D-bil-Vox result interference

IVD International Clinical Application Department

Sang

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Case Background

Background

Nakasero hospital-Crown Uganda with BS-600M had a concern about Direct bilirubin (vox) Negative value patients results for some neonates. The Sample handling protocol preanalytical, calibration, QC and Water quality are all ok. The competitor machine results are giving positive value and make sense.

Complain

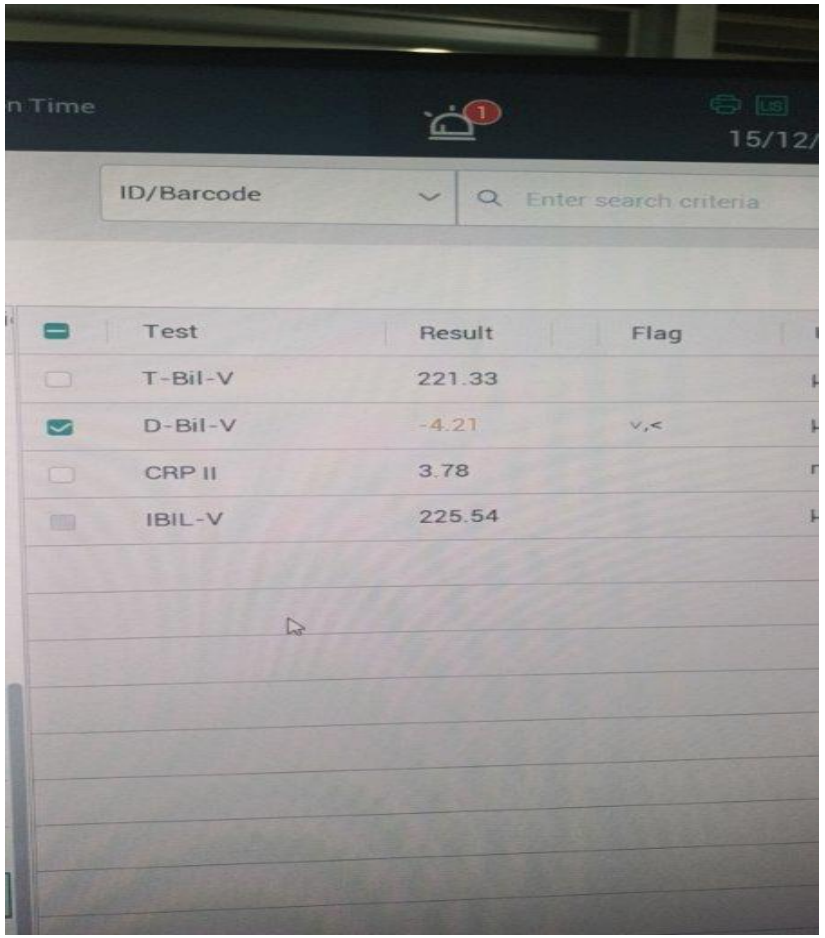
The customers complain about the Mindray Direct bilirubin results do not correlate with other platforms and with good QC results. The Negative Direct bilirubin is unreliable, thus leading to unnecessary rerun and repeats.

Expectation

The customer wanted crown Uganda and Mindray to find out the root cause of this issue and provide solution.

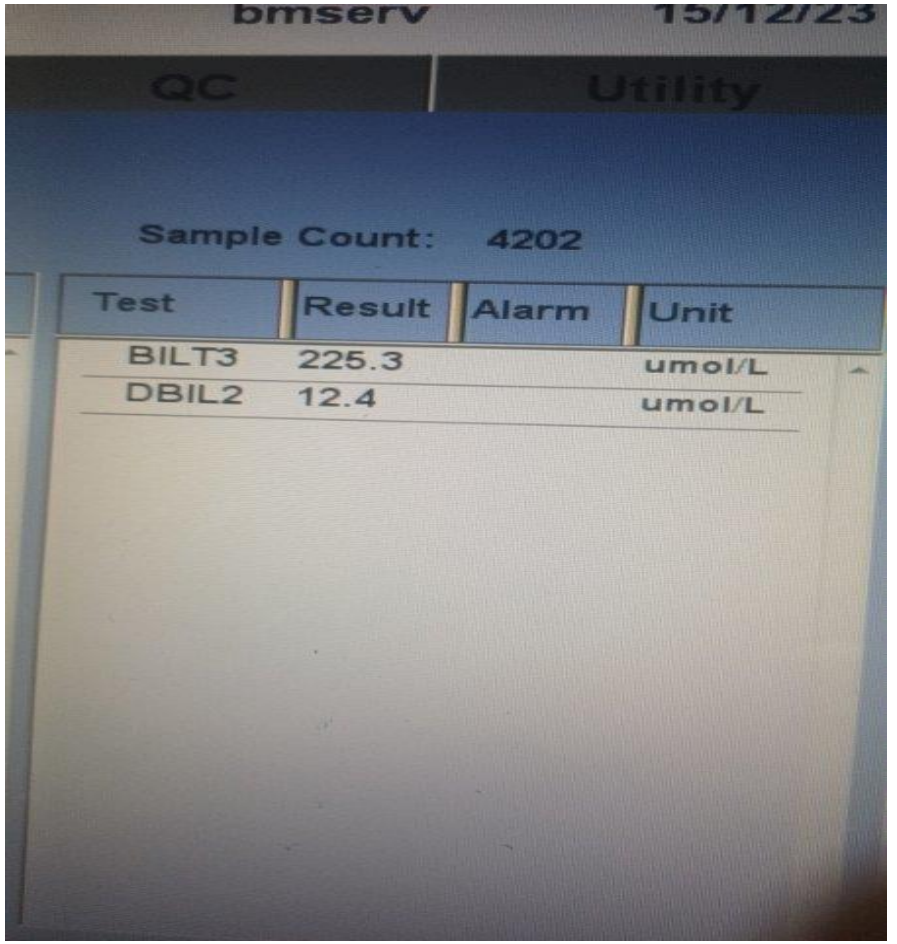
Case Background

Initial direct bilirubin Negative results



Unreliable Direct bilirubin result.

Reliable Total Bilirubin result.



Competitors machine results (Roche)

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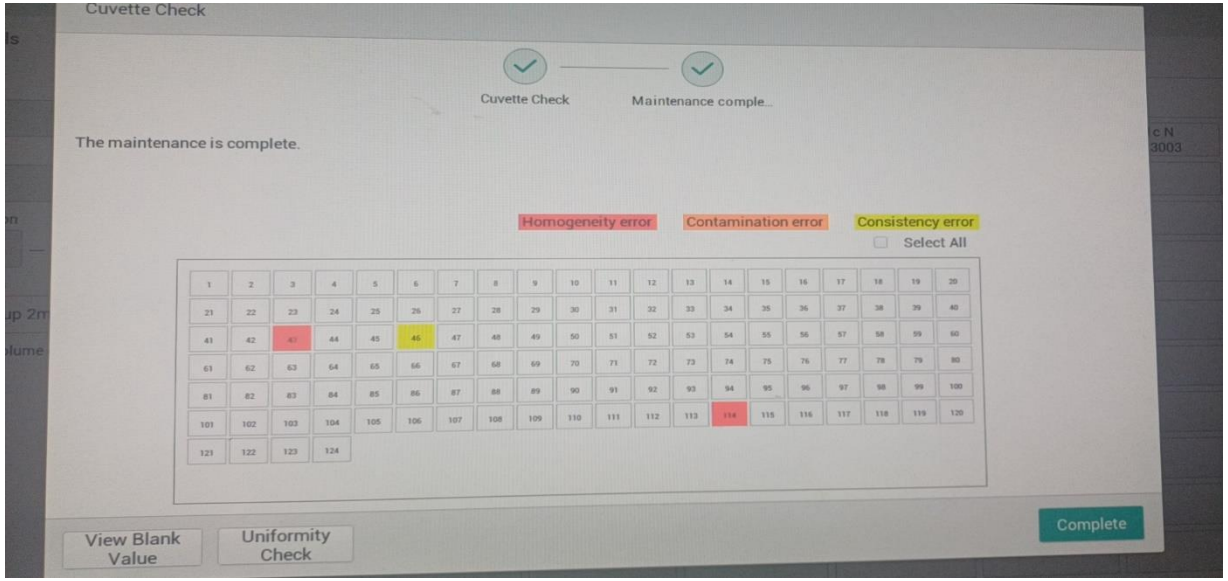
Rule out root cause ideas

