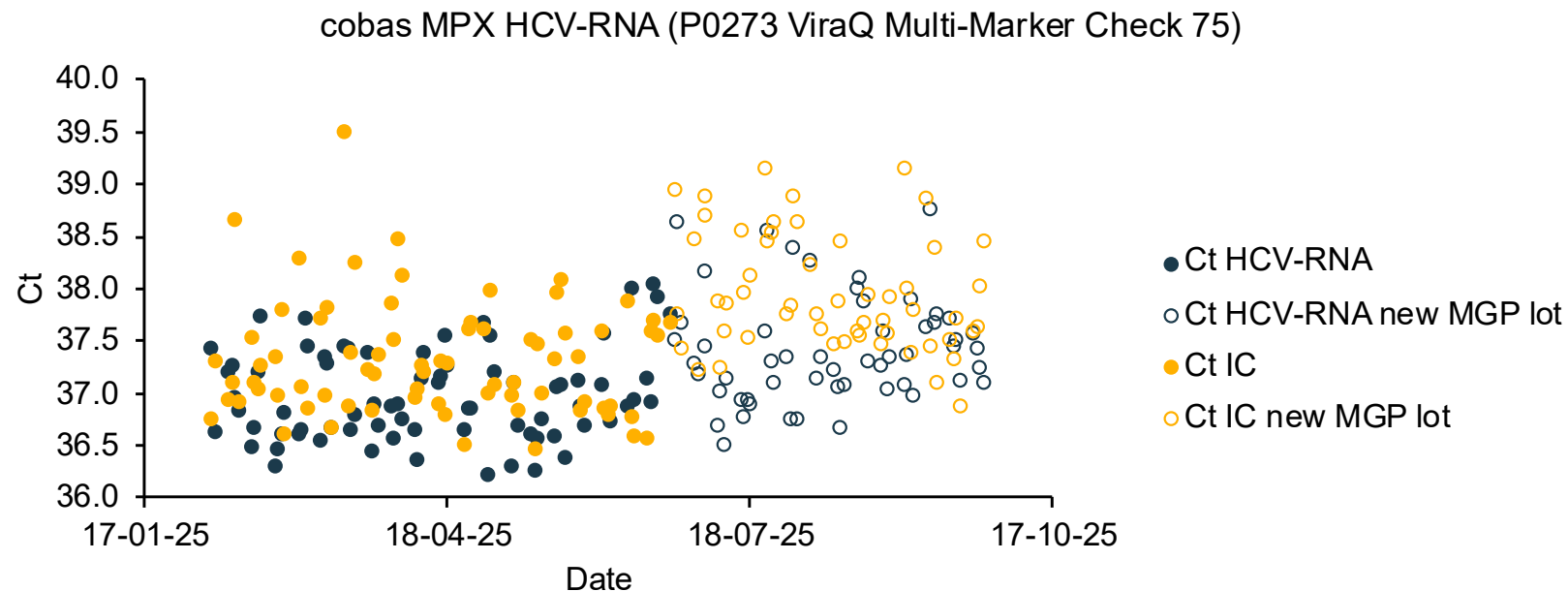
- Procleix Ultrio Elite results on our HCV-RNA run control
- Positioning (concentration) of the run control is crucial

Figure 2. Scatter plot of customer results by Product Batch / Test Reagent Lot combination



Automatic data transfer to DataQ Analytics allows for more in-depth analysis

- External quality control (EQC) data files contain additional test parameters
- Extraction reagent in cobas NAT assays: Magnetic Glass Particles (MGP)
- Ct values on both run control and internal control (IC) increased upon new MGP lot (open circles)



Conclusions

- New run control reproducibility report enables comparison of test parameters and provides QC assessment
- Root cause analysis of deviating results is facilitated by the new report
- DataQ Analytics automatic data transfer further improves the effectiveness of monitoring