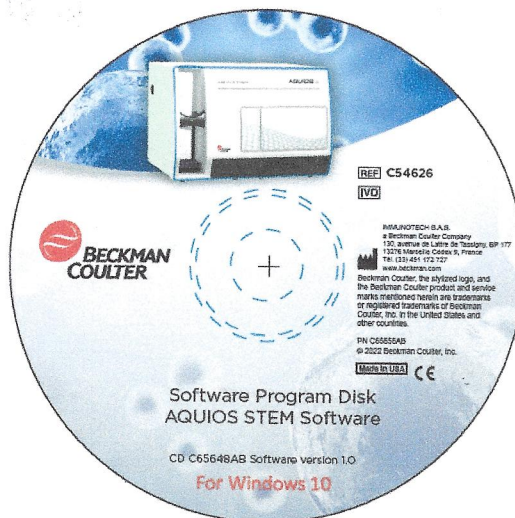


PROYECTOS DE RÓTULO EXTERNO

Nota: por art. 1° de la Disposición n° 4043/2005 ANMAT, se acepta el uso de los 24 símbolos descritos y definidos en el Anexo I de la citada norma en reemplazo del texto de la información requerida en la presente Disposición en los rótulos de los productos para diagnóstico de uso in vitro.

RÓTULO ORIGINAL DEL PRODUCTO



1. Nombre del Producto	AQUIOS STEM Software Kit
2.	
a) Nombre y dirección del Importador	Rótulo Local
b) Nombre del Director Técnico	Rótulo Local
c) Nombre y dirección del Elaborador	Rótulo Local
d) Nombre y dirección del Fabricante Legal	Immunotech S.A.S., A Beckman Coulter Company, 130 Avenue de Latre de Tassigny-BP177- 13276 Marseille, Cedex 9-France
3. Leyenda "Autorizado por la ANMAT"	Rótulo Local
4. Número de lote o partida	LOT
5. Fecha de Vencimiento	
6. Constitución del equipo (relación de los componentes)	1 unidad
7. Leyenda "Uso In Vitro"	IVD

8. Descripción de la finalidad de uso del producto	
9. Descripción de las precauciones	
10. Indicación de las condiciones adecuadas de almacenamiento y transporte del producto	NA

RÓTULO LOCAL (APUESTO POR EL IMPORTADOR/DISTRIBUIDOR EN ARGENTINA)

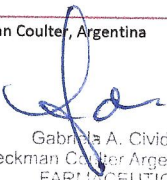
Beckman Coulter Argentina, Gral. Martín M. Güemes. 4168 B1603EN Villa Martelli, Bs. As
 Directora Técnica: Farmacéutica Gabriela A. Cividino
 Fabricante: Immunotech S.A.S., A Beckman Coulter Company, 130 Avenue de Lattre de Tassigny-BP177- 13276 Marseille, Cedex 9-France.
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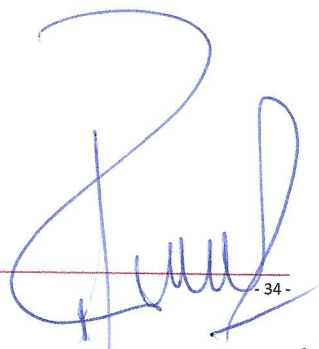
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- 34 -

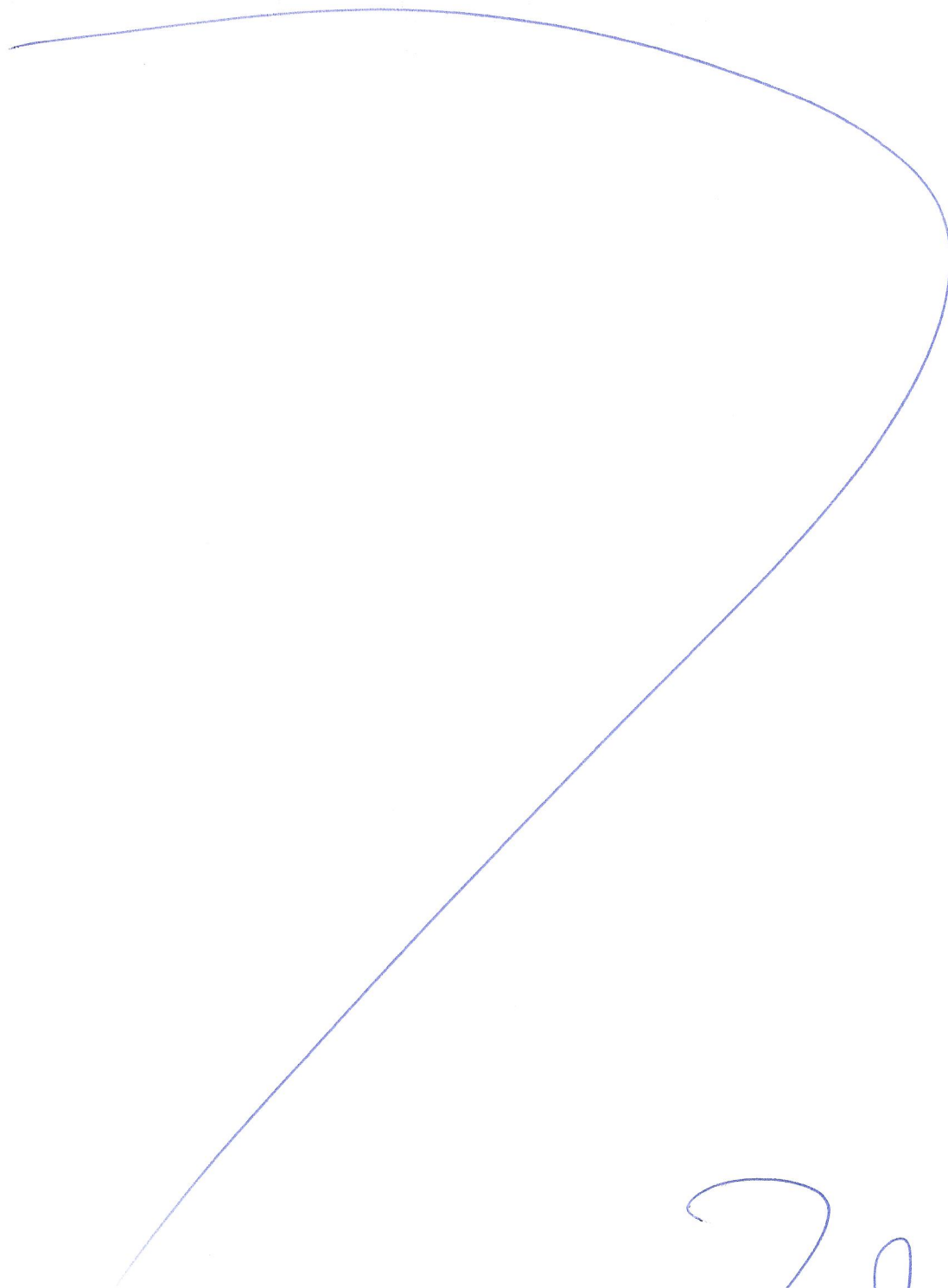

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PROYECTO DE MANUAL DE INSTRUCCIONES

Ver adjunto Instrucciones de Uso del Producto.



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- 35 -

System Guide

AQUIOS STEM

Rx Only in the U.S.A.



B75978AA
March 2022



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Beckman Coulter STEM Software System Guide
B75 78AA March 2022

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Glossary of Symbols is available at
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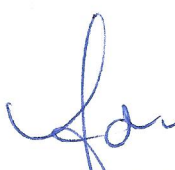
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Revision History

B75978AA, March 2022

Initial Issue

Software version 1.0

This document applies to the latest software listed and higher versions. When a subsequent software version affects the information in this document, a new issue will be released to the Beckman Coulter Web site. For labeling updates, go to www.beckman.com and download the latest version of the manual for your instrument.

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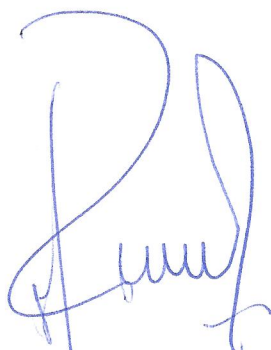
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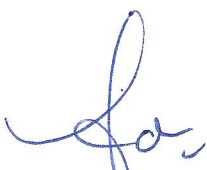
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iii




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Safety Notice

Read all product manuals and consult with Beckman Coulter-trained personnel before attempting to operate instrument. Do not attempt to perform any procedure before carefully reading all instructions. Always follow product labeling and manufacturer's recommendations. If in doubt as to how to proceed in any situation, [Contact Us](#).

Beckman Coulter, Inc. urges its customers and employees to comply with all national health and safety standards such as the use of barrier protection. This may include, but it is not limited to, protective eyewear, gloves, and suitable laboratory attire when operating or maintaining this or any other automated laboratory analyzer.

Alerts for Warning and Caution

WARNINGS and CAUTIONS alert you as follows:

WARNING

WARNING indicates a potentially hazardous situation which, if not avoided, could result in death or serious injury. May be used to indicate the possibility of erroneous data that could result in an incorrect diagnosis.

CAUTION

CAUTION indicates a potentially hazardous situation, which, if not avoided, may result in minor or moderate injury. It may also be used to alert against unsafe practices. May be used to indicate the possibility of erroneous data that could result in an incorrect diagnosis.

CAUTION

System integrity could be compromised and operational failures could occur if:

- This equipment is used in a manner other than specified. Operate the instrument as instructed in the Product Manuals.
- You introduce software that is not authorized by Beckman Coulter into your computer. Only operate your system's computer with software authorized by Beckman Coulter.
- You install software that is not an original copyrighted version. Only use software that is an original copyrighted version to prevent virus contamination.

 CAUTION

If you purchased this product from anyone other than Beckman Coulter or an authorized Beckman Coulter distributor, and, it is not presently under a Beckman Coulter service maintenance agreement, Beckman Coulter cannot guarantee that the product is fitted with the most current mandatory engineering revisions or that you will receive the most current information bulletins concerning the product. If you purchased this product from a third party and would like further information concerning this topic, [Contact Us](#).

 WARNING

Risk of operator injury if:

- All doors, covers, and panels are not closed and secured in place prior to and during instrument operation.
- The integrity of safety interlocks and sensors is compromised.
- Instrument alarms and error messages are not acknowledged and acted upon.
- You contact moving parts.
- You mishandle broken parts.
- Doors, covers, and panels are not opened, closed, removed, and/or replaced with care.
- Improper tools are used for troubleshooting.

To avoid injury:

- Keep doors, covers, and panels closed and secured in place while the instrument is in use.
- Take full advantage of the safety features of the instrument. Do not defeat safety interlocks and sensors.
- Acknowledge and act upon instrument alarms and error messages.
- Keep away from moving parts.
- Report any broken parts to your Beckman Coulter Representative.
- Open/remove and close/replace doors, covers, and panels with care.
- Use the proper tools when troubleshooting.

Contents

Revision History, iii

Safety Notice, v

Alerts for Warning and Caution, v

Introduction, xv

Overview, xv

How to Use Your AQUIOS Manuals, xv

Before You Begin, xvi

About Your Cytometer Software, xvi

About this System Guide, xvi

Conventions, xvii

Symbols, xviii

Graphics Icons, xviii

CHAPTER 1: Use and Function, 1-1

Overview, 1-1

Intended Use, 1-1

Intended User, 1-2

System Components, 1-2

AQUIOS STEM System, 1-2

Unique Load & Go Feature, 1-3

AQUIOS STEM Test, 1-3

Consumables and Supplies, 1-3

Preparation, 1-4

AQUIOS STEM Lysing Solution, 1-4

Monoclonal Antibodies, 1-4

AQUIOS STEM-Count Fluorospheres, 1-5

Acquisition, 1-5

AQUIOS Sheath Fluid, 1-5

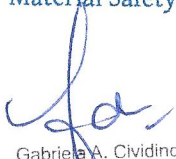
Quality Control, 1-5

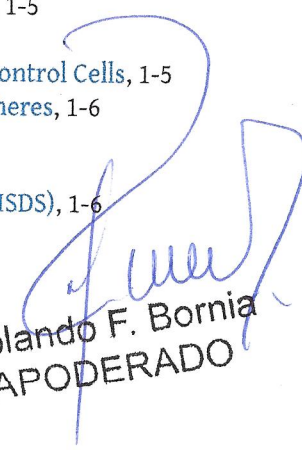
AQUIOS STEM CD34 Control Cells, 1-5

Flow-Check Fluorospheres, 1-6

Limitations, 1-6

Material Safety Data Sheets (SDS/MSDS), 1-6


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CHAPTER 2: Operating Principles, 2-1

Overview, 2-1

Principles of AQUIOS STEM Tests, 2-1

Testing with the AQUIOS STEM Kit Reagents, 2-2

Light Source Configuration, 2-2

CD34+HPC Enumeration Panels, 2-3

AQUIOS STEM Tests, 2-3

Analysis Algorithm Overview, 2-4

Introduction to Gating Strategy, 2-4

Gating Strategy: AQUIOS STEM Panel, AQUIOS STEM Duