Celltrion Healthcare Singapore

One Raffles Quay North Tower, Level 25, Singapore 048583

URGENT: Medical Device Safety Notification

To:

Chairman Medical Board
Relevant Head of Departments

8 August 2019

Dear Sir/Madam,

This document contains important information of the affected product. Please ensure that all potential users in your facility are made aware of this safety notification and the recommended actions. Please keep this document in your records.

With regards to below stated medical device, Celltrion Healthcare SG has received a notification from the manufacturer to implement a corrective action.

Product name: IMMUNDIAGNOSTIK REMSIMA® MONITOR TOTAL ADA ELISA
Device class: Class B, IVD
License no: DE0502825
Manufacturer: Immundiagnostik AG, Germany

Brief description:
This notification is about interferences in some assays to biotin in patient samples. The same notification has been submitted to the German Federal Institute for Drugs and Medical Devices (BfArM). One of the products affected by such interferences is the Remsima Monitor total ADA ELISA, K 9664.

Safety issue:
Interferences are detected in some assays to biotin in patient samples; the high levels of biotin in patient samples may lead to false lowered results on the affected kits. For more information, please refer to the letter attached.

Corrective action:
Update on the Instructions for Use (IFU) to include information about biotin interferences. Revised IFU has been submitted to HSA and approved in the system.

Safety action:
Please ensure that all users of the affected product and other relevant personnel of within your organization is informed of this information. Please keep record of this notice to ensure the effectiveness of the corrective action.

Yours Sincerely,

[redacted]

Kim Jitae, Director
Celltrion Healthcare Singapore, One Raffles Quay North Tower, Level 25, Singapore 048583

Immundiagnostik AG · Stubenwald-Allee 8a · D-64625 Bensheim

Important Notification

Immundiagnostik AG started a corrective action concerning the following products:

Product / Part Number	LOT	Expiry Date
IDKmonitor® Infliximab total ADA / K 9654	All lots (including future lots until IFU has been updated)	Several
IDKmonitor® Adalimumab total ADA / K 9651		
Remsima® Monitor total ADA / K 9664		
25(OH)-Vitamin D direct day ELISA / K 2108		
25(OH)-Vitamin D dried blood ELISA / K 2108DBS		
PreventID® Cardiac Troponin I / KSTCTI402		
PreventID® Vital-D / KST80100		

Dear Customer,

Immundiagnostik AG is about to prepare a corrective action for the products mentioned above. This letter contains important information about Biotin interferences. We kindly ask for your special attention.

Description:
Immundiagnostik AG identified all of their assays using a Biotin system referring to a recently published letter by the German Federal Institute for Drugs and Medical Devices (BfArM) alerting health care providers, lab personnel, and lab test developers that Biotin can significantly interfere with certain lab tests and cause incorrect test results which may go undetected. In order to investigate interference from Biotin several samples were spiked with up to 1200 ng/ml Biotin and analyzed in the respective assays.

Result:

Product / Part Number	Effect
IDKmonitor® Infliximab total ADA / K 9654	Possibility of lowered results when biotin concentration is **>100 ng/ml**
IDKmonitor® Adalimumab total ADA / K 9651	Possibility of lowered results when biotin concentration is **>150 ng/ml**
Remsima® Monitor total ADA / K 9664	Possibility of lowered results when biotin concentration is **>150 ng/ml**
25(OH)-Vitamin D direct day ELISA / K 2108	Possibility of lowered results when biotin concentration is **>100 ng/ml**
25(OH)-Vitamin D dried blood ELISA / K 2108DBS	Possibility of lowered results when biotin concentration is **>100 ng/ml**
PreventID® Cardiac Troponin I / KSTCTI402	Possibility of lowered results when biotin concentration is **>100 ng/ml**
PreventID Vital-D / KST80100	Possibility of lowered results when biotin concentration is **>100 ng/ml**

Risk assessment:
Biotin in patient samples can cause falsely low results. Incorrect test results may lead to inappropriate patient management or misdiagnosis. The likelihood to misinterpret test results is low and limited to cases in which blood was taken from patients who are ingesting levels of biotin above the recommended daily dose before the level has decreased to an extent that does not interfere with the assay.

Actions to be taken:

- Interpret the test result in the context of the whole clinical presentation.
- Discuss this notification with your medical director and clarify if corrective actions are necessary. A retrospective re-evaluation of test results is not recommended.
- Immundiagnostik AG has already started to update the manuals of the affected products in order to point out the risks of interferences in patients receiving a biotin therapy. This corrective action will be completed by July, 1st 2019. The latest version of the manual will then be available from our website. Please obtain a copy and consult for further information.

Pass on this information:
Please ensure that all users of the above mentioned products and other relevant personnel within your organization got knowledge of this information. If you have passed these products to a third party please forward a copy of this information or contact the person mentioned below. Please store this information at least until all actions have been completed.

The German Federal Institute for Drugs and Medical Devices (BfArM) received a copy of this notification. Please return the attached confirmation of receipt within 10 working days in order to let us know that you have acknowledged this notification.

We regret any inconvenience this incident may have caused and would like to thank you for your collaboration with Immundiagnostik AG.

Sincerely yours

[redacted]

Dr. Franz Paul Armbruster, CEO

If you have concerns or further questions please contact:

Immundiagnostik AG
Stubenwald-Allee 8a
64625 Bensheim, Germany

Dr. Bettina Hafen / Quality Manager
Tel.: +49 (0) 6251 70190 107 / Fax: +49 (0) 6251 849430
Email: [redacted]

Acknowledgement of Receipt

- Please complete this form and return it.
Immundiagnostik AG must demonstrate records of this corrective action –

FAX back to:

+49 6251 849430

Customer Name and Address /stamp:

Acknowledgement of receipt of the Important Notification about
Biotin interferences in the following products:

Product / Part Number	LOT	Expiry Date
IDKmonitor® Infliximab total ADA / K 9654	All lots (including future lots until IFU has been updated)	Several
IDKmonitor® Adalimumab total ADA / K 9651		
Remsima® Monitor total ADA / K 9664		
25(OH)-Vitamin D direct day ELISA / K 2108		
25(OH)-Vitamin D dried blood ELISA / K 2108DBS		
PreventID® Cardiac Troponin I / KSTCTI402		
PreventID® Vital-D / KST80100		

Please complete this form and fax it to the number above. By returning this form you confirm that you received the important notification and got knowledge of its content and if applicable, took actions as recommended in the notification. If you have passed these products to Third Parties you herewith also confirm that you have traceable records of having forwarded this information to all relevant parties. Thank you.

Signed by: _____ Date: _____

Name: _____ Title: _____