

Case handling on abnormal UA results

IVD International Clinical Application Department

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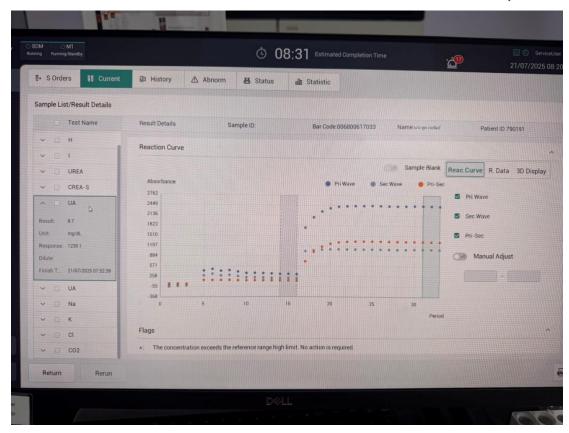
04. Case Summary

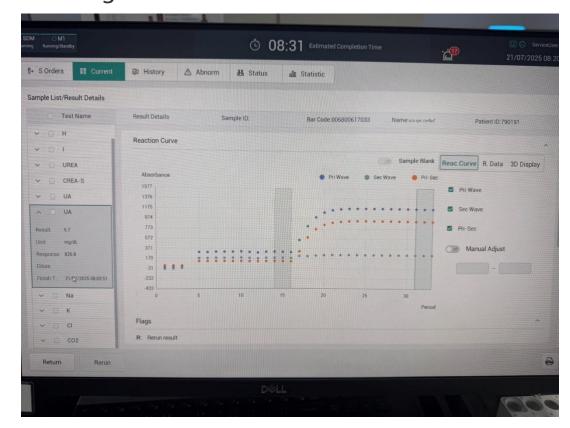


Case Background

Feedback from Hospital B(Large testing volume 500-700 samples per day): There have been multiple cases where the initial test results and the faulty results showed interference or abnormal reaction curve,--Can be the 1st results lower than the 2nd one, and can the 1st higher than the 2nd

Background





1st result

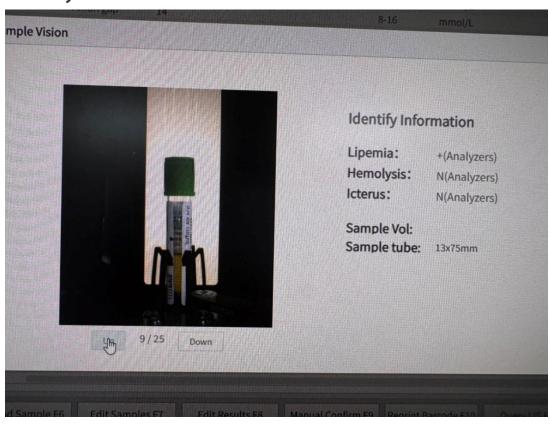
2nd result

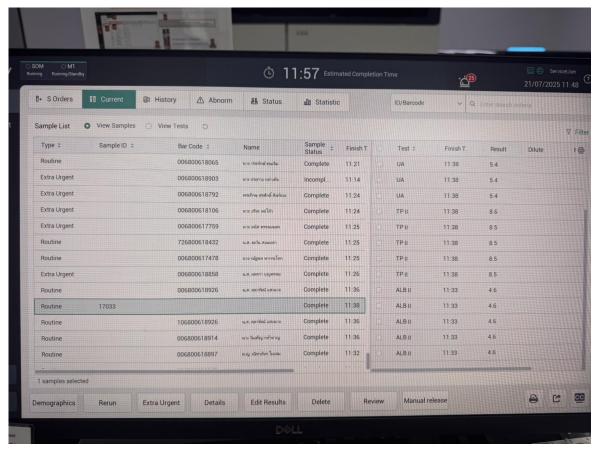


Case Background

Feedback from Hospital B: There have been multiple cases where the initial test results and the

faulty results showed interference or abnormal reaction curve





Sample SI information

Sample Repeatability



Troubleshooting Conducted

- Full system maintenance: All probes and mixers were cleaned and maintained, but the issue persisted.
- Adjustment of testing sequence and carryover pair: Test sequence follow the default setting; Carryover pairs were set for ALB/TP (ALB/TP not the carryover pairs of UA, just avoid the higher immunoglobulin which might cause cross-contamination to UA). However, anomalies still occurred on the 22nd July.
- Replacement of reagent carousel water: To address the serum index showing "L+", all water in the reagent carousel was replaced with sterile water for injection.
- Exclusion of endogenous interference: On the 21st and 22nd, ALB and TP were measured for samples 621624 and Sample 617033. The reference range for Globulin (Glo) is 2–3 g/dL, but both samples slightly exceeded the upper limit:
 - 1)Sample 621624: TP = 8.3 g/dL; ALB = 4.6 g/dL; Glo = 3.7 g/dL
 - 2) Sample 617033: TP = 8.6 g/dL; ALB = 4.6 g/dL; Glo = 4.0 g/dL
- Sample pretreatment confirmed: 4500rpm, 10mins; Heparin tube
- Reagent/Calibrator confirmed: within the onboard stability;

