

Urgent Field Safety Notice

FSN 1-2021

30. August 2021

Please forward to all end users of the products!

Dear customer,

Our products are continuously optimised and are subject to comprehensive quality control measures, aimed at ensuring the highest product quality possible. As part of these investigations, the following product has been showing effects of leakage:

Order no. 93957

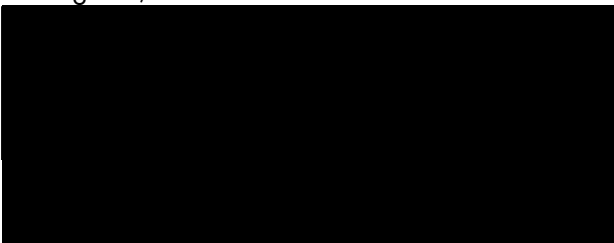
96 Deep Well Filter Plates **MassTox**® Immunosuppressants in whole blood - ONEMINUTE Test (Lot no. 1120 and 0121)

Please review this Urgent Field Safety Notice and **complete and return the Reply Form** as we are required to document receipt of the corrective action.

We apologise for any inconvenience this may cause.

Please contact Chromsystems Support if you have any questions and we will endeavour to respond as quickly as possible. You can reach us on the hotline + **49 89 18930-111** or by e-mail at **support@chromsystems.com**. Alternatively, you can contact your local sales representative.

Regards,



Urgent Field Safety Notice

FSN 1-2021

30. August 2021

Please forward to all end users of the products!

We would like to inform you that Chromsystems Instruments & Chemicals GmbH issues a corrective action for the below-mentioned product. Our records show that you have received this affected product.

Product description	Order No.	Lot No.
96 Deep Well Filter Plates MassTox ® Immunosuppressants in whole blood - ONEMINUTE Test	93957	1120; 0121

Table 1: Identification of the affected IVD medical device

Problem description including the identified cause

Internal investigations demonstrate that the existing lots #1120 and #0121 on the market of 96 Deep Well Filter Plates **MassTox**® Immunosuppressants in whole blood - ONEMINUTE Test (order no. 93957) show effects of leakage, as described in the following. Chromsystems Instruments & Chemicals GmbH is already in contact with the plate manufacturer in order to provide you with error-free 96 Deep Well Filter Plates again as soon as possible.

When using the mentioned filter plates, a liquid transfer may occur from column 2 into column 1 and from column 11 into column 12, and vice versa (see Figure 1).

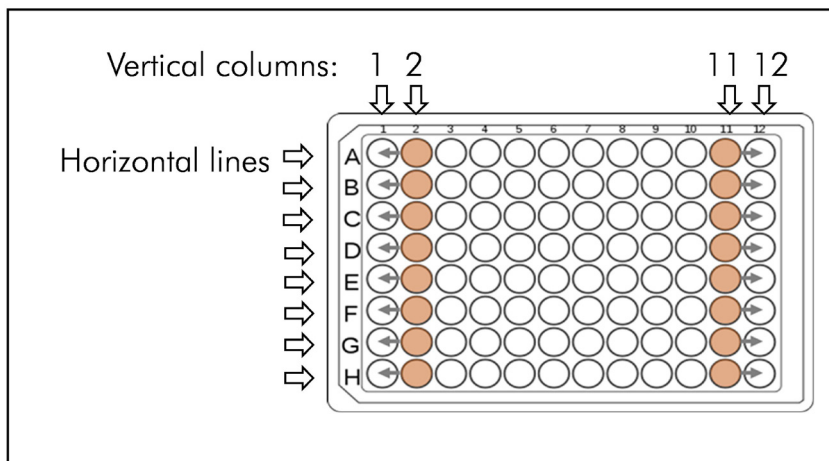


Figure 1: Schematic representation of the 96 Deep Well Filter Plate, order no. 93957

Urgent Field Safety Notice

FSN 1-2021

30. August 2021

Please forward to all end users of the products!

It could be shown that due to a production error at our supplier, leakage in the material can lead to an unwanted transfer of liquid into neighbouring deep wells. This can result in mixing of the liquids of neighbouring cavities in columns 1/2 or columns 11/12, respectively (e.g. transfer of liquid from A2 to A1 and vice versa, or B2 to B1 and vice versa, or H11 to H12 and vice versa, etc.). The liquid transfer apparently takes place mainly during centrifugation.

According to current findings, other columns are also affected by leakage in batch #1120, while in batch #0121 only mixing of columns 1/2 or columns 11/12 is observed. No carryover between adjacent horizontal lines was observed (A↔B, B↔C, C↔D, D↔E, E↔F, F↔G, G↔H).

The use of the affected 96 deep well filter plates can lead to falsified measurement results for the analytes **cyclosporin A**, **everolimus**, **sirolimus** and/or **tacrolimus**. Currently, a falsification of the measured values by up to 5 % can be detected in columns 1/2 and 11/12. This sample carryover only has a clinically relevant effect if a sample with a high immunosuppressant concentration is located next to a sample with a low concentration. In the worst case, sample carryover results in a sample below the therapeutic range being falsely quantified in the therapeutic range.

We evaluate the risk based on the following considerations:

The quantitative determination of the immunosuppressants cyclosporin A, everolimus, sirolimus and/or tacrolimus in whole blood by LC/MS-MS is used for therapeutic monitoring after organ transplantation. In addition, these drugs are used to suppress immune activity in autoimmune diseases.

In the case of leakage and liquid transfer into neighbouring deep wells as described above, there is a risk of false determination of calibrators and controls as well as patient samples.

In patient samples where drug levels are actually below the therapeutic range, but this test erroneously determines immunosuppressant concentrations within the therapeutic range, there is a risk of organ rejection with life-threatening consequences for the patient (worst case scenario). This scenario is to be expected in rare cases and only if several factors come together: Use of a defective filter plate, presence of a patient sample with a very high drug concentration (e.g. C_{max} determination after drug intake), presence of a patient sample below the therapeutic range and positioning of these samples in adjacent wells of the filter plate.

In patient samples whose drug levels are actually above the therapeutic range and are determined to be slightly lower by this test, there is a small risk of nephrotoxic effects from the immunosuppressants.

We strongly recommend that you coordinate the decision on clinical relevance of this finding with the attending physician(s).

Urgent Field Safety Notice

FSN 1-2021

30. August 2021

Please forward to all end users of the products!

We would like to point out that there are no universally established therapeutic ranges for cyclosporine A, everolimus, sirolimus or tacrolimus in whole blood. Each user should establish his or her own therapeutic ranges based on clinical assessments. In addition, individual results cannot be used as the sole indicator for making changes in the treatment regimen. Each patient should be thoroughly evaluated clinically before treatment adjustments are made, because significant inter-individual variability exists with respect to the effects of immunosuppressive drugs, which means that individual patients may require more or less robust immunosuppressive therapy (literature reference: Lothar Thomas (Hg.) (2021): Clinical Laboratory Diagnostics 2020, Chapter 40: Therapeutic Drug Monitoring, <https://www.clinical-laboratory-diagnostics-2020.com/k40.html>).

What measures should be taken by the addressee

If you have already used the products listed in Table 1 for your measurements, please check with the attending physician(s) whether it is necessary to review the results of cyclosporin A, everolimus, sirolimus and/or tacrolimus.

- Do not use 96 Deep Well Filter Plates (Order no. 93957) of batch #1120.
- Please indicate the number of 96 Deep Well Filter Plates (Order no. 93957) of batch #1120 that you still have available in the enclosed response letter. We will arrange for the pickup and exchange of this affected batch #1120.

Use only 96 Deep Well Filter Plates (Order no. 93957) of batch #0121 and follow the safety instructions below:

- Do not pipette samples into columns 1 and 12.
- When using the 6PLUS1® Multilevel Whole Blood Calibrator Sets and/or the **MassCheck**® Immunosuppressants Whole Blood Control Level I - IV, this results in the maximum number of samples listed in Table 2 that can be processed on the 96 Deep Well Filter Plates (Order No. 93957) in addition to the controls and calibrators, if applicable.
- Avoid the worst case scenario described above by repeating the processing and measurement of adjacent samples of samples with very high immunosuppressant concentrations.

Urgent Field Safety Notice

FSN 1-2021

30. August 2021

Please forward to all end users of the products!

First column to be used	Max. number of patient samples	
	When using calibrators and controls	When using controls (without calibrators)
2	69	76
3	61	68
4	53	60
5	45	52
6	37	44
7	29	36
8	21	28
9	13	20
10	5	12

Table 2: Maximum number of wells that can be used for patient samples

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

If you have forwarded any of the products mentioned in this letter to another laboratory, please inform that laboratory of the content of this letter and forward a copy.

Please document your measures on the attached document (attachment Response) and return your response until 10.09.2021 (contact details provided in the attachment Response).

Urgent Field Safety Notice

FSN 1-2021

30. August 2021

Please forward to all end users of the products!

Passing on the information described here

Please make sure that all users of the products mentioned above and other persons affected in your organization are informed about this „urgent field safety information“. If you have provided third parties with these products, please forward a copy of this information or inform Chromsystems at: regulatory@chromsystems.com.

Please follow this notice and the resulting action to ensure the effectiveness of this corrective action. Please retain this information at least until the action has been completed.

Your responsible national authority has been informed and has received a copy of this „urgent field safety information“.

We are currently working under high pressure to solve this problem and hope to be able to provide you with error-free filter plates again as soon as possible. We apologize for the inconvenience caused by this situation. The continuous inspection of our products ensures their high quality. However, this process can also lead to corrections like this being necessary and executed. We would like to thank you in advance for your support in implementing the necessary measures and look forward to continuing our good cooperation.

Urgent Field Safety Notice

FSN 1-2021

30. August 2021 - **reply form**

Please forward to all end users of the products!

Product description	Order No.	Lot No.
96 Deep Well Filter Plates MassTox ® Immunosuppressants in whole blood - ONEMINUTE Test	93957	1120; 0121

Customer Details

Organization

Address

Contact Name

Title/Function

Phone

E-mail

Customer Action (To be filled out by the customer or check N/A)

I confirm receipt of this Field Safety Notice and that I have read and understood its content.

Yes Patient data on cyclosporin A, everolimus, sirolimus and/or tacrolimus were obtained using the products listed above.

No **If Yes:** Decision on clinical relevance of results was made with attending physician.

N/A **If No:** No further actions to be taken by user.

↓ Continued on page 8

Urgent Field Safety Notice

FSN 1-2021

30. August 2021 – **reply form**

Please forward to all end users of the products!

Customer Action (To be filled out by the customer or check N/A)

Yes The information that 96 Deep Well Filter Plates **MassTox®** Immunosuppressants in whole blood - ONEMINUTE Test (**Order no. 93957, Lot no. 1120**) must not be used has been brought to the attention of all relevant users and implemented.

N/A

Following amount of 96 Deep Well Filter Plates (**Best.-Nr. 93957, Charge #1120**) are still available and need to be picked up and exchanged.

Amount
packaging units

Amount
single plates

Yes The information that **columns 1 and 12** (see figure 1) of 96 Deep Well Filter Plates (**Order no. 93957, Lot no. 0121**) must not be used due to leakage and potential liquid spillage between columns 1/2 and 11/12 has been brought to the attention of all relevant users and implemented.

N/A

Yes Are you aware of any adverse medical events and direct negative effects on patients related to the products listed in this FSN?

No

Yes I have identified and notified my customers or others to whom products affected by this letter have been or may have been sent.

N/A Date and type of notification

↓ Continued on page 9

Urgent Field Safety Notice

FSN 1-2021

30. August 2021 – **reply form**

Please forward to all end users of the products!

I have a query, please contact me.

Brief description of query:

Date / Name /

Signature _____

With my signature I confirm receipt of this Field Safety Notice 1-2021 and that I have read and understood its content.

Please send the completed form by E-Mail or Fax until 10.09.2021 to:

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

It is important that your organization takes the actions listed in FSN 1-2021 and confirms that you have received the FSN 1-2021.

Your organization's reply is the evidence we need to monitor the progress of the corrective actions.