



November 20th, 2014.

FIELD SAFETY NOTICE (FSN)

(Please refer to Annex 5 of the Guideline: [MEDDEV 2.12-1 REV.8 Guideline Vigilance](#))

In Vitro Diagnostics Medical Devices : Type: Instruments for professional use.

<u>Attention</u>	:	To all users of Tosoh Automated Glycohemoglobin Analyzers:		
		<u>IVD</u>	<u>Catalogue nr</u>	<u>CE Registration</u>
		HLC-723G7	0019327	BE-CA02-877-03
		HLC-723G7 LA	0019757	BE-CA02-261-05
		HLC-723G8	0021560	BE-CA02-037-07
		HLC-723G8 LA	0021674	BE-CA02-377-07
		HLC-723GX	0023130	BE-CA02-185-11
<u>FSCA reference</u>	:	NC37486_FSCA_EN		
<u>Our reference</u>	:	NC37486_2_FSN_CU_EN		
<u>Reference IE CA</u>	:	V21588 IE-14-09-000084		
<u>Type of actions:</u>	:			

Please note that this FSN replaces the previous FSN from October 27th 2014.
The previous FSN should not be taken into consideration and should be discarded.
This new FSN contains more detailed information concerning the circumstances and the actions to be taken.

Dear Customer,

Tosoh Europe N.V., authorised representative of Tosoh Corporation Japan, is initiating a field safety corrective action (FSCA) for the instruments listed above.

This “**Field Safety Notice**” (FSN) contains important information that requires your immediate attention.

Please note that the national competent authority (CA) has been informed of this field safety corrective action.

Description of the problem:

Erroneously high HbA1c results (between 3-5 mmol/mol higher) were reported for patient samples using Tosoh Automated Glycohemoglobin Analyzers HLC-723G7/G8 (Variant Analysis Mode).

Note: 3 - 5 mmol/mol in IFCC units means 0.3 - 0.5% in NGSP units

Our investigations on the issue have indicated that such effect was caused by non-microbiological contamination of the analysers.

A method has been developed to verify the status of an analyser and to decide if it is affected.

Potential impact on the clinical outcome:

Accurate measurement of HbA1c is crucial for decision making in diabetic control and diagnosis/screening for diabetes type 2.

For follow up of diabetic patients the critical difference between two subsequent results within a subject is +/- 4 mmol/mol.



So in this case it could be possible that for some patients the subsequent HbA1c value was 5 mmol/mol higher compared to an initial HbA1c value, potentially triggering a change in treatment. This possible inappropriate increase or excess use of insulin could result in severe hypoglycaemia, particularly in Type 1 diabetic patients.

Therefore, in all cases, the follow up of a patient should be done with HbA1c data trending over a longer period of time and recent values must be interpreted in combination with the patients' own glucose monitoring values.

In cases where any discrepancies are observed between the obtained HbA1c value and the blood glucose values, the clinician is to take a confirmatory sample or wait for the next examination before changing the patient's treatment plan.

Recently HbA1c has been accepted as a tool for diagnosis and screening for diabetes type 2. The recommended cut off value is 48 mmol/mol. Thus, the possible higher results observed have the potential to cause over diagnosis of Type 2 Diabetes, when General Practitioners chose to follow the American Diabetes Association diagnostic criterion of HbA1c > 48 mmol/mol (6.5%). This could then lead to some patients having to undergo additional tests (e.g. oral glucose tolerance testing).

Conclusions:

These higher observed results for HbA1c were not detected by the internal and external QC. There could be a minor impact on the treatment of diabetic patients and some non-diabetic patients could be sent for further investigation to confirm if they are indeed diabetic.

Additional information

Since the moment that the original incident was reported to the local competent authorities, Tosoh Europe N.V. has performed a multitude of investigations, in cooperation with its organisations in Japan and the USA. Objective of these investigations was to determine the root cause of the problem and to implement proper corrective actions.

The procedure described in Annex I is the outcome of these investigations.

Even if this procedure indicates the option between either Tosoh HbA1c controls or patient samples to perform the test, **we would like to advise you using both, controls AND patient samples.**

By doing so, you will obtain the best possible and unambiguous view on the actual status of your analyser and allow you to judge if your analyser is due for preventive maintenance.

At the same time Tosoh Europe N.V. has put in place some improved preventive maintenance procedures for your analyser. These consist of:

- New maintenance kits, containing more parts to replace than before (and in that way ruling out any possibly remaining contamination)
- A more frequent preventive maintenance schedule. As from now on preventive maintenances on your analyser will be carried out every 20,000 injections (in that way anticipating re-occurrence of any contamination).

These new preventive maintenance kits and improved procedures will mainly be handled by your local Tosoh service representative. Nevertheless we want you to be informed about all additional corrective actions that were taken.



