Please distribute the attached customer letter.
To the Laboratory Manager
To the attention of the Healthcare center Chairman

Address
City, Date

Our reference: FSCA#5436

**IMPORTANT:**

**URGENT FIELD SAFETY NOTICE**

**Ref. 415386 and 415386-30 - VIDAS® High-sensitive Troponin I**

**Risk of false positive results**

Dear bioMérieux Customer,

Our records indicate that your laboratory received one/some of the following bioMérieux products: VIDAS® High-sensitive Troponin I Ref. 415386 and/or 415386-30

The aim of this communication is to inform you about the investigation outputs related to not repeatable over-estimated results that lead to potential false positive results when using VIDAS® High Sensitive Troponin I (Ref. 415386 and 415386-30) and provide you recommendations and advices in case you encounter the issue**.**

**Description of the issue**

Since January 2021, based on complaints received from the field related to critical non-repeatable overestimated results (changing interpretation according to the cutoff value, 19 ng/L, in the frame of the three hours algorithm that lead to a change in clinical interpretation) that lead to false positive results by some customers, bioMérieux initiated an investigation that is still ongoing.

It is important to keep in mind that it is commonly acknowledged among experts that both conventional and high sensitive Troponin assays can lead to abnormally non-repeatable overestimated values especially in the lower part of the measuring range.

The rate of critical non-repeatable overestimated results observed during product design of VIDAS® High-Sensitive Troponin I Ref. 415386 was ≤ 1%. It was concluded that this low rate has negligible medical impact as it will not impact the expected clinical performance of the assay.
In addition, the clinical performances presented in our Product Instructions for Use were estimated on all obtained results, including potential non-repeatable overestimated results.

Until the end of November 2021, despite quality data analysis (control chart analysis, raw material history), visits at customer's sites and lots monitoring before release, it was not possible to reproduce internally the high non-repeatable overestimated result rate observed by some customers.

Since the end of November 2021, new analysis and testing were performed internally. The results showed a rate of critical non-repeatable overestimated results closed to the rates observed by some complaining customers (>=1%).

A new plan is currently in progress to test different conditions in order to assess the potential root-causes and aggravating factors

**Impact to customer:**

Considering what has been shared above, the critical non-repeatable overestimated High-Sensitive Troponin I results are leading to false positive results.

**Reminder of good practices for the VIDAS® High Sensitive Troponin I use**

1. **Good laboratory practices regarding pre-analytical steps**

We kindly remind you good practices to reduce **risk of having non-repeatable high cTn values by** limiting analytical interfering factors (such as fibrin clots, hemolysis, etc). It is an anticipated phenomenon, largely described in the scientific literature for most cTn assays, it is key to execute pre-analytical steps in accordance with good laboratory practices:

• Sample preparation: occasional non-repeatable overestimated result can occur when heparin plasma samples have not been well-mixed after blood collection which may lead to the formation of microclots invisible to the naked eye.
Laboratories encountering this phenomenon may opt for a combination of higher relative centrifugal force (g), or longer centrifugation time and/or filtering to avoid these potential microclots. Samples containing suspended fibrin particles or erythrocyte stroma should be centrifuged before testing.

• Blood sampling tube: it is recommended to validate the type of collection tubes before use as some may contain substances which interfere with test results and to follow the manufacturer's recommendations for use. For a given patient, serial troponin testing must be performed using the same type of sample tube.

According to international guidelines (WHO) and good sample collection practices, it is generally recommended:

• Plasma:
- Respect ratio between the anticoagulant and the sample.
- After sampling, the filled tube must be turned upside down in order to mix the sample with the anticoagulant.
- Then, the tube can be centrifuged (at least 15 min at 2000 to 3000 g).

These steps are essential to prevent coagulation and avoid the formation of microclots.

• Serum:
- Wait for the complete formation of the clot before performing a centrifugation (at least 1500g for 10 min) Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting times.

• Special case of frozen samples:
- Mix thawing samples, using a Vortex-type mixer.
- Centrifuge sample before testing

*Always refer to the tube manufacturer recommendations.

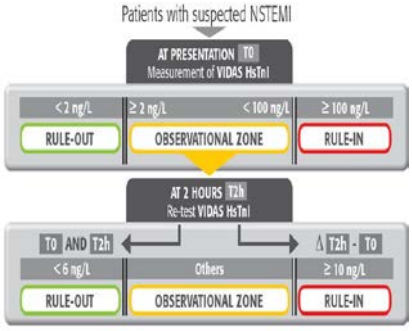
## 2. Best practices of clinical troponin use

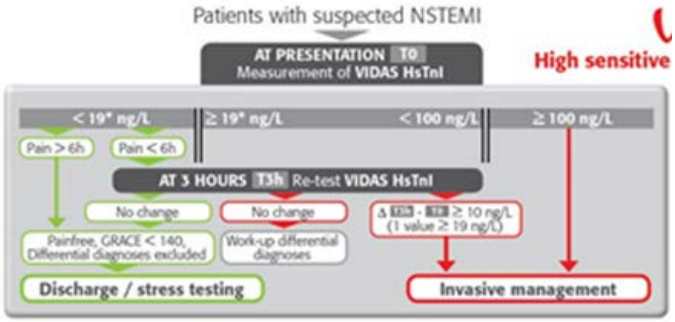
1) Clinical evidence of acute myocardial ischemia (= symptoms, most often – chest pain) is cornerstone for Acute Myocardial Infarction (AMI) suspicion and start of diagnostic workup

2) ECG (electrocardiography) is a first-line instrumental tool in patients with suspected Acute Coronary Syndrome (ACS) and allows to identify a quarter of Acute Myocardial Infarction cases (so-called, **STEMI,** AMI with ST-segment elevation). ECG is mandatory in all patients with ACS suspicion. In STEMI troponin is not needed to establish a diagnosis.

3) Introduction of troponin detection methods with improved sensitivity has allowed to detect and quantify even very slights changes in troponin concentrations. This technical advance has allowed to develop specific algorithms, based on serial troponin measurements, to aid in NSTEMI rule-in and rule-out. In most cases of elevated troponin results on admission (and especially if not concordant with clinical picture), a new testing 3 or 2 hours later will provide information on troponin kinetics, helping in differentiation of true false-positive from pathological elevations.

Here are the existing validated algorithms, available for VIDAS® High-sensitive Troponin I test:




**Suggested actions of high importance:**

We recommend you to take the following actions at this time:

- Please distribute this information to all appropriate personnel in your laboratory, retain a copy in your files, and forward this information to all parties that may use this product, including others to whom you may have transferred our product.
- Suggested actions if you face a suspected not repeatable over-estimated result, according to existing algorithms, described above:

  • **If you perform** VIDAS® High-sensitive Troponin I **testing in hospital settings** :
  Re-test the same sample as soon as possible in case the initial result is > 100 ng/L.

  • **If you perform** VIDAS® High-sensitive Troponin I **testing outside hospital settings**:
  For accurate troponin algorithms application (0/3h or accelerated 0/2h) hospital environment is preferred and, after eventual discussion with prescriber (clinician), patient may be either oriented

rapidly towards closest ED or, if clinical context is not in line with troponin results, the same sample may be retested to eliminate a case of potential non-repeatable overestimated result.

bioMérieux is committed to providing our customers with the highest quality product possible.

We sincerely apologize for any inconvenience that this may have caused you. If you need additional assistance or have any questions, please contact your local bioMérieux Customer Service representative.

Yours faithfully,

Customer Service

**Attachment A: Acknowledgement Form.**

**URGENT FIELD SAFETY NOTICE**

**FSCA 5436 - VIDAS® HS TN I Ref. 415386/415386-30 - False Positive Results**

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**TO BE RETURNED TO YOUR BIOMERIEUX CUSTOMER SERVICE AT THE FOLLOWING FAX NUMBER** : XXXXXXXX

Name of the laboratory:

City:

**Customer number:**

☐ I acknowledge receipt of the bioMérieux letter regarding the "**VIDAS® HS TN I Ref. 415386/415386-30 - False Positive results**"

☐ I will implement the required actions as indicated in the Urgent Field Safety Notice.

☐ Have you encountered impact on patients' results, or reports of illness or injury related to the identified issue ?

☐ Yes ☐ No

**DATE** ..... **SIGNATURE** : .....