CHROMSYSTEMS
DIAGNOSTICS BY HPLC & LC-MS/MS

Urgent Field Safety Notice
Urgent safety information
FSN 3-2022
18.05.2022

Please forward to all end users
of the products!

Target value correction for glycine in Dried Blood Spot Control Level I and II, lot no. #2821 using an underivatised LC-MS/MS analytical method

Dear customer,

Within the framework of our quality control, we have determined that the **target values for glycine** must be adjusted for the following products:

MassCheck® Amino Acids, Acylcarnitines incl. Succinylacetone

Dried Blood Spot Control Bi-Level (I+II) (order no. 0191, batch no. **#2821**)
Dried Blood Spot Control Level I (Order No. 0192, Batch No. **#2821**)
Dried Blood Spot Control Level II (Order No. 0193, Batch No. **#2821**)

Therefore, please be sure to read the following Urgent Field Safety Notice. We also ask you to complete the accompanying response form, as we need proof of receipt of the corrective action.

We apologise for the inconvenience caused by this situation. Chromsystems support is always available to answer any further questions you may have and will deal with your request quickly and reliably.

You can reach us via the hotline + 49 89 18930-111 or by e-mail at support@chromsystems.com.

You are also welcome to contact our field staff.

We thank you in advance for your support in carrying out the necessary measures and look forward to continued good cooperation.

Yours sincerely,

Dr Ralf Fischer

Head of Regulatory Affairs Department

Chromsystems Instruments & Chemicals GmbH

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This letter is to advise you that Chromsystems Instruments & Chemicals GmbH is taking corrective action on the products listed in Table 1. Our records show that you have been supplied with the listed products.

Table 1: Affected products / batch.

Product designation	Order no.	Batch no.
MassCheck® Amino Acids, Acylcarnitines incl. Succinylacetone		
Dried Blood Spot Control Bi-Level (I+II)	0191	#2821
Dried Blood Spot Control Level I	0192	#2821
Dried Blood Spot Control Level II	0193	#2821

Description of the problem including the identified cause

A too low concentration of glycine (**analytical method "LC-MS/MS, underivatised"**) was detected in the dried blood controls of the batch 2821 of the products listed in Table 1.

Therefore, we have made the following adjustment to the values given on the package inserts for glycine (**analytical method "LC-MS/MS, underivatised"**) (see Table 2).

Table 2: Changed values, package insert 0192 #2821, 0193 #2821.

	Substance	Analysis method	Unit	Target value	Range		
0192 #2821	Glycine	LC-MS/MS, underivatised:	µmol/l	Original value: 211	153	-	268
				Update: 367	267	-	467
0193 #2821	Glycine	LC-MS/MS, underivatised:	µmol/l	Original value: 488	343	-	632
				Update: 805	566	-	1044

The values for the analysis method "LC-MS/MS, derivatised" as well as the values of all other substances are not affected and do not change.

We assess the risk on the basis of the following considerations

Glycine is used in newborn screening as a marker for some inborn errors of metabolism. These include the following very rare disorders:

Non-ketotic hyperglycaemia [2], propionazidaemia [1], methylmalonic aciduria [1], whereby in propionazidaemia and methylmalonic aciduria glycine is only used as a secondary marker.

In order to assess the impact on the patient of low set concentration values for glycine in the Dried Blood Spot Controls 0191, 0192, 0193 #2821, the following worst case example is discussed:

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Due to the unacceptable measurement results for glycine in the controls, it is possible that a laboratory may assess the setting of the analytical system for glycine of the newborn screening method used to be out of order and subsequently introduce or adjust a factorisation for glycine. If the results of the controls are about twice the target value, the laboratory would include a factor of about 0.5 in the calculation. This would also cause all patient samples to measure falsely too low by the factor of about 0.5. If this happens without a simultaneous factorisation of the cut-off value, there is a risk that the disease will not be detected in the newborn screening due to falsely too low results.

In this described worst case scenario, a life-threatening situation exists for patients suffering from one of the above-mentioned diseases if the disease is not detected or not detected in time.

What measures are to be taken by the customer/user

- If you have used the Dried Blood Spot Control Level I and II (order no. 0191, 0192, 0193) of batch 2821, please check whether you have determined glycine.
- Replace the old package insert (release date 10.09.2021) with the updated package insert with release date 18.05.2022.
- If you have determined glycine, clarify with the attending physician or laboratory director, if necessary, whether a back-check of the values for glycine is required.
- If you have given any of the products mentioned in this letter to another laboratory, inform that laboratory of the contents of this letter and forward a copy.
- Please document your measures on the enclosed response form and send us your reply by 01.06.2022.

If you have any questions, please contact our support team at +49 89 18930-111 or by e-mail at support@chromsystems.com.

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Passing on the information described here

Please ensure that all users of the above products and other persons in your organisation who need to be informed are made aware of this "Urgent Safety Information". If you have given the products to third parties, please forward a copy of this information or inform us by e-mail at:

regulatory@chromsystems.com

Please follow this notice and the resulting action to ensure the effectiveness of the corrective action and keep this information at least until the action is completed.

The competent national regulatory authority has been informed of this "Urgent Safety Information".

We thank you in advance for your support in carrying out the necessary measures and look forward to continued good cooperation.

Yours sincerely,

Dr Ralf Fischer
Head of Regulatory Affairs Department
Chromsystems Instruments & Chemicals GmbH

Literature:

[1] la Marca (2014) Mass spectrometry in clinical chemistry: the case of newborn screening, Journal of Pharmaceutical and Biomedical Analysis, 101, 174-182.
[2] Sweetman et al. (2006) Naming and counting disorders (conditions) included in newborn screening panels, Pediatrics, 117, S308-S319.

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Reply form

Product designation	Order no.	Batch no.
MassCheck® Amino Acids, Acylcarnitines incl. Succinylacetone		
Dried Blood Spot Control Bi-Level (I+II)	**0191**	**#2821**
Dried Blood Spot Control Level I	**0192**	**#2821**
Dried Blood Spot Control Level II	**0193**	**#2821**

1. Customer information (to be filled in by the customer)	
Organisation	
Address	
Contact Name	
Title/Function	
Phone	
Email	

2. Customer action (to be filled in by the customer)		
☐ Yes ☐ No	The information that the value of glycine (analytical method LC-MS/MS, underivatised) in products 0191, 0192, 0193 #2821 has been updated is brought to the attention of all relevant users and implemented. The package insert was exchanged for the new package insert.	To be filled in by the client or enter n/a.
☐ Applies ☐ Does not apply	Patient data on glycine are not collected. FSN 3-2022 is therefore not relevant for the laboratory.	To be filled in by the client or enter n/a.
☐ Yes ☐ No	Are you aware of any adverse medical events and direct negative effects on patients related to the products listed in this safety communication?	If "yes": Please provide details of this event (to be completed by the client):

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☐ Yes ☐ n/a	I have identified and notified my customers or other affected third parties to whom products affected by this letter were shipped.	Enter the date and type of notification or n/a.
☐ Yes	I have a question, please contact me.	Short description of the request:

With my signature, I acknowledge receipt of Safety Notice FSN 3-2022 and that I have read and understood its contents.

Name	
Signature	
Date	

Please return the completed form by e-mail or fax by 01.06.2022 to:

E-mail: regulatory@chromsystems.com / Fax: +49 89 189 30 199

It is important that your organisation takes the actions listed in the FSN and confirms that you have received the FSN.

Your organisation's response is the evidence we need to monitor the progress of corrective action.

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