Actions a user can take to verify analyser status:

1. Carefully read and, when in doubt, perform the methods described in Annex I:
The proposed methods are provided for the HLC-723G8, Standard Analysis Mode/Variant Analysis Mode, HLC-723G7, Standard Analysis Mode/Variant Analysis Mode, HLC-723GX, Variant Analysis Mode, and are intended to check for contamination.
2. Please share this information with your laboratory staff and retain this Field Safety Notice (FSN) as part of your laboratory Quality System documentation. If you have forwarded any of the affected products listed above to another laboratory, please provide them a copy of this letter.
3. Please complete and **return the enclosed Reply Form within 10 days** so we are assured you have received this important communication. Returning the Customer Reply Form promptly will prevent you from receiving repeat notifications. Once your reply form has been received you will be contacted to organize an appointment that is suitable for you should your instrument be due for preventive maintenance after performing the proposed methods listed in Annex I.

We sincerely apologize for any inconvenience this may have caused.
Tosoh Europe is committed to providing you with the highest quality diagnostic products and support services to meet the needs of your laboratory and the patients you serve.
We thank you for your understanding and support in helping us deal with this issue and highly appreciate your continuous loyalty to our company;

If you have any further questions regarding this information, please contact your local Tosoh Service Engineer.

Sincerely,

Luc Goyens

Quality Assurance Manager - EMEA

Tosoh Europe N.V.



Annex I:

The proposed methods are provided for the HLC-723G8, Standard Analysis Mode/Variant Analysis Mode, HLC-723G7, Standard Analysis Mode/Variant Analysis Mode, HLC-723GX, Variant Analysis Mode, and are intended to check:

- (i) the effectiveness of annual/preventive maintenance, and
- (ii) if it is time for preventive maintenance or not

Materials and Methods

This test is done with Tosoh Hemoglobin A1c Control Set, but whole blood samples can be used alternatively.

Materials required:

- Tosoh Hemoglobin A1c Calibrator Set (**0018767**)
- Tosoh Hemoglobin A1c Control Set (**0021974**)
(hereinafter referred to as "A1c control")
- In case whole blood samples are used please use 2 normal (= not containing Hb variants) fresh (less than 48 hours old) patient samples with a concentration of HbA1c around 30 mmol/mol and around 80 mmol/mol (*).
- Sample vials (volume capacity of 500 µL or more)
- Tosoh HSi Hemolysis & Wash Solution (**018431L**) (hereinafter referred to as "H&W Solution")
- Purified water

Method:

- (1) Calibrate the instrument according to the IFU (Instructions for Use).

A. In the case the A1c control is used:

- (2) Reconstitute a vial of the A1c control, Level 1, adding 0.5 mL of purified water and gently swirl it to ensure homogeneity according to the IFU. Reconstitute a vial of the A1c control, Level 2 in the same way.
- (3) For Level 1, pipette 10 µL of the reconstituted material into a sample vial and dilute it with 0.5 mL of purified water according to the IFU (A). In the same way, pipette another 10 µL of the reconstituted material into another sample vial and dilute it with 0.5 mL of H&W Solution (B).
- (4) In the same way, prepare diluted samples for Level 2 control material.
- (5) Measure each of the above (A) and (B) for both levels, a total of 4 samples, on the instrument in triplicate (12 results).
- (6) If the result for either of the two levels of A1c controls meets the criteria below, the performed preventive maintenance is not sufficient, or it would be time for preventive maintenance.

Absolute difference between the HbA1c result (mean of triplicate results) diluted in purified water (A) and the HbA1c result (mean of triplicate results) diluted in H&W Solution (B):

- >= 0.3 NGSP% or 3 mmol/mol for the A1c control, Level 1.
- >= 0.5 NGSP% or 5 mmol/mol for the A1c control, Level 2.



B. In case whole blood samples are used:

- (2) Aliquot the samples. Dilute one aliquot of the samples 1/200 with purified water (A) and 1/200 with H&W Solution (B). Use another aliquot as undiluted samples (C).
- (3) Measure each of the above (A), (B) as diluted samples and (C) as undiluted samples in triplicate.
- (4) If the result for either of the two concentrations of the samples meets the criteria below, the performed preventive maintenance is not sufficient, or it would be time for preventive maintenance.

Absolute difference between the HbA1c result (mean of triplicate results) diluted in purified water (A) and the HbA1c result (mean of triplicate results) diluted in H&W Solution (B), or absolute difference between the HbA1c mean of triplicate results diluted in H&W Solution (B) and that undiluted (C):

>= 0.3 NGSP% or 3 mmol/mol for the low concentration sample.

>= 0.5 NGSP% or 5 mmol/mol for the high concentration sample.

(*) Note: 30 mmol/mol and 80 mmol/mol correspond to 4.9 NGSP% and 9.5 NGSP%, respectively.



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Annex II:
Customer Reply Form

PLEASE FAX THIS COMPLETED FORM TO: +32 (0)13 61 85 09 or email to info.raqa@tosoh.com

Our Reference: **NC37486-2-FSN-EN:** Tosoh Automated Glycohemoglobin Analyzers HLC-723:

Model	:	G7	/	G7 LA	/	G8	/	G8 LA	/	GX
Product Code	:	0019327	/	0019757	/	002156	/	0021674	/	0023130

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Please use Block Capitals.

1	Facility Name and Address:	
2	Customer Reply Form completed by:	
3	Title	
4	E-mail and/or Telephone Number (including Area Code)	

Your signature below indicates that you have received, read and understood the attached FSN; and disseminated this information to staff or facilities as applicable.

Date: (DD/MM/YYYY):/...../ 2014

Customer Signature: