



November 19, 2018

Revised and Updated Notification
URGENT MEDICAL DEVICE RECALL – FA-30417XL

COULTER® EPICS® XL™ Flow Cytometer with System II Software
COULTER EPICS XL-MCL™ Flow Cytometer with System II Software

Product	Part Numbers	Software Versions
COULTER® EPICS® XL™ Flow Cytometer (new, reconditioned or refurbished) with System II Software	All	All
COULTER EPICS XL-MCL™ Flow Cytometer (new, reconditioned or refurbished) with System II Software		

Dear Beckman Coulter Life Sciences Customer,

This notification supplements our previous **Urgent Medical Device Recall Letter dated January 9, 2018 – FA-30417XL** concerning an internal electronic component on the circuit “Amplifier” boards in the FC 500 system that may be affected by a manufacturing defect. This letter contains important information that needs your immediate attention.

This letter provides new and/or enhanced information for the following topics. **The updated information is shown in blue, bold text within the letter:**

- Actions that you should take if you observe any of the issues described in this letter (see Action # 5 below and Attachment 1, FAQ # 4)

ISSUE:	As a result of customer complaints and subsequent internal investigations, Beckman Coulter Life Sciences has determined that an internal electronic component on the circuit “Amplifier” boards in the EPICS XL/XL-MCL Flow Cytometry systems may be affected by a manufacturing defect. Each EPICS XL/XL- MCL system contains up to seven (7) of the potentially affected Amplifier boards. All instruments are potentially impacted.
---------------	--

IMPACT:	<p>There may be impact to patient results due to this issue when using the EPICS XL/XL-MCL for any application.</p> <p>This manufacturing defect may result in failures causing signal loss and/or signal drifting as follows:</p> <ul style="list-style-type: none">▪ The failure could present itself as signal loss and/or signal drifting resulting in absence of data or a shift in the population in the data plots.▪ Customers have reported sudden loss of signal, intermittent signal loss, sudden upward or downward shift in signal, upward or downward drift in signal over time, fluctuating signal, suboptimal compensation, erroneous results on affected parameters, and/or increased coefficients of variation (CV) of Flow-Check beads (see Attachment 1 – FAQ for more details).
----------------	---

ACTIONS:	<p>Implement the following actions for the applications you use * -</p> <ol style="list-style-type: none"> 1. <u>For All Applications including Laboratory Developed Tests:</u> <ol style="list-style-type: none"> a. As per the product documentation all data must be reviewed by a laboratory professional prior to the release of reported results from the lab. b. Immediately implement the collection of TIME as a parameter and create TIME versus Parameter plots which will allow the monitoring of signal integrity as instructed in Attachments 2 and 3. c. Review data as described below: <ol style="list-style-type: none"> i. Review of all TIME plots for each parameter. ii. Monitor consistent Forward Scatter, Side Scatter and all fluorescence data over time as shown in Attachment 3. iii. Unexpected fluctuations in the events over time may indicate signal integrity or data acquisition conditions resulting from board failure; or compromised fluidics, iv. All data must be reviewed prior to the release of any results from the laboratory, via an LIS or any other mechanism. 2. <u>For tetraONE:</u> <ol style="list-style-type: none"> a. As it is not possible to add TIME as a parameter to these protocols, discontinue use of the automated tetraONE application. b. You can continue to use the tetraCHROME reagents with the manual gating instructions provided in the product labeling. Refer to CYTO-STAT tetraCHROME IFU, PN B90108 (for tetraCHROME CD45-FITC/CD4-RD1/CD8-ECD/CD3-PC5, PN 6607013 and tetraCHROME CD45-FITC/CD56-RD1/CD19-ECD/CD3-PC5, PN 6607073). <ol style="list-style-type: none"> i. Ensure to follow the instructions in the preceding step to add time as a parameter and create the TIME vs Parameter plots. ii. If your laboratory uses Panel Reports, the panels and corresponding panel report templates will need to be constructed as well. iii. Create a separate Data Review TIME Plot protocol for data review including TIME, for the manual tetra application (Attachment 3). iv. Follow the Data Review instructions in the IFU and respective System Guides, as well as the instructions attached to this notification (Attachment 4). 3. <u>For stemONE:</u> <ol style="list-style-type: none"> a. By default, the stemONE IVD locked protocols have TIME included as a parameter. There are no additional requirements to create a manual stemONE IVD protocol. b. Create a separate Data Review TIME Plot protocol for data review including TIME, for the stemONE application (Attachment 3).
-----------------	---