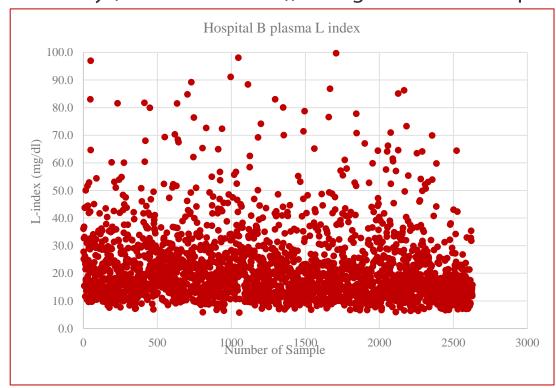


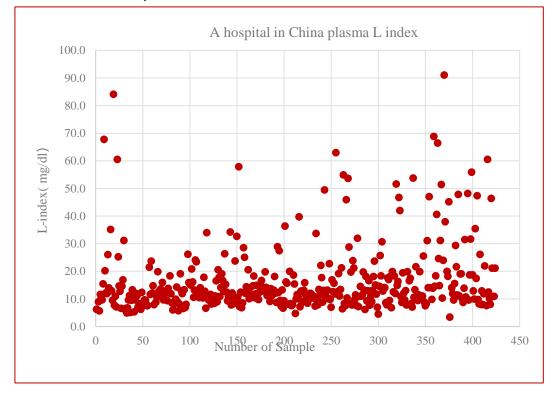


Analysis on Sample Pretreatment

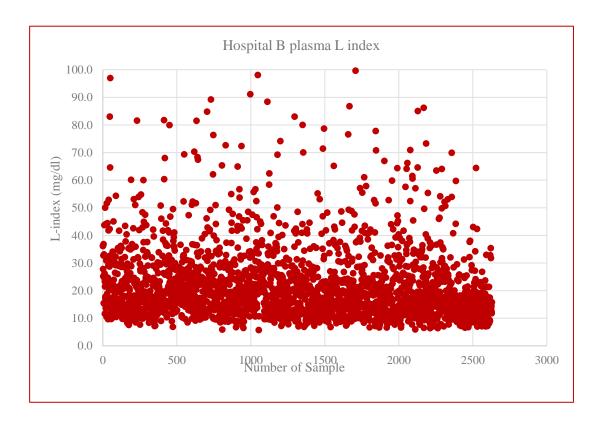
Analysis of Matrix component Content in Plasma

Lipemic index in test samples form insoluble particles that do not participate in the main reaction but cause turbidity (with absorbance), acting as "Matrix component" in the reaction system.





Analysis of Matrix component Content in Plasma



Flag	L	Н	I
N	40	50	4
+	225	150	15
++	450	300	25
+++	900	450	35
++++	1800	900	55
++++			

Mindray Serum Index Tier Classification criteria

When compared with hospitals of the same level in China, the L serum index in samples from Hospital B is elevated. However, most of the samples still have an L serum index within the normal range (less than 40 mg/dl). The matrix component content in the plasma samples from Hospital B is also within the normal range.



Property comparison between Serum and Plasma

ltem	Serum	Plasma
Matrix component Composition	Fibrin, charged with adsorbed ions; occasional severe lipemia	Polymers of hydrophobic substances adsorbed by negatively charged heparin
Change Trend	The size of Matrix component tends to increase, hard to decrease (stable structure)	The size of Matrix component can either be increased or decreased (unstable structure, limited by charge effects)
Change Impact	Absorbance increases	Absorbance may increase or decrease
Influencing Factors ©2021 深圳迈瑞生物医疗电子	Weak surfactants cause Matrix component aggregation 股份有限公司版权所有	Strong surfactants disperse Matrix component; weak surfactants cause aggregation

■ Summary:

Plasma: Matrix component cannot be completely eliminated and are unstable.

- If the reaction system is contaminated by an amount of strong surfactants that exceeds its anti-interference capacity, the impurities will disperse, and the turbidity will decrease.
- If the reaction system is contaminated by an amount of weak surfactants that exceeds its anti-interference capacity, the impurities will aggregate, and the turbidity will increase.

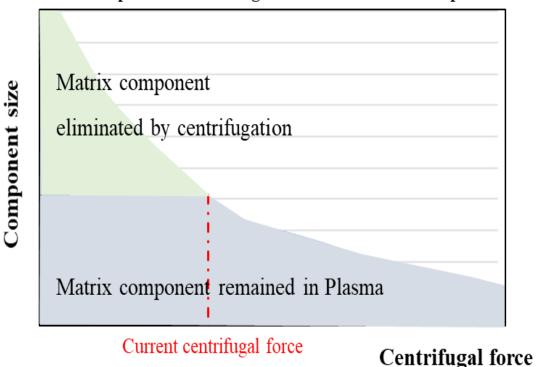
Serum: Serum is a more stable sample type for analysis because with a proper sample pre-processing can effectively eliminate fibrinogen (a key impurity). By switching to serum samples, this may significantly reduce this issue that are often caused by these impurities.



Characteristics of Plasma Matrix component

In plasma, heparin is a strongly negatively charged substance. This property allows it to attract and adsorb numerous hydrophobic substances, forming particulate matter(particles). Large particles are easily removed by centrifugation, while small particles are difficult to eliminate.

Relationship between centrifugal and residual matrix components



Summary:

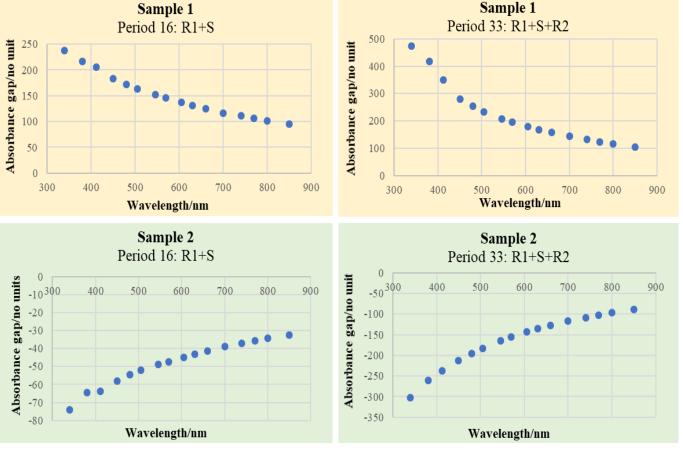
- 1. The current centrifuging condition could minimize the matrix component effect in plasma but they cannot remove them as completely as with serum.
- 2. Changes in the matrix component size and quantity lead to changes in turbidity which cause a change in absorbance.
- The primary focus for troubleshooting this issue is to eliminate contamination from excessive surfactants, as matrix component effect are unavoidable.



Analysis on Reaction Curve

When sample impurities enter the UA reaction system, they are influenced by contamination, which causes them to aggregate. This leads to differences in turbidity changes.

The graphs below illustrate this effect in two abnormal samples:



Experiment:

To assess the impact of contamination, select 2 contaminated UA test samples. Then measure at 2 specific points in the reaction with the individual absorbance at 16 different wavelengths and record the trend of the absorbance changes on the spectrum:

- Point1: At the time of adding R1 reagent to the samples
 (Cycle 16: R1+S)
- Point2: After the mixture of R1, the sample, and R2 has been fully mixed and equilibrated (Cycle 33: R1 + Sample + R2
 - X-axis: 16 wavelengths provided by BS-2800M (Unit: nm)
 - **Y-axis**: The absorbance gap/differences between first abnormal test and rerun

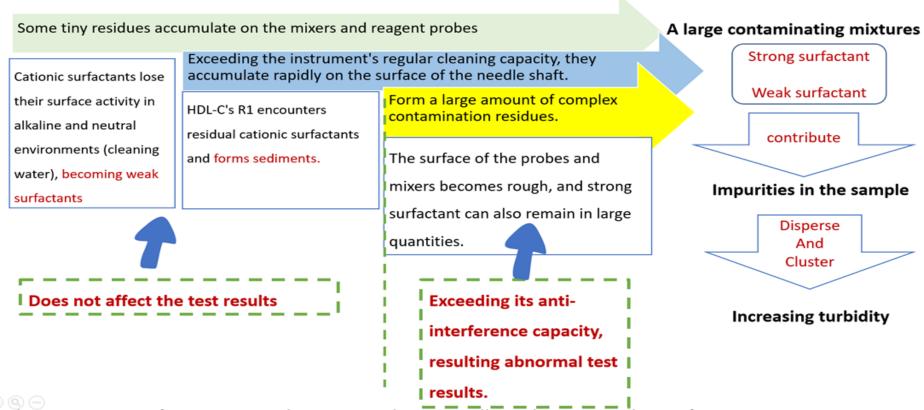
Fig. samples absorbance distribution on multiple wavelengths before and after reaction



Analysis on matrix component

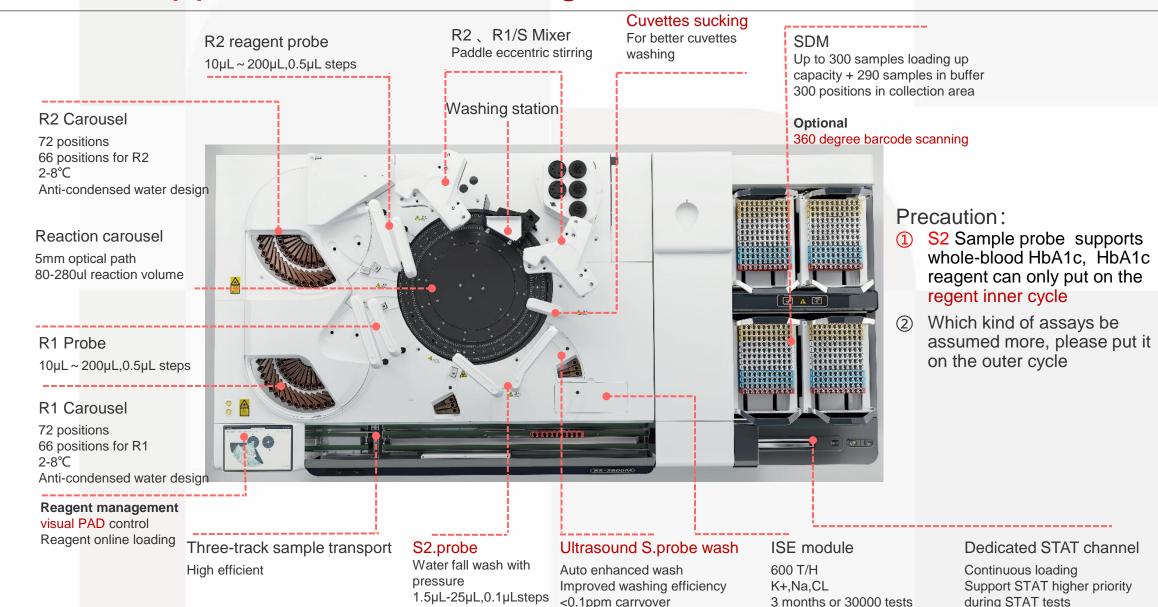
Sources of Contamination Causing Matrix component Aggregation/Dispersion

Surfactant residues and contamination pathways



- Initial residue: Cationic surfactants in acidic reagents leave small residues on probe surfaces.
- Deposit formation: Residues react with HDL-C reagent R1, forming deposits.
- Surface alteration: Probe surfaces become rough, altering their properties.
- Increased contamination: Substances that previously did not leave residues now accumulate, worsening

1.1 Overall appearance and configuration



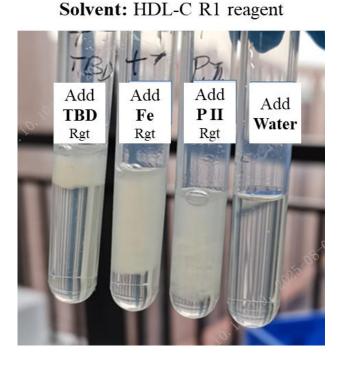
Avoid manual washing

stability

Analysis on allocation and Sequence

• The current allocation of items in the reagent carousels require adjustment.

Inner Ring		Outer Ri	ng
Parameter	Tests	Parameter Test	
ALB II	152	a-AMY Manual	8
ALP	129	AST	148
ALT	146	Ca	58
CK	12	D-bil-D II	118
CO2	174	Fe	18
CREA-S	263	Glu-H	120
D-Bil-V	7	HDL-C	52
HbA1c-3	53	LDL-C	36
HS-CRP	11	Mg lI	28
LDH	9	PII	61
T-Bil-V	7	T-bil-D II	117
TP II	122	TC	55
TPUC	30	TG	59
UIBC	15	UA	89
		UREA	191
In total	1130	In total	1158





- Fig. 1(left) Current allocation of parameters in the reagent carousel
- Fig. 2 (right) Experiments of HDL-C R1 reagent producing precipitation by acidic reagent

- Four acidic reagents are allocated in one ring (same reagent carousel ring), and three of them are used frequently (have a high testing frequency).
- Residue or sedimentation from acidic reagents such as DBD, TBD, Fe, P which are acidic reagents, and HDL-C can leave over a large amount of weak surfactants. This causes impurities to aggregate within the reaction system, which in turn leads to an increase in turbidity and results in elevating or increasing absorbance.
- Residue of strong surfactants from TC, LDL-C, and cleaning agents can remain on a rough reagent probe surface. This causes impurities within the reaction system to disperse, which in turn can lead to a decrease in turbidity.

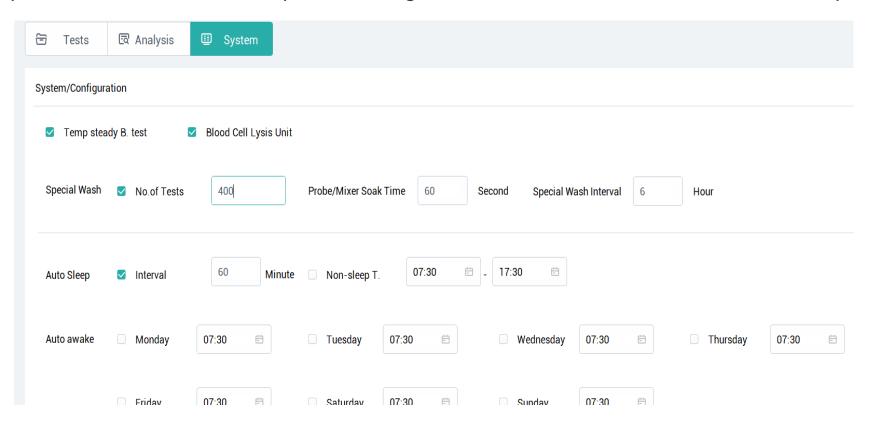


Recommendations

Instrument Cleaning and Deposit Removal

Ensure cleaning water covers ≥4mm of the reagent probe's outer wall and fully submerges stirrer paddles.

- 1. Enable "Interval Test Insert Cleaning" (default: 400 tests) to enhance cleaning;
- 2. Temporarily replace DA with DC for intensive probe cleaning (restore DA afterward) to remove surfactant deposits.



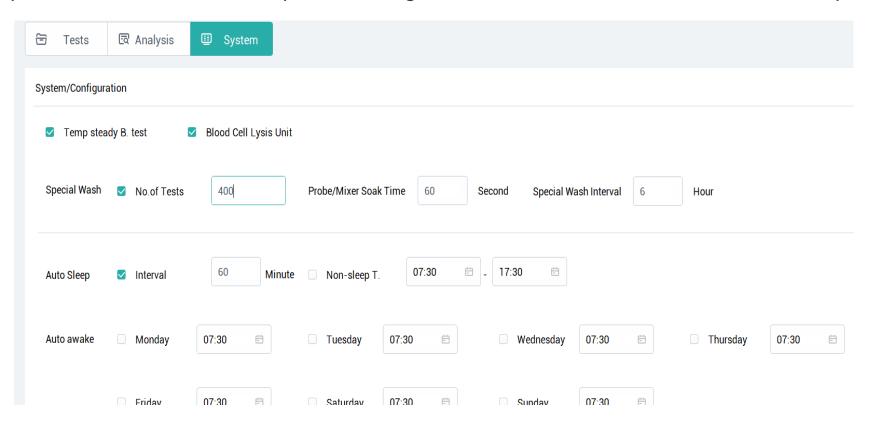


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Recommendations

2. Adjust Test Sequence of both the inner and outer

СУ

رحلم			
1	α-ΑΜΥ	18	UA
2	AST	19	TPUC
3	ALT	20	CREA-S
4	T-Bil-V	21	TG
5	T-Bil-D	22	HDL-C
6	РΠ	23	TC
7	D-Bil-V	24	LDL-C
8	D-Bil-D	25	ТРШ
9	Fe	26	TP
10	UIBC	27	ALBΠ
11	Ca	28	LDH
12	MgⅡ	29	UREA
13	ALP	30	HS-CRP
14	GLU-H	31	Hb-3
15	CK	32	HbA1c-3
16	CO2	33	Water
17	LIP		

2. Adjust the reagent allocation

Inner R	ing		Outer Ring	
Parameter	Tests	Parame	eter Tests	
ALT	146	a-AMY M	Ianual 8	
T-Bil-V	7	AST	148	
T-bil-D II	117	D-bil-D) II 118	
PII	61	Fe	18	
D-Bil-V	7	UIBO	C 15	
ALP	129	Ca	58	
CO2	174	Mg l	I 28	
CREA-S	263	Glu-F	H 120	
TG	59	UA	89	
ALB II	152	HDL-	C 52	
LDH	9	TC	55	
TPUC	30	LDL-	C 36	
HbA1c-3	53	TP I	I 122	
		UREA	A 191	
		HS-CI	RP 11	
		CK	. 12	
In total	1207	In tot	al 1081	

Words in Blue indicates that the positions of the inner and outer rings need to be adjusted.

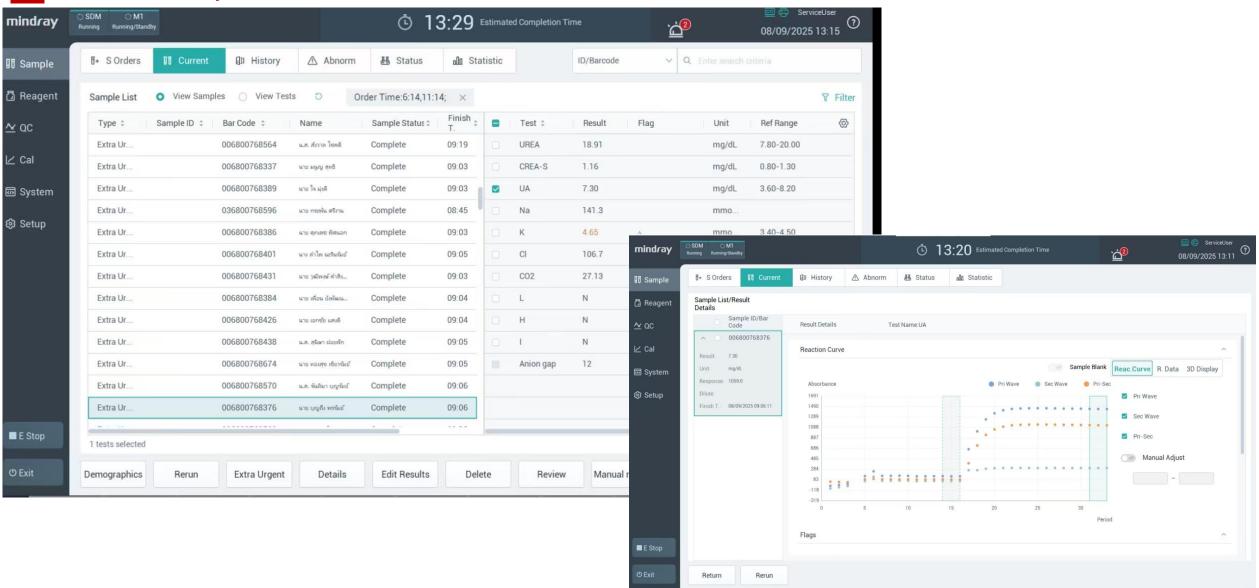


So with all these measures taken, this problem should be resolved.

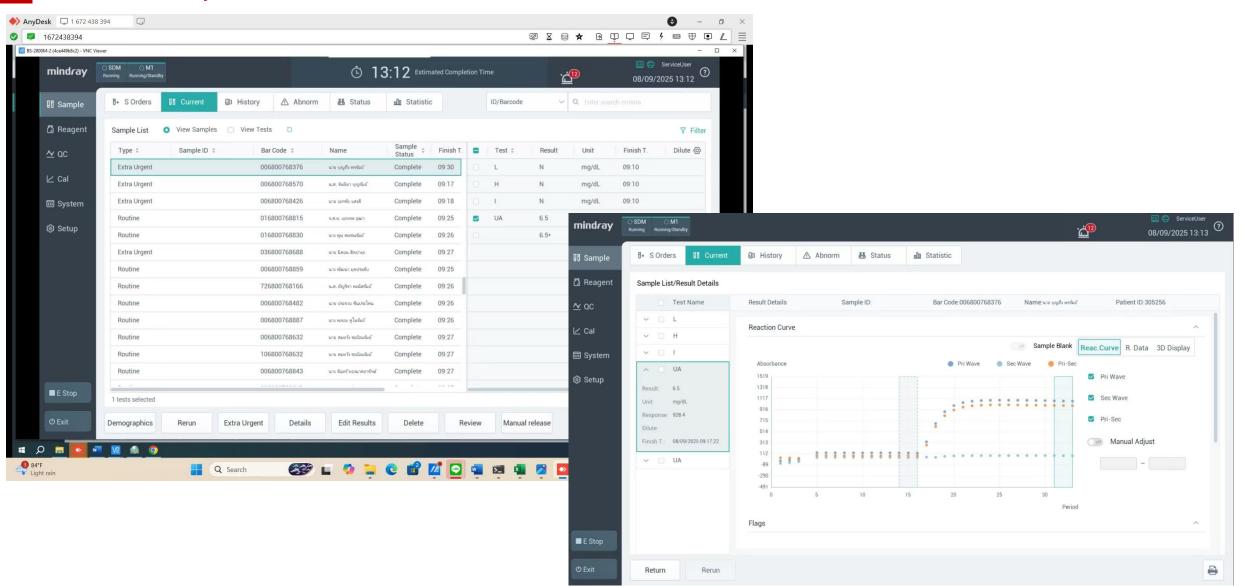
However, although the frequency of the problem has been reduced, the problem itself still persists



Case Analysis



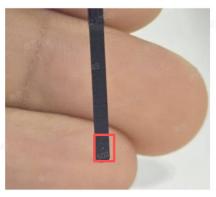
Case Analysis



Case Analysis





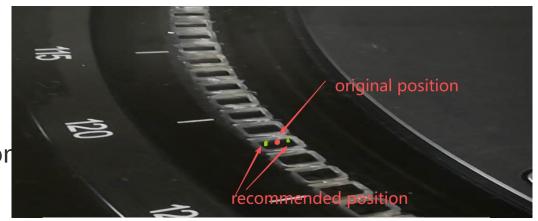


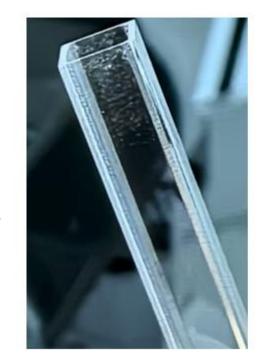


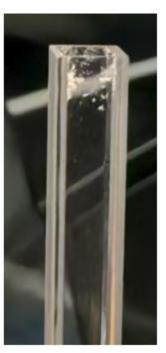


Case Solution

- 1. Move D-bil-D Π and Fe from the outer ring to the inner ring, and move ALP from the inner ring to the outer ring.
- 2. Use a flashlight to check for contamination above the reaction cup. If there is any contamination, it needs to be taken out and cleaned with CD80;
- 3. Shut down the machine for debugging, and debug the R1 reagent probe of each instrument:
- 1) The probe must be adjusted by service tool in a horizontal way;
- 2) Adjust the position of the probe 1mm to the left or right in the direction of movement; do not center it.





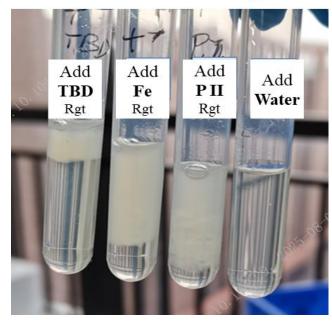


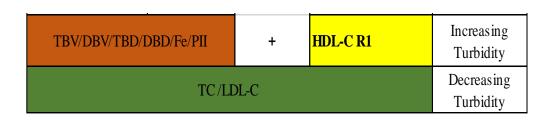
Case Analysis

The first measure aims to cut off pollution sources, mainly considering the impact of acidic reagents on turbidity. Previously, it was suggested that acidic reagents should not be overconcentrated, but now it is necessary to avoid the impact of all acidic reagents. Therefore, DBD and Fe need to be moved to the inner circle. Meanwhile, to balance the number of tests in the inner and outer circles, the position of ALP will be adjusted to the outer circle.

Inner Ring			Outer Ri	ng
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TP II	122		TC	55
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UIBC	15		UA	89
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Solvent: HDL-C R1 reagent





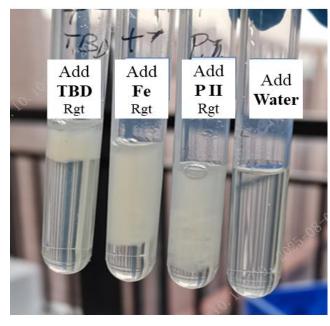


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TPUC	30	TG	59
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		UREA	191
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Solvent: HDL-C R1 reagent







Case Summary

The second measure is a preventive one. If the first two measures are properly implemented, UA will temporarily return to normal. However, if splashing occurs, long-term use will inevitably lead to accumulated contamination in the reaction cups, along with other risks such as value jumps.









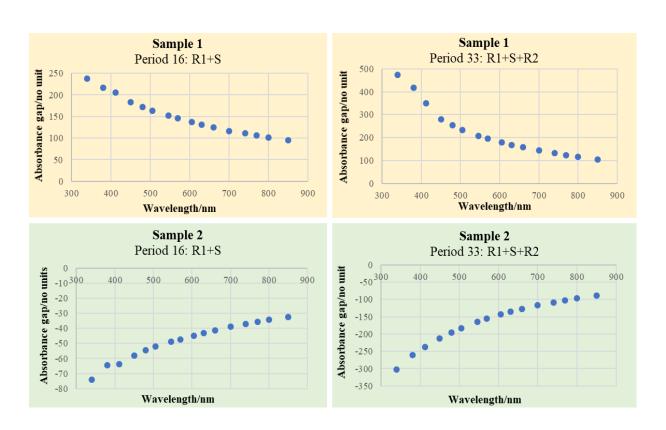




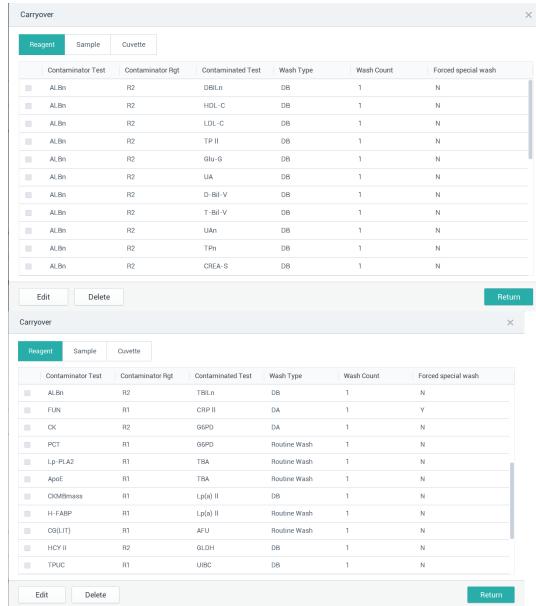


Case Summary

The third measure is intended to remove residual pollutants from the adjusted system. As the reaction characteristics clearly indicate the impact of other reagents on turbidity, the only paths for such reagent contamination are reagent probes and **reaction cuvette.** For reagent needles, their cleaning and maintenance processes are fully visible, so the risk of contamination is very low. However, if there is splashing from the reagent needles, it may affect the reaction cups. Hence, it is necessary to remove residual pollutants from the reaction cups.



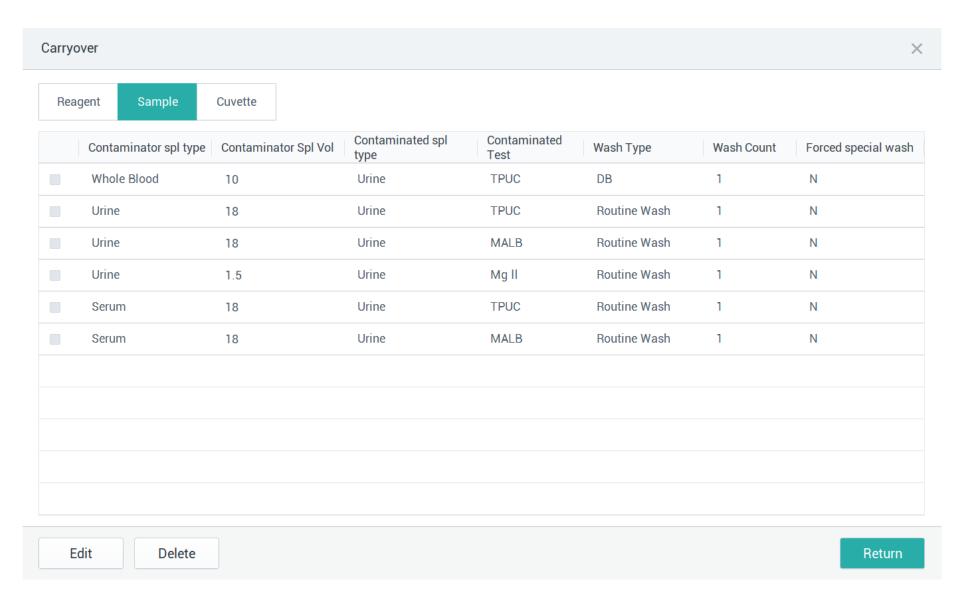
China domestic setting



Carryo	over						×
Rea	agent Sample	Cuvette					
	Contaminator Test	Contaminator Rgt	Contaminated Test	Wash Type	Wash Count	Forced special wash	
	ApoE	R1	TBA	Routine Wash	1	N	
	CKMBmass	R1	Lp(a) II	DB	1	N	
	H-FABP	R1	Lp(a) II	Routine Wash	1	N	
	CG(LIT)	R1	AFU	Routine Wash	1	N	
	HCY II	R2	GLDH	DB	1	N	
	TPUC	R1	UIBC	DB	1	N	
	FUN	R1	UIBC	DA	1	Υ	
	LIP	R1	TBA	DB	1	N	
	TG	R1	LIP	DB	1	Υ	
	TC	R1	LIP	DB	1	N	
	FUN	R1	CHE	DA	1	Υ	
E	Edit Delete					Returi	n _

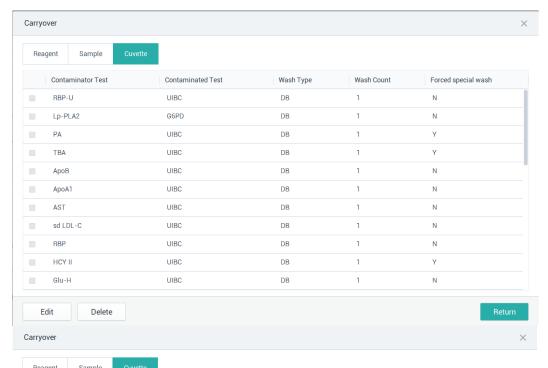
Solution

China domestic setting





China domestic setting



Hea	gent Sample Cuvette				
	Contaminator Test	Contaminated Test	Wash Type	Wash Count	Forced special wash
	Fe	UIBC	DB	1	N
	ASO II	UIBC	DB	1	N
	AFU	UIBC	DB	1	N
	C3	UIBC	DB	1	Υ
	C4	UIBC	DB	1	Υ
	DA	UIBC	DB	1	Υ
	β-НВ	UIBC	DB	1	Υ
	IgM	UIBC	DB	1	Υ
	IgA II	UIBC	DB	1	N
	PII	UIBC	DB	1	Υ
	DC	Fe	DB	1	N

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Delete

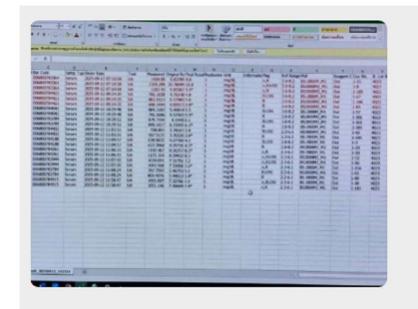
Rea	ngent Sample Cuvet	te			
	Contaminator Test	Contaminated Test	Wash Type	Wash Count	Forced special wash
	IgM	UIBC	DB	1	Υ
	IgA II	UIBC	DB	1	N
	PII	UIBC	DB	1	Υ
	DC	Fe	DB	1	N
	UIBC	Fe	Routine Wash	1	N
	TPUC	UIBC	DB	1	Υ
	LDH	UIBC	DB	1	Υ
	IgG	UIBC	DB	1	Υ
	UIBC	UIBC	DB	1	Υ
	T-Bil-V	UIBC	DB	1	Υ
	D-Bil-V	UIBC	DB	1	Υ



Solution

Background

- For this case, after doing the machine maintenance, reagent allocation and probe alignment, UA results temporarily return to normal;
- Long-term stability on sample depends on the dual guarantee of regular instrument maintenance and improvement of sample quality.



Today's results,M1 had no abnormal