April 12, 2018

# URGENT MEDICAL DEVICE CORRECTION NOTIFICATION

## High number of total images/unassigned events in some patients for CELLSEARCH® Circulating Tumor Cell Kits (IVD), (Product Code 7900001)

Dear Valued Customer:

This is to inform you of an Urgent Medical Device Correction Notification for the following:

| Product Name | Product Code | Lot | Expiry Date |
|---|---|---|---|
| CELLSEARCH® Circulating Tumor Cell Kits (IVD) | 7900001 | S038 | 10AUG2018 |
| | | S038R | |
| | | S038S | |
| | | S038T | |
| | | S038U | |
| | | S038V | |

This an Urgent Medical Device Correction Notification has been initiated by Menarini Silicon Biosystems Inc. due to reports of an unusually high number of unassigned events observed with some patient samples when reviewing the image gallery.

### Investigation Summary

We have received reports from a limited number of customers about the intermittent occurrence of an unusually high number of total images / unassigned events (more than 10,000) in the image gallery for some patient samples using the CELLSEARCH® Circulating Tumor Cell Kits (IVD), (Product Code 7900001) listed in the table above. An internal review of data and testing has defined and confirmed the occurrence of a high number of unassigned events intermittently. Testing has also confirmed that although a high number of unassigned events may be observed, the staining reagents in the affected kits function otherwise as intended for detecting Circulating Tumor Cells and White Blood Cells. However, in the course of this investigation, an isolated manufacturing process discrepancy was found in the production of the affected kit lots. It is not known at this time if this process discrepancy contributes to, or is the root cause of the reported issue. See the Question and Answer section for further details.

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**Required Actions**

- Please dispose of any affected product in your current inventory.
- Report any previous occurrence of unusually high number of total images / unassigned events in patient samples to Customer Technical Support.
- Complete and return the enclosed Confirmation of Receipt form no later than **April 27, 2018.**

## Impact to Results

The same Cell Interpretation Guidelines as described in the CellTracks Analyzer II User Guide can be followed to determine if the cells or objects in the image gallery meet the criteria of a CTC. However, the unusually high number of total images / unassigned events may require additional time and effort for the operator to review all the images and may cause a delay in reporting the results. In extreme cases, the operator may declare the sample non-evaluable. During internal testing in replicating the issue, no false positive or false negative enumeration of CTCs were observed. There was also no indication of false positive or false negative CTCs related to this issue in the reported complaints. Based upon our initial evaluation of the complaints, we do not believe that previously obtained test results are affected.

Patient results generated using CELLSEARCH® Kits should be used in conjunction with the overall clinical information derived from diagnostic tests (i.e., imaging and laboratory tests), physical examination and the complete medical history in accordance with appropriate patient management procedures.

It is important that you are aware of the potential impact, as described above, and that you report the occurrence in patient samples to Customer Technical Support.

## Resolution

An isolated manufacturing process discrepancy has been identified as the most likely root cause and the investigation is ongoing to further determine root cause and corrective and preventive actions. At this time, the instrument is not implicated as the source.

We apologize for the inconvenience this may cause your laboratory. We have anticipated questions you may have in the following Question and Answer section. If you have additional questions about this issue, contact Customer Technical Support at 800 (0)8374339.

Sincerely,

John Clay
*Quality Assurance Director*

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Questions and Answers

1. **Can I use my current inventory of the affected lots?**

No, please dispose of any affected product in your current inventory. Although we have confirmed the performance of the affected lots to date, the continued stability and performance of the affected kits is unknown. For tests already performed, see the **Impact of Results** section of the letter for potential impact to results.

2. **What is considered an unusually high number of total images / unassigned events?**

Though there is no standard range of unassigned events to be expected from each test; based on the customer reports, typical numbers range from 100 to 1,000, and limited reports of more than 10,000 unassigned events has been received for the affected lots.

3. **What about previously reported results?**

Internal testing has shown that apart from generating higher numbers of unassigned events in some patient samples, to date, the staining reagents in the affected kits otherwise function as intended for detecting Circulating Tumor Cells and White Blood Cells. Patient results generated using CELLSEARCH® Kits should be used in conjunction with the overall clinical information derived from diagnostic tests (i.e., imaging and laboratory tests), physical examination and the complete medical history in accordance with appropriate patient management procedures. You should discuss any concerns you may have regarding previously reported results with your Laboratory Medical Director or with the requesting physician.

4. **Are there other lots available to replace my existing inventory?**

We are working on a re-supply plan to ensure you receive replacement for the existing inventory. Upon return of the enclosed confirmation form, we will communicate shortly regarding product availability date.

5. **Will I receive credit for my tests if I observe the issue described above?**

Customers who have reported a complaint to Technical Support and are unable to report patient results will be issued a credit. Customers who have destroyed remaining inventory and returned confirmation form to the indicated email address will also be issued a credit.

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Customer Confirmation of Receipt and Action

# URGENT MEDICAL DEVICE CORRECTION NOTIFICATION

## High number of total images/unassigned events in some patients for CELLSEARCH® Circulating Tumor Cell Kits (IVD), (Product Code 7900001)

*Please return this form to us no later than* **April 27, 2018.**

**Attn:** ***Field Action Coordinator***

**EMAIL:** cs-correction@siliconbiosystems.com

**Section I – Acknowledgement**

I read and understood the Urgent Medical Device Correction Notification and will do as instructed.

**Section II – Confirmation**

Your Name: _____ Name of Facility: _____

Your Signature: _____

Date: _____ Telephone: _____

*(Your signature provides confirmation that you have received and understood this notification.)*

**Section III – Traceability of Products**

Product Code: 7900001. Lot Number(s): _____

Quantity of Kits On-Site: _____ Quantity of Kits Unopened: _____

Quantity of Kits Opened: _____ Date Opened: _____

No. of Tests Performed: _____

Quantity of Kits Disposed: _____

Your Name: _____ Title: _____

Your Signature: _____

Date: _____ Email: _____

*(Your signature provides confirmation that you have destroyed the remaining inventory at your site.)*