	<p>c. Follow the Data Review instructions in the stemONE System Guide, PN 4277322, Chapter 4 as well as the instructions attached to this notification (Attachment 5).</p> <p>4. <u>For Laboratory Developed Tests:</u> In addition to the actions described above, follow the instructions in Attachment 4 to:</p> <ul style="list-style-type: none"> a. Ensure that the appearance of the data patterns are reviewed and look for suboptimal compensation. b. Ensure that the pattern appearance matches the statistical data reported. <p>5. If you detect any of the issues described, follow the instructions below:</p> <ul style="list-style-type: none"> a. Reject results of the sample b. Stop acquiring samples and immediately contact Beckman Coulter Life Sciences Customer Technical Support Center to determine if the signal loss is potentially caused by a defective Amplifier Board. Your local Beckman Coulter Life Sciences Representative who will gather additional information and schedule an on-site visit. <ul style="list-style-type: none"> i. If the signal loss is suspected stop using the instrument until your Beckman Coulter Life Sciences Service Engineer arrives. ii. During the on-site service visit, Beckman Coulter Life Sciences Service will inspect your instrument to confirm the issue. If it is confirmed to be caused by a defective Amplifier board(s), Beckman Coulter Life Sciences will not be able to repair your device as the parts are no longer available. As explained further in the Resolution below, Beckman Coulter Life Sciences will work with you on options to migrate your existing flow sample workload to a currently available research or clinical cytometer. <p>6. Consult with your Medical Director to determine if a retrospective review of results is warranted.</p>
RESOLUTION:	<p>Beckman Coulter Life Sciences discontinued the manufacturing of new EPICS XL/XL-MCL units. On December 31, 2018, we are discontinuing the service support and the supply of spare parts and system-specific reagents/ controls/ assay target values. We will be contacting you regarding available options to completely retire the units which are not actively used and/ or to assess options to migrate your existing flow sample workload to a currently available research or clinical cytometer.</p>

	<p>* Continue following the above actions for the applications you use, as long as you use your system.</p>
--	---

Please share this information with your laboratory staff and retain this notification as part of your laboratory Quality System documentation. If you have forwarded any of the affected product listed above to another laboratory, please provide them a copy of this letter.

So that we are assured you have received this important communication, please respond within 10 days in one of the following ways:

- Electronically, if you received this communication via email.
- Manually, complete and return the enclosed Response Form.

If you have any questions regarding this notification, please contact:

- From our website: <http://www.beckman.com>
- By phone: call 800-369-0333 in the United States and Canada (Monday – Friday, 8:00 am EST – 8:00 pm EST).
- By email – US and Canada only: LScustomerLetter@Beckman.com
- Outside the United States and Canada, contact your local Beckman Coulter Life Sciences representative.

We apologize for the inconvenience that this has caused your laboratory.

Sincerely,



Nancy Nadler
Vice President, Quality Assurance and Regulatory Affairs
Enclosure: Response Form

Attachment 1

Frequently Asked Questions (FAQ)

1. What is the impact of the issue?

- There may be impact to patient results due to this issue when using the EPICS XL/XL-MCL for any application.
- Implementation of the actions provided in this letter allow for the detection of signal loss and/or signal drifting that could impact patient results.

2. Is my instrument potentially impacted?

- There is the potential that it could be impacted.
- Implementation of the actions provided in this letter allow for detection of signal loss and/or signal drifting that could impact patient results.

3. How can I confirm if my instrument has this issue?

- Implementation of the actions provided in this letter allow for the detection of signal loss and/or signal drifting that could impact patient results.
- Review of these plots, in addition to those used for assay/application result determination, should be part of routine data review, prior to reporting results. Please see additional information in the Attachments.

4. If my instrument demonstrates symptoms of this issue after the implementation of the actions in this letter, what are the next steps to resolve the issue?

- **If your instrument displays the indicated issues follow Action # 5 in this updated notification. Contact Beckman Coulter Life Sciences Customer Support or your local Beckman Coulter Life Sciences Representative for additional guidance and support.**

5. Where can I find the instructions how to implement the immediate recommendations?

- See Attachments 2 through 5 of this communication.

6. How can I confirm there is no issue with previous data if TIME parameter was not selected?

- Unexpected fluctuations in the events over time may indicate compromised data acquisition conditions (see Special Procedures and Troubleshooting Manual for the EPICS XL/XL-MCL (PN 4237296)) for instructions on handling compromised fluidics or optics conditions).

7. How can I get updates on the resolution of this issue?

- Beckman Coulter Life Sciences will be contacting you regarding available options for resolution of this issue.

Attachment 2

Instructions for Creating TIME Plots in System II Unlocked Protocols

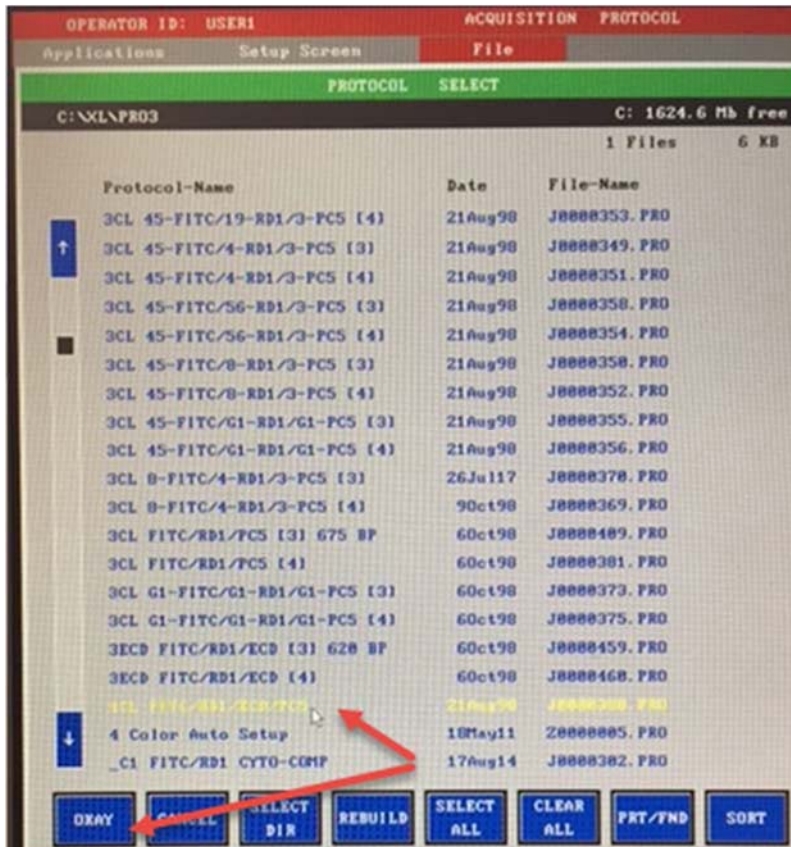
Please refer to COULTER® EPICS® XL Flow Cytometer COULTER EPICS XL-MCL Flow Cytometer SYSTEM II Software Getting Started manual, PN 4237238, Chapter 4, Creating Protocols for additional instructions. The following instructions apply to any unlocked protocol in the System II Software.

A. Adding Time Plots to Unlocked Protocols

1. Select Setup Screen >> Protocols



2. Select **File>> Select** to view the Protocols.
3. Click on a desired protocol to select it and the OKAY:



- The protocol will display (this example is a 4 color protocol). Make note of the Signal Sources box at the lower right of the display.

Edit the protocol to ensure that TIME is selected as a parameter for data collection by selecting the "X" next to TIME in the Signal Sources box. Observe that TIME is now listed in the protocol parameters as an added signal to be acquired. (Example in screen shot below is a 4 Color protocol).

SIGNAL SOURCES			
Sensor	Lin	Log	Peak
FS	X	X	X
SS	X	X	X
FL1	X	X	X
FL2	X	X	X
FL3	X	X	X
FL4	X	X	X
TIME	X		
PRISM	X		
RATIO	X	NUM:??	
		DEN:??	
AUX	X	SIG:??	

PARAMETERS	
Signal	User Name
TIME	TIME
FS	FS
SS	SS
FL1 LOG	FL1 LOG
FL2 LOG	FL2 LOG
FL3 LOG	FL3 LOG
FL4 LOG	FL4 LOG

Erase Hist/Param

- Select **File >> Save**.

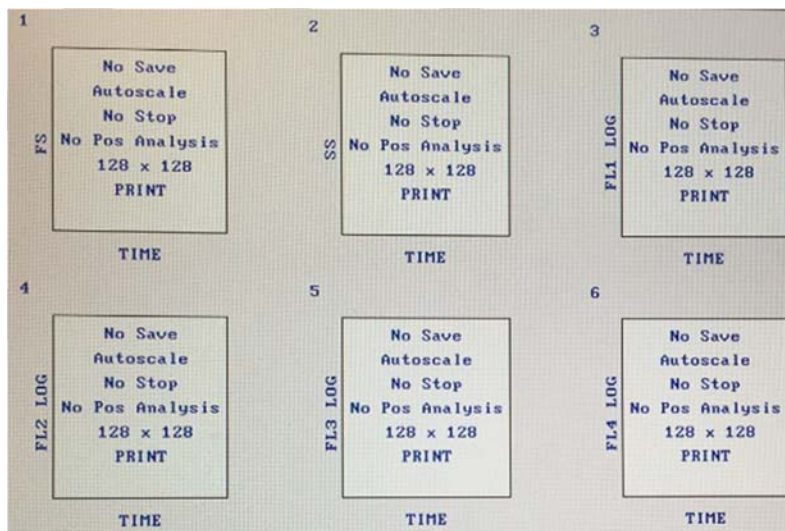
Note: System II protocols allow a maximum of 8 plots. If the unlocked protocol just updated cannot accommodate an individual TIME plot for each parameter, a separate Data Review protocol using 2-parameter histograms of TIME versus each parameter (i.e. FS/TIME, SS, TIME, FL1/TIME, FL2/TIME, FL3/TIME, and FL4/TIME) is created per the instructions in Attachment 3.

Attachment 3

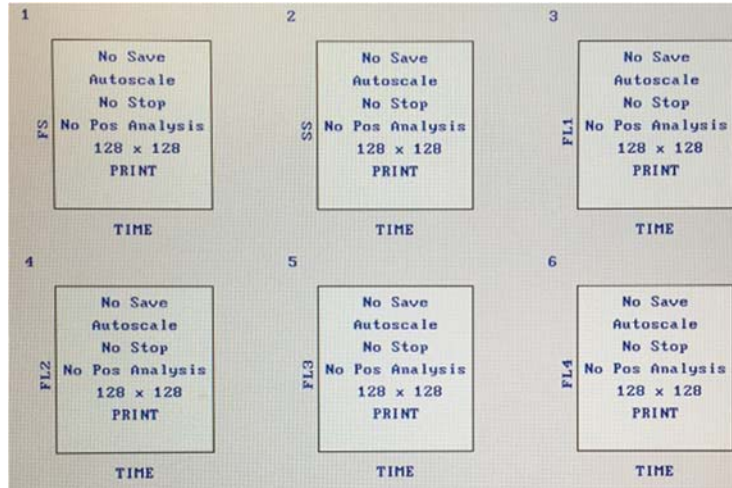
Instructions for Creating a Data Review Protocol with Time Plots For Listmode Replay Data Review

A. Creating a Data Review Protocol with Time Plots

1. Select **Setup Screen >> Protocol**.
2. Either open an existing 4 color (log fluorescence) protocol or create a new 4 color protocol following the instructions beginning in Section 4-2 to create the protocols. Ensure this protocol has the following signals selected:
 - a. FS Lin
 - b. SS Lin
 - c. FL1 Log
 - d. FL2 Log
 - e. FL3 Log
 - f. FL4 Log
 - g. TIME
3. Assign parameters to plot axes:
 - a. Click on TIME in the Parameter box and assign TIME to the X-axis of Plots 1 through Plot 6.
 - b. Click on the next Parameter Signal, for example, FS, and click on the Y-axis of Plot 1.
 - c. Repeat Step 3b to assign the remaining parameters (SS, FL1, FL2, FL3 and FL4) to the Y-axis of the remaining histograms. The protocol should appear as shown below:



4. Select **File >> Save As ...** and enter a name for the protocol: i.e. Data Review Log FL-TIME Plots.
5. If Linear fluorescent signals are selected to be collected, repeat Step 1 through Step 4 selecting FS-Lin, SS-Lin, FL1-Lin, FL2-Lin, FL3-Lin, FL4-Lin and TIME. When saving the protocol, enter a name for the protocol: i.e. Data Review Lin FL-TIME Plots:

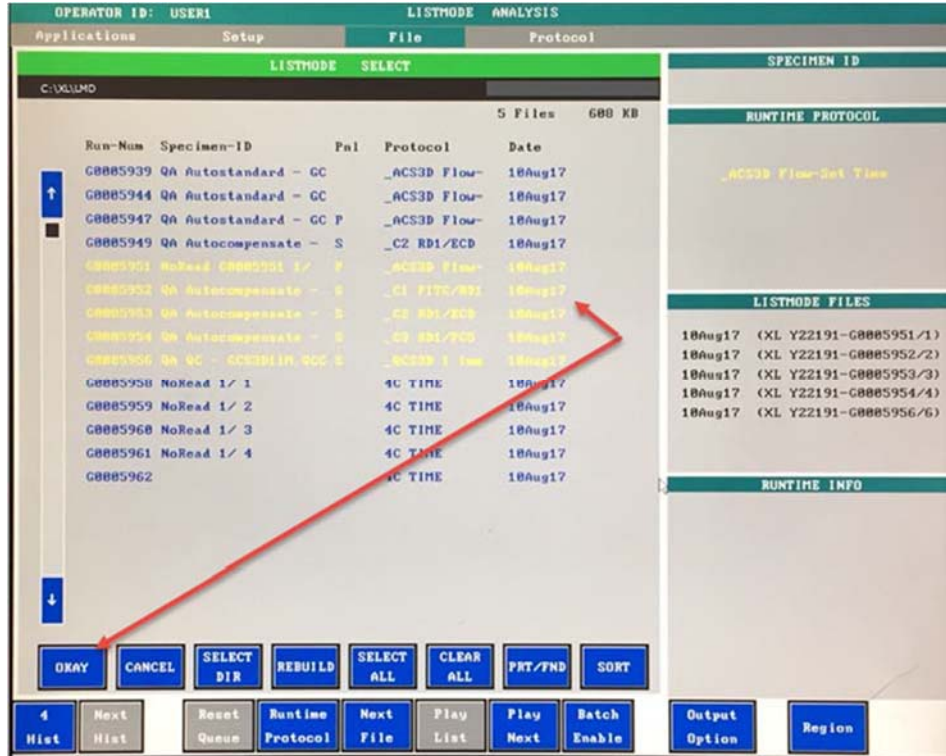


6. If your laboratory uses panels to acquire samples, refer to the COULTER® EPICS® XL Flow Cytometer COULTER EPICS XL-MCL Flow Cytometer SYSTEM II Software Getting Started manual, PN 4237238, Chapter 6, Creating Panels for additional instructions.
7. If your lab uses panel reports, please refer to the COULTER® EPICS® XL Flow Cytometer COULTER EPICS XL-MCL Flow Cytometer SYSTEM II Software Data Management manual, PN 4237237, Chapter 4, Creating Reports for the necessary instructions.
8. Refer to Procedure B of this document for instructions on Listmode Replay using the Data Review using TIME Plots.

B. Listmode Replay using the Data Review Protocol with TIME Plots

Refer to COULTER® EPICS® XL Flow Cytometer COULTER EPICS XL-MCL Flow Cytometer SYSTEM II, Instructions for Use Manual, PN 4237297, Chapter 5, Listmode Analysis, for additional instructions regarding Listmode replay in System II software.

- Select **Applications >> Listmode**.
- Select **File >> Select** and click on all desired listmode files for data review, then select **OKAY**:



Runtime
Protocol

- Click on the Runtime Protocol button at the bottom of the screen to toggle to

New
Pnl/Pro

- Select **Protocol >> Select** and select the Data Review Protocol (i.e. Data Review Log FL-TIME Plots created in Procedure B of this Attachment) and then select **OKAY**.

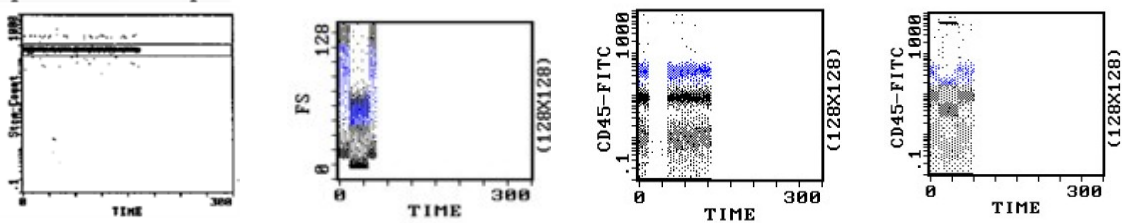
Play
Next

- Click on the Play Next to review each listmode file data on each Time versus parameter plot.

Data review must include the following:

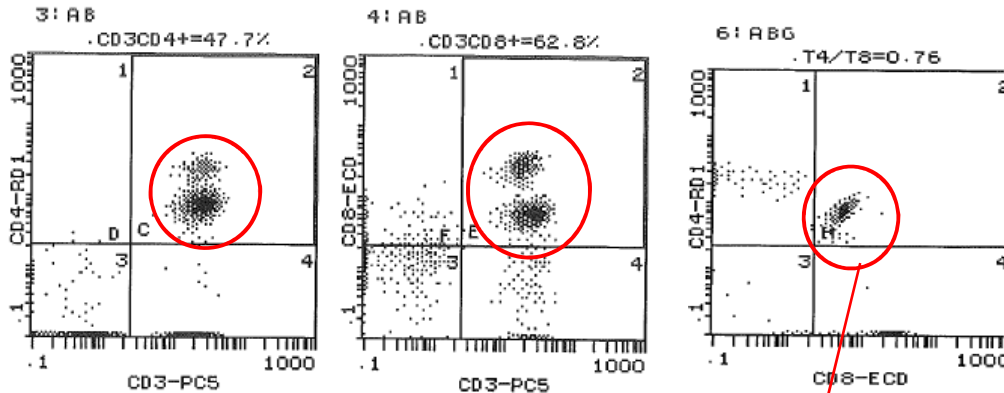
- Review of all TIME plots for each parameter.
- Monitor consistent Forward Scatter, Side Scatter and all fluorescence data over time as shown in the example below.

Examples: Stable Acquisition Examples: Compromised Acquisition



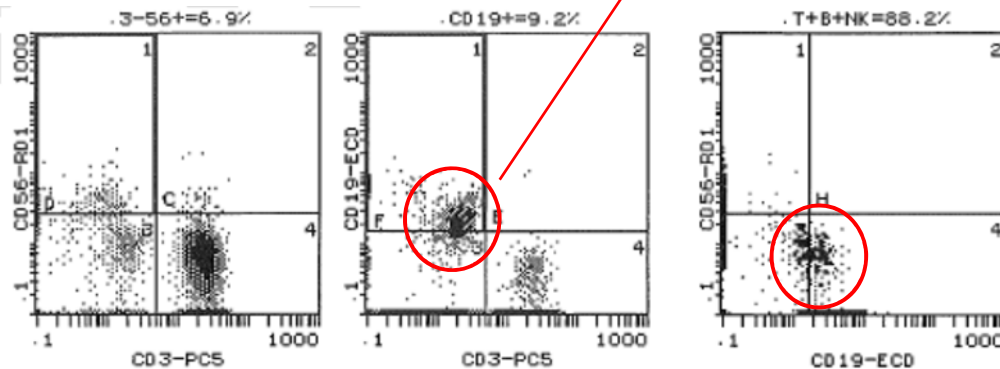
- Unexpected fluctuations in the events over time may indicate compromised data acquisition conditions (see Special Procedures and Troubleshooting Manual for the EPICS XL/XL-MCL (PN 4237296) for instructions on handling compromised fluidics or optics conditions).
- Review the data plots for the application in question. Below are examples of data plots from the tetraONE application demonstrating signal loss:

tetraONE 45/4/8/3



This also demonstrates an example of suboptimal compensation

tetraONE 45-56-19-3

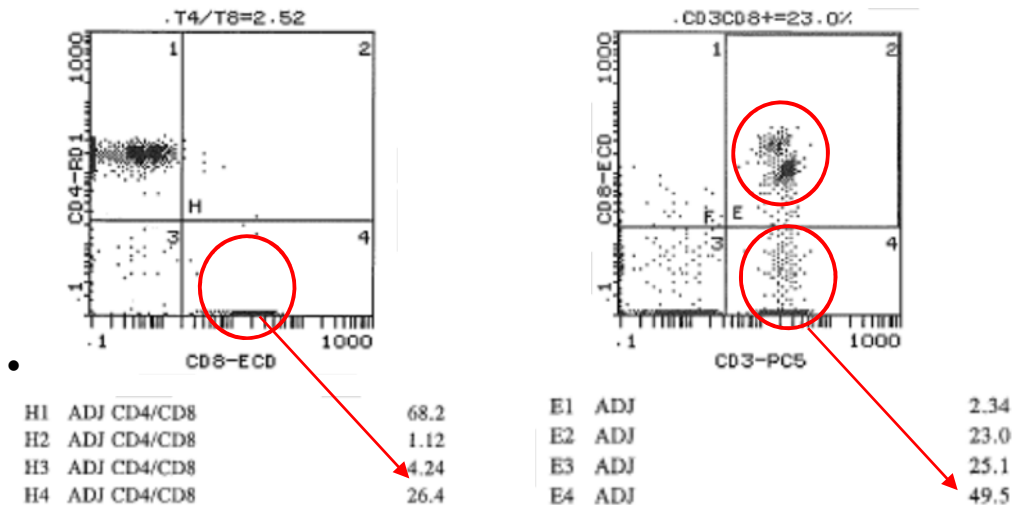


Attachment 4

Additional Information for Laboratory Developed Tests

In certain applications, the implementation of the TIME vs Parameter plots may not always result in detection of the failure. Therefore:

- Ensure that the appearance of the data patterns are reviewed, look for suboptimal compensation (as shown on the previous page). In some instances, the finding may be especially subtle. In this case, a similar pattern could be due to a small compensation error. Consider the possibility that this may be an Amplifier board failure.
- Ensure that the pattern appearance matches the statistical data reported. The following are examples of data where the pattern appearance does not match the statistical data reported below the plots, and the population appearance is not appropriate:



- Follow the Data Review instructions in the respective IFU(s) and System Guides, as well as the instructions included in this notification.

Attachment 5**Instructions for IVD Locked Protocols
stemONE / tetraONE****Manual IVD Protocol Creation**

These instructions provide guidance for the tetraONE and stemONE locked IVD applications for the purpose of data review with TIME plots.

A. stemONE IVD locked protocols

1. By default, the stemONE IVD locked protocols have TIME included as a parameter. There are no additional requirements to create a manual stemONE IVD protocol. Attachment 3 addresses creating a separate Data Review TIME Plot protocol for data review including TIME, for the tetraONE and stemONE applications. Refer to Attachment 3 for instructions on 'Creating a Data Review Protocol with TIME Plots' for data review.
2. For all stemONE listmode data, perform listmode replay using the Data Review Protocol with TIME Plots instructions provided in this document (Attachment 3).

B. tetraONE IVD locked protocols

1. Locate the indicated product instructions for use at www.beckman.com.
2. Scroll down to the option to search by Item/REF/Document Number
1. Enter the following information to locate the tetraCHROME IFU:
 - Item/REF/Document Number: B90108 CYTOSTAT tetraCHROME IFU
 - Document Category: Consumable IFU/CIS/Setting Sheet



Technical Documents	My Technical Documents	Safety Data Sheets (SDS/MSDS)	Software Download	* Indicates required fields
Search By Product				
Search By Reagents/Calibrators/Controls				
Search By Item/REF/Document Number				
Item/REF/Document Number	Document Category	Language		
B90108	Consumable IFU/CIS/Setting Sheet	English		
Search	Search Tips			
Search By Lot Number				
Search By Serial Number				
Search By Keyword				

3. Follow the CYTOSTAT tetraCHROME reagent IFU for instructions on creating unlocked manual protocols.
4. Ensure TIME is selected as a parameter for data collection in the unlocked tetraCHROME manual protocol(s). The unlocked tetraCHROME protocol(s) will be used for data collection.
5. If your laboratory uses panels to acquire samples, refer to the COULTER® EPICS® XL Flow Cytometer COULTER EPICS XL-MCL Flow Cytometer SYSTEM II Software Getting Started manual, PN 4237238, Chapter 6, Creating Panels for additional instructions.

6. If your lab uses panel reports, please refer to the COULTER® EPICS® XL Flow Cytometer COULTER EPICS XL-MCL Flow Cytometer SYSTEM II Software Data Management manual, PN 4237237, Chapter 4, Creating Reports for the necessary instructions.
8. For all tetra application listmode data, perform listmode replay per the *Listmode Replay using the Data Review Protocol with TIME Plots* instructions provided in this document (Attachment 2).