# Medical Devices Safety Notice

**The National Health Regulatory Authority would like to alert all governmental and private healthcare facilities, local agents and distributors that the below medical device:**

| Device Details | |
|---|---|
| **Device Name** | Triglycerides 250 tests<br>Triglycerides 4X50 tests<br>Triglycerides 1000 tests |
| **Device Model** | 20767107322<br>04657594190<br>08058687190 |
| **Manufacturer** | Roche Diagnotics |
| **Country of Origin** | Germany |
| **Reference** | attached |
| **Reason of Alert** | NHRA initiates this FSN due to updates in the Method Sheets for Triglycerides (TRIGL). Changes include:<br>1. Icterus Interference: Reducing the interference claim for unconjugated bilirubin from 35 to 10.<br>2. Prozone Check: Clarifying wording about false low results due to oxygen depletion.<br>3. Calibration Interval: Implementing a 56-day calibration interval for cobas® c 303 and cobas® c 503. |
| **Action should be taken** | Please refer to "Actions to be taken by Customer/ User" in the attached FSN<br>And for more information please contact the authorized representative General Medical W.L.L at registration.medics@intercol.com & meher.medics@intercol.com |

**Your cooperation is highly appreciated in improving health services in the Kingdom of Bahrain.**

**For more information please contact Medical_Devices@nhra.bh**

FSCA 2024 0048

03/JUL/2024

**Quality Notification**

**13 June 2024**

# Subject: Triglycerides (TRIGL): Method Sheet Update of Icterus (I index), Prozone Check wording in section "Limitations - Interference", and additional timeout calibration interval

| Product | Quant. | GMMI |
|---|---|---|
| Triglycerides (250 tests) | N/A | 20767107322 |
| Triglycerides (1000 tests) | N/A | 08058687190 |
| Triglycerides (4 x 50 tests) | N/A | 04657594190 |
| Triglycerides (800 tests) | N/A | 05171407190 |
| Triglycerides (800 tests) | N/A | 05171407214 |

| | |
|---|---|
| **Instrument/System** | **cobas**® c 111 analyzer<br>**cobas**® c 303 analytical unit<br>**cobas**® c 311 analyzer<br>**cobas**® c 501 module<br>**cobas**® c 502 module<br>**cobas**® c 503 analytical unit<br>**cobas**® c 701 module<br>**cobas**® c 702 module<br>COBAS INTEGRA® 400 plus analyzer |
| **Component** | Documentation<br>Reagent<br>System |
| **Target Group** | Application |



روش دياجنوستيكس ميدل ايست ش م ح
شركة ذات مسؤولية محدودة تأسست بموجب القانون رقم ٢ سنة ١٩٨٦
ووفقا للائحة التنفيذية رقم ١ لسنة ١٩٩٩
رقم السجل التجاري: ١٥٠٤١٦ –رقم الرخصة: ١٣٠٢٩٤
**Roche Diagnostics Middle East FZCO**
Formed Pursuant to Law No. 2 of 1986
& Implementing Regulation No. 1 of 1999 with Limited Liability
Registration No.: 150416 – License No.: 130294

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# Subject

This Quality Notification covers three changes in the Method Sheets and instrument settings:

Topic 1) “Limitations – interference” Icterus: Update of the interference claim for unconjugated bilirubin (without setting change).

Topic 2) “Limitations – interference” Prozone Check: Improvement of the wording (without setting change) regarding the results for oxygen depletion during assay reaction.

Topic 3) Implementation of an additional timeout calibration interval of 56 days during the 26 weeks on board stability for cobas ® c 303 and cobas ® c 503.

| Cat. No. | Analyzer | Test Short Name/ ACN/Test ID | Topic 1 - I index claim | Topic 2 - Oxygen depletion | Topic 3 - calibration interval |
|---|---|---|---|---|---|
| 20767107322 | **cobas**® c 311 | ACN 781 | x | x | unchanged |
| | **cobas**® c 501 | ACN 781 | x | x | |
| | **cobas**® c 502 | ACN 8781 | x | x | |
| | COBAS INTEGRA® 400 plus | Test ID 0-010 | unchanged | x | |
| 08058687190 | **cobas**® c 303/ 503 | ACN 21130 | x | x | x |
| 04657594190 | **cobas**® c 111 | ACN 781 | unchanged | x | unchanged |
| 05171407190 | **cobas**® c 701 | ACN 8781 | x | x | unchanged |
| 05171407214 | **cobas**® c 702 | | | | |

**Topic 1 - Icterus: I index interference claim for unconjugated bilirubin**

For cobas ® c systems (except cobas ® c 111):
The I index interference claim for unconjugated bilirubin is reduced from 35 to 10 (corresponding to the approximate unconjugated bilirubin concentration of 599 µmol/L (35 mg/dL) to 171 µmol/L (10 mg/dL), respectively).
The I index interference claim for conjugated bilirubin is not affected and remains at 10.

As a consequence, the value for the I index in the application settings for the TRIGL assay remains at 10, since the I index measurement does not discriminate between conjugated and unconjugated bilirubin.
Customers need to be informed about the I index interference claim reduction for unconjugated bilirubin in the TRIGL Method Sheets for cobas ® c systems.

No customer action is required regarding the application settings on the instrument.

For COBAS INTEGRA ® 400 plus and cobas ® c 111:
The I index interference claim in the TRIGL Method Sheet for COBAS INTEGRA ® 400 plus and for cobas ® c 111 remains valid and unchanged at 5 for both conjugated and unconjugated bilirubin.

**Topic 2 - Prozone Check: Results for oxygen depletion during assay reaction**

For cobas ® c systems (except cobas ® c 111):
Currently, it is stated that "False normal results are due to oxygen depletion during assay reaction". It is possible that low TRIGL results outside the reference range are generated, due to oxygen depletion.
For better clarification, the wording is changed to "False low results are due to oxygen depletion during assay reaction".

For COBAS INTEGRA ® 400 plus and cobas ® c 111:
The Antigen Excess-Check is not implemented in the TRIGL applications on COBAS INTEGRA ® 400 plus and cobas ® c 111.
Reason: Due to the technical design of the mixing procedure, the risk for oxygen depletion on these two systems is very low. No false low values for TRIGL on both systems were reported so far. The wording "Extremely lipemic samples (triglycerides greater than 3000 mg/dL) can produce false low results." is implemented precautiously.

**Topic 3 - Implementation of additional timeout calibration interval of 56 days during the 26 weeks on board stability**

For cobas ® c 303, cobas ® c 503
For TRIGL, a reagent aging effect was detected. This aging effect could cause recovery drifts in QC and patient samples. Therefore, an additional timeout calibration interval of 56 days during the 26 weeks OBS is implemented.

For cobas ® c 501/502, cobas ® c 701/702 and cobas ® c 311 systems:
These systems are not affected because the reagent on board stability claim is already at 56 days for cobas ® c pack small and 14 days for cobas ® c pack large.

For COBAS INTEGRA ® 400 plus and cobas ® c 111 systems:
These systems are not affected due to the different test principle. The blank value of the reagent is measured first before the addition of the sample. Therefore, any change of the blank reagent absorbance is subtracted within every measurement, thus eliminating the effect caused by reagent aging.

## Root Cause

**Topic 1 - Icterus: I index interference claim for unconjugated bilirubin**
The current I index claim for unconjugated bilirubin interference (35) is based on the interference testing on cobas ® c 501 master system according to a requirement for interference testing at only one concentration. During application work for cobas ® c 503, the bilirubin interference was tested at two concentrations.
The interference claim for 35 mg/dL unconjugated bilirubin was not met for the sample with elevated triglyceride concentration on cobas ® c 503 and cobas ® c 501. The scientific explanation is that the TRIGL assay shows an unusual behavior regarding unconjugated bilirubin interference. This interference is more pronounced at pathological (high) triglyceride concentration compared to triglyceride concentration around the medical decision point.

**Topic 2 - Prozone Check: Results for oxygen depletion during assay reaction**
For cobas ® c systems (except cobas ® c 111): The wording was improved as false low values that are not in the normal range are flagged by the Prozone Check, and thus invalid. The Prozone Check is encoded in the instrument settings for these systems.
For COBAS INTEGRA ® 400 plus and cobas ® c 111: The statement that extremely lipemic samples may produce false low results is added to the Method Sheets precautiously.

**Topic 3 - Implementation of additional timeout calibration interval of 56 days during the 26 weeks on board stability**
The reagent darkens over time. The TRIGL reagent is based on an enzymatic, colorimetric test principle. The TRIGL reagent is a mono reagent containing all ingredients in one solution. During on board storage time, the blank absorbance of the reagent increases due to color formation of the reagent solution.

# Risk Assessment

**Severity**

The probability of occurrence of harm in combination with the issue related severity the overall risk has been determined as acceptable residual risk. Thus, an HHE is not required. For further information, please refer to the upcoming SN-RDS-CoreLab-2024-093.

**Customer Details:**

| |
|---|
| Facility Name:<br>Contact Name:<br>Position:<br>Phone:<br>Date:<br>Signature and Stamp: |

If you have any questions, please do not hesitate to contact our Application Support Team or your local Account Manager.

Yours sincerely,

For on behalf of
**Roche Diagnostics Middle East FZCO**

**Venkatesan Veeraraghavan**
Regional Quality Manager

**Hassan Kassem**
Regional Quality & Product Safety Lead, Middle East