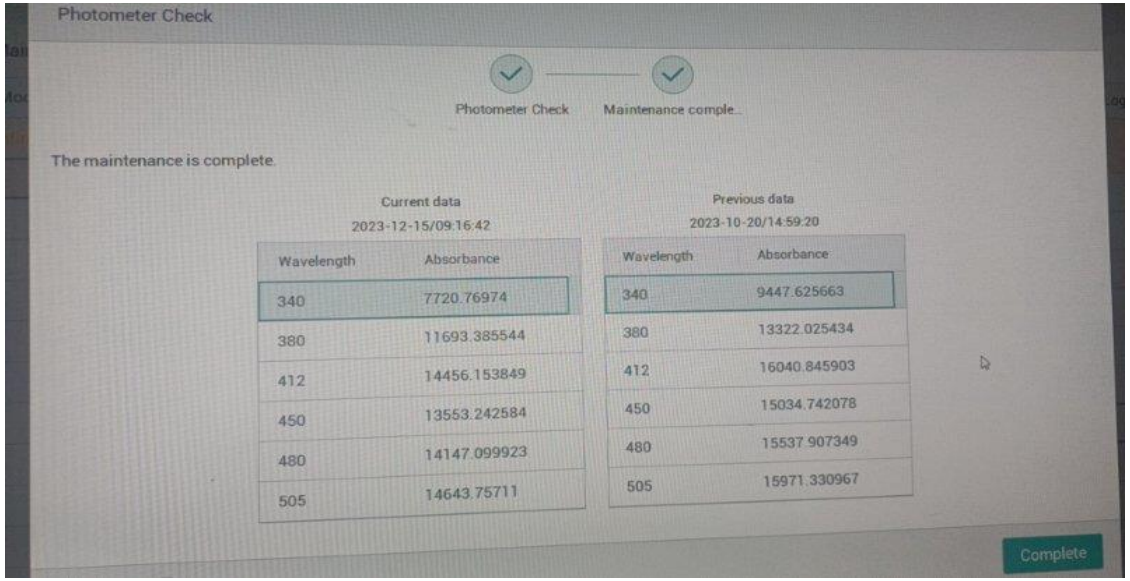
Sample status:

- sample clot
- Abnormal sample status (hemolysis, jaundice, lipemia); serum index excluded sample status interference.

Cross contamination:

perform maintenance on the analyzer. run cuvette check and photometer check.





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Rule out root cause ideas

Bad precision:

Run one sample five times. The precision is ok

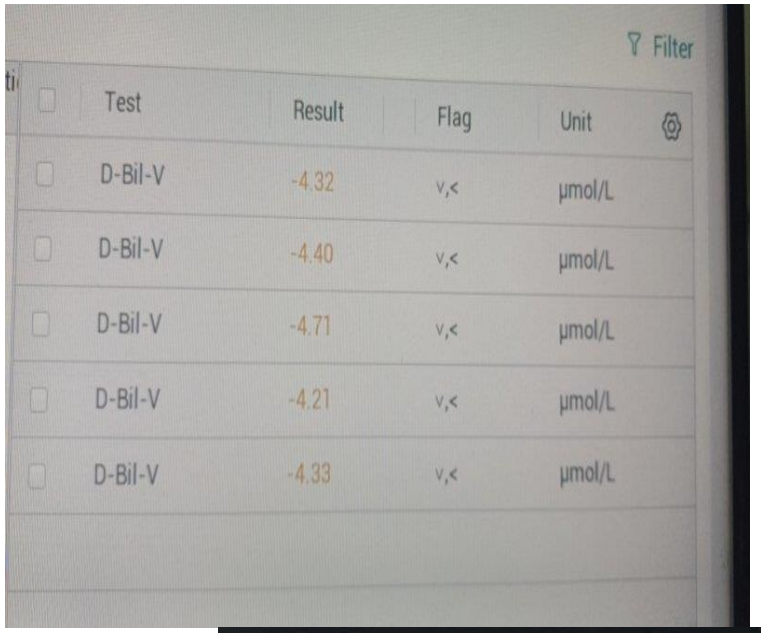
Interference:

Perform sample Dilution 1:10 results

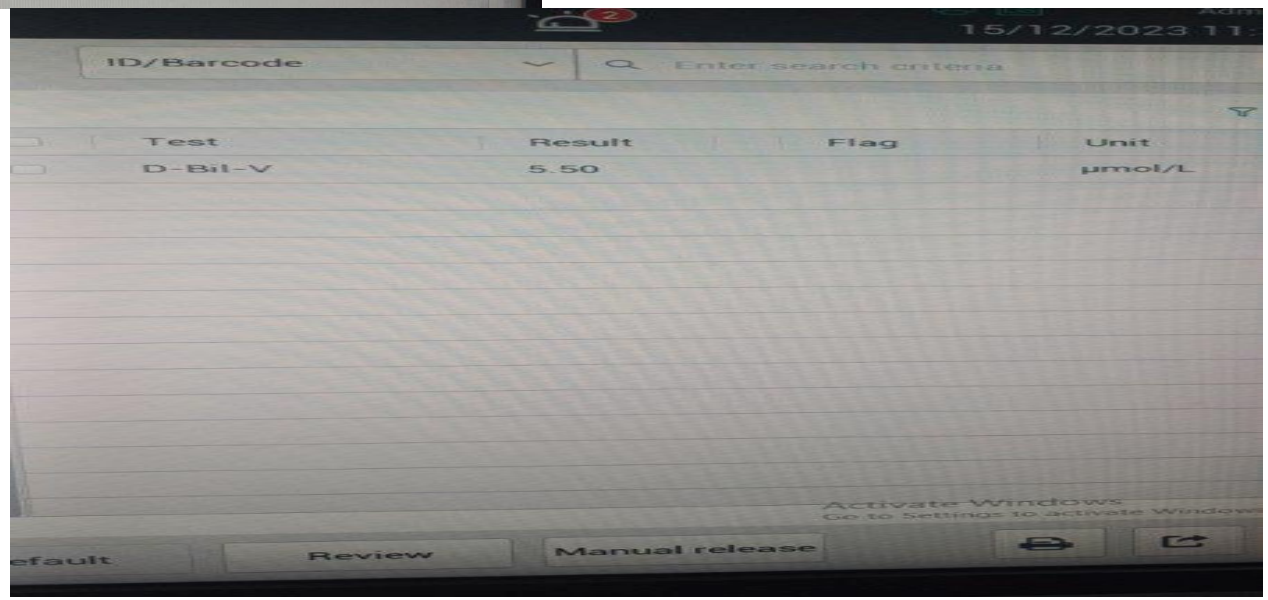
Which after dilution the results became 5.50 umol/l.

Recommendation:

The negative results may be caused by globulin interference. I would recommend you test the TP and ALB on sample and calculate the GLO.



1	-4.32
2	-4.4
3	-4.71
4	-4.21
5	-4.33
AVE	-4.394
SD	0.189
CV	-4.31%



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Case Idea Notice

D-Bil-V

Sample Stability

- Calibrators, QC materials and samples should be kept from light and heat. For calibrators and QC materials, after reconstitution and equilibrium to room temperature, they should be tested at once.

Methodology Comparison

- The reagent was improved from lot 140721004, the reagent with more updated lot number has better performance when comparing with Fujifilm Wako reagents.

Interference

- Result can be interfered by unknown medicine.
- γ-globulin can interfere test results, and cause negative results.

Results Issue

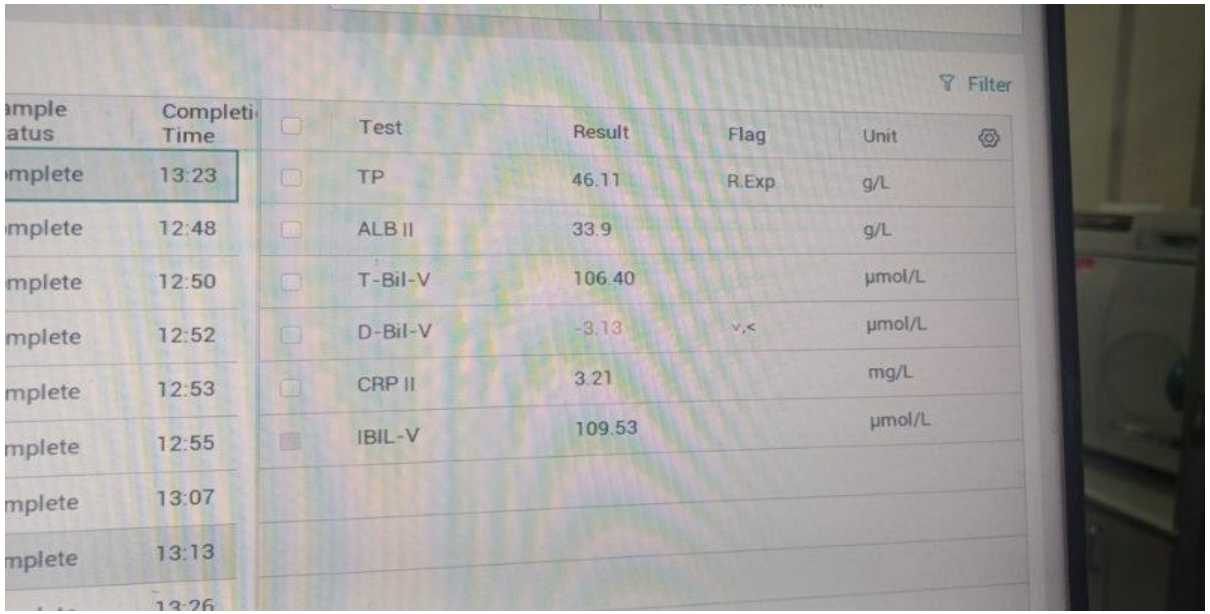
- Mindray reagents cannot test the Beckman L3 level QC, neither does the Fujifilm Wako reagent.
- Expired reagent, γ-globulin interference, expired calibration and cross-contamination could cause negative results.

Case Solution

Troubleshooting for gamma globulin interference.

The negative results is caused by globulin interference. It is recommended to test the TP and ALB on sample and calculate the GLO.

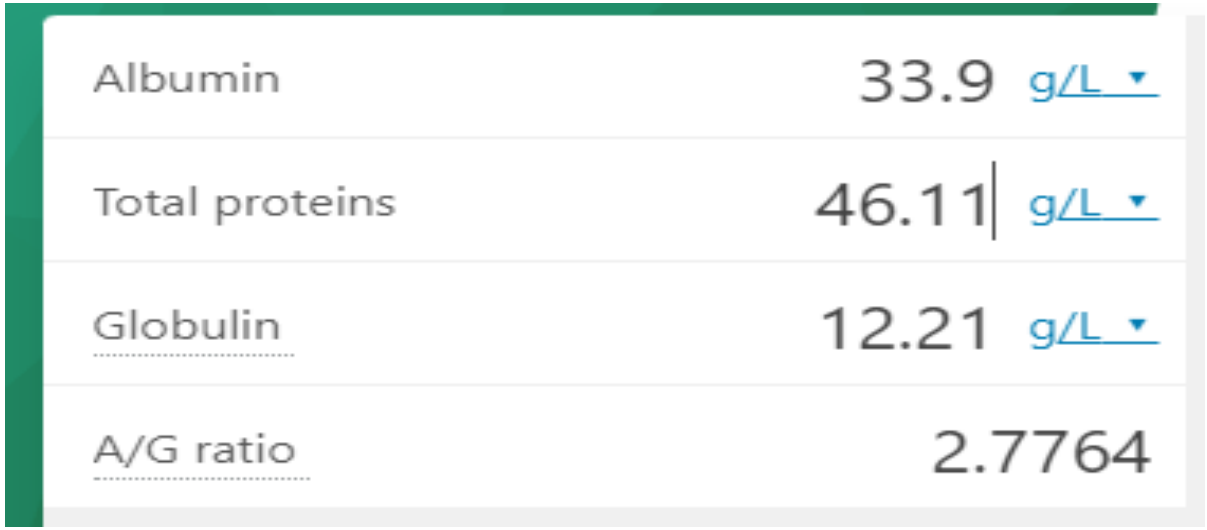
Other IgM, IgG, IgA and RF but not done



Globulin reference range:

- Globulin - 8.0 -16.0 g/L

Result were within normal range or neonate, denying immunoglobulin interference from the sample.



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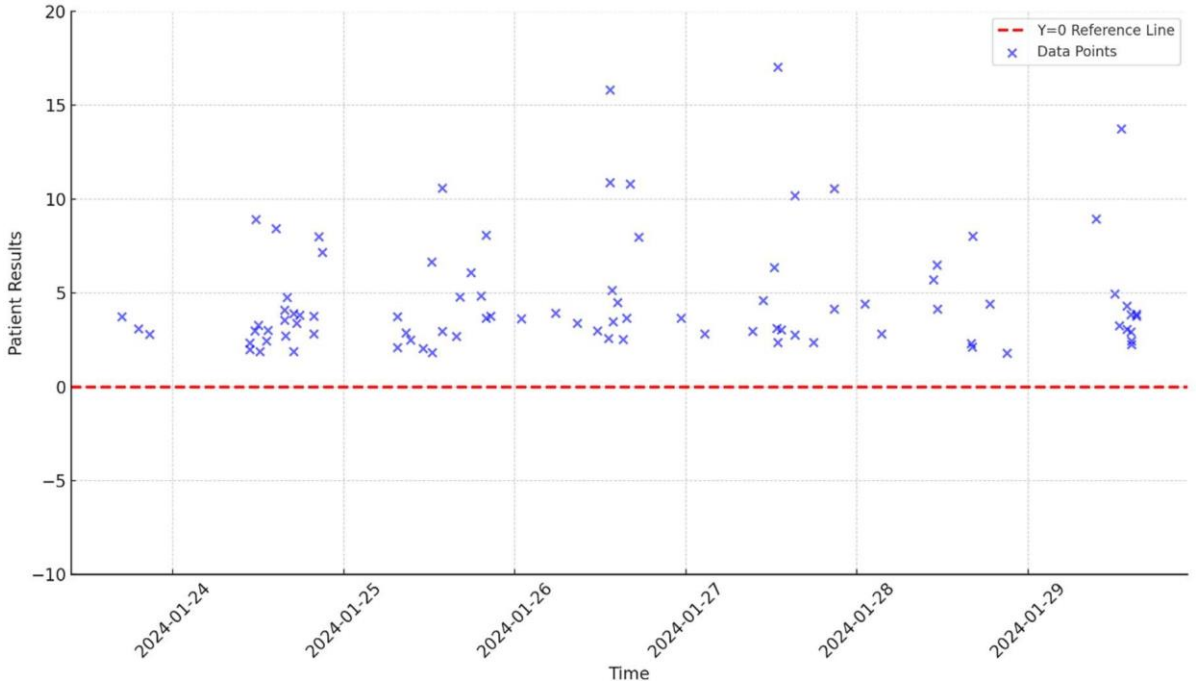
Case Solution

Medicine interference.

Having investigated we concluded that the direct bilirubin negative result may be because of unknown medicine interference from the sample.

We loaded Direct bilirubin (DSA) reagent on the analyzer performed calibration, quality control and run patient's samples. On the graph below no negative results was recorded.

Date of Analysis	Results	Date of Analysis	Results	Date of Analysis	Results	Date of Analysis	Results
23/01/2024 15:55:37	6.10	25/01/2024 07:28:40	3.74	26/01/2024 14:24:02	4.50	28/01/2024 10:45:55	5.70
23/01/2024 16:50:22	3.75	25/01/2024 07:29:16	2.08	26/01/2024 15:09:59	2.52	28/01/2024 11:13:13	6.48
23/01/2024 19:11:38	3.10	25/01/2024 08:40:58	2.88	26/01/2024 15:41:54	3.67	28/01/2024 11:19:36	4.14
23/01/2024 20:42:24	2.79	25/01/2024 09:19:00	2.51	26/01/2024 16:12:09	10.80	28/01/2024 16:03:00	2.31
24/01/2024 10:48:25	2.34	25/01/2024 10:11:42	29.31	26/01/2024 17:22:34	7.98	28/01/2024 16:09:53	2.12
24/01/2024 10:48:49	1.98	25/01/2024 11:07:17	2.03	26/01/2024 23:05:17	28.25	28/01/2024 16:15:58	8.03
24/01/2024 11:30:48	2.99	25/01/2024 12:20:16	6.66	26/01/2024 23:17:51	3.66	28/01/2024 18:41:39	4.42
24/01/2024 11:38:05	8.92	25/01/2024 12:21:52	1.81	27/01/2024 01:46:11	37.72	28/01/2024 21:02:04	1.80
24/01/2024 12:01:18	3.29	25/01/2024 13:46:30	10.58	27/01/2024 02:39:27	2.82	28/01/2024 22:20:24	85.32
24/01/2024 12:13:59	1.89	25/01/2024 13:46:42	2.96	27/01/2024 03:12:18	22.55	29/01/2024 09:36:43	8.95
24/01/2024 13:09:47	2.43	25/01/2024 15:45:06	2.68	27/01/2024 09:22:58	2.95	29/01/2024 12:10:35	4.95
24/01/2024 13:19:39	3.01	25/01/2024 16:16:30	4.79	27/01/2024 10:51:41	4.61	29/01/2024 12:48:16	3.26



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Case Solution

Medicine interference.

Considering all the D-BIL (vox) results were negative values, while D-BIL(DSA) result was normal, it was suspected there was interference material from the sample.

We need to establish by checking on patient treatment history to identify the drug causing the interference.

Note the following similar findings have been noted on T-Bil (vox method).

1) After checking the medicine history of the patient within 1 week, Esomeprazole Sodium interference was suspected.

2) R&D department did verification, it was found that when serum sample with 0.08 mg/dL of this medicine, T-BIL-V test would be interfered, but the bias was acceptable (bias within -10%）. This concentration was far more than the absorbed concentration in human body (in terms of total absorption).

Conclusion:

Customer would continue to use D-Bil-DSA due to evidence of medicine non-interference.

Case Summary

Any quantitative or qualitative test could be interfered, such interference could be categorized as endogenous or exogenous.

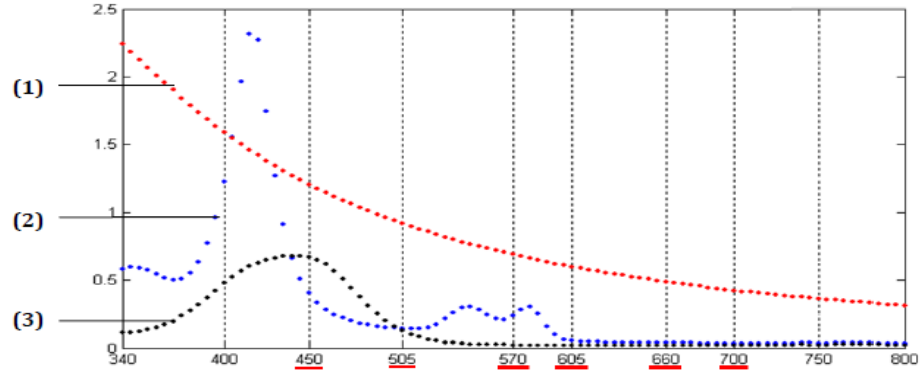
Considering the methodologies of the tests, possible endogenous interference from patient sample mainly contains:

- sample clot;
- abnormal sample status (hemolysis, jaundice, lipemia);
- other abnormal metabolites in patients (Immunoglobulin IgM, IgG, IgA, Rheumatoid factors, etc.);
- **medicine history (prescription drugs and over-the-counter drugs);**
- sample additives (anticoagulant such as EDTA, Heparin, citrate, oxalate, etc.);
- preservatives (NaF, Iodoacetate, HCl, etc.).

Case Summary: Identification & Solutions to Interference

Abnormal Sample Status – Serum Index

Serum index (serum index, SI) is an important indicator for measuring the quality of samples. Unqualified samples may seriously affect the accuracy of routine biochemical tests. It is commonly used to judge the quality of a sample by naked eye. Due to its strong subjective ability, standardization cannot be realized. Therefore, it cannot accurately reflect the actual condition of the sample.



The figure above shows the absorption spectrum of interferents in serum samples. (1) refers to lipemia, (2) refers to hemolysis, and (3) refers to icterus.

- Hemolysis index (H): Monitor the hemolysis degree of the sample. The higher the value, the higher the hemolysis degree;
- Icterus index (I): Monitor the degree of icterus of the sample. The higher the icterus, the higher the icterus.
- Lipemia index (L): Monitor the degree of lipemia of the sample. The higher the index, the higher the lipemia.

Common interference handling measures:

- Lipemia: 1. the lipemia is removed by ultracentrifugation. 2. gradient dilution
- Icterus sample: gradient dilution
- Hemolysis sample: For severe hemolysis, re-collect blood.
- Fibrin filaments or clots: remove clots and centrifuge again

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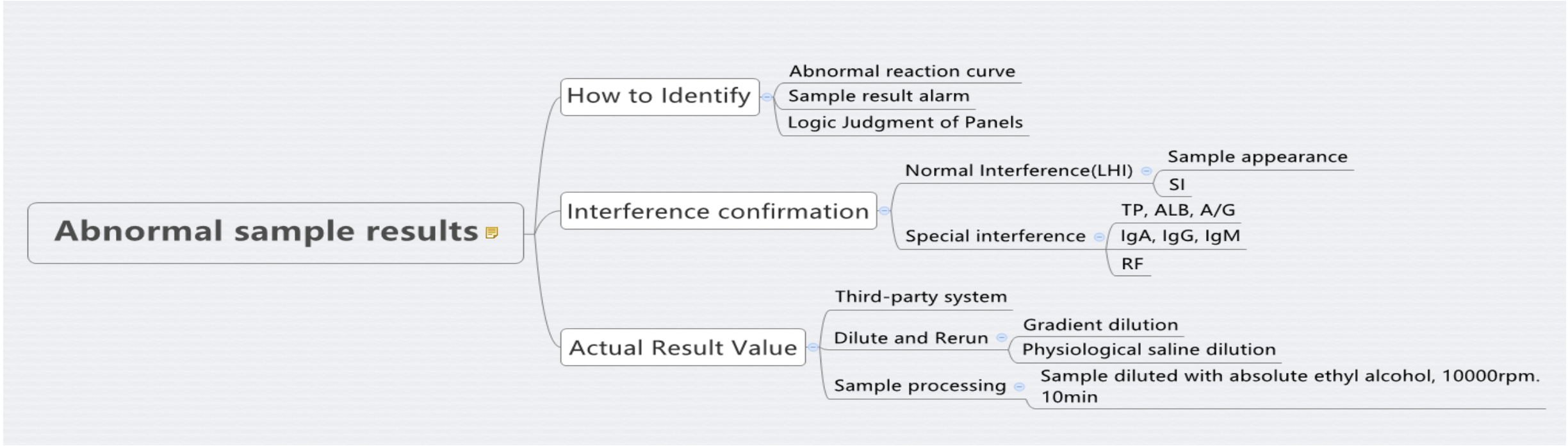
Case Summary: Identification & Solutions to Interference

Sample interference types:

- Abnormal Sample Status
- Globulin Interference
- RF Interference
- Drug Interference
- Special Interference(Tube heparin)



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Case Summary

Medicine Interference Checking:

1) Collection of medicine history of the patient within 1 week prior to testing.
2) Share the findings to R&D for further analysis when sample result are abnormal, and medicine interference was suspected

Thanks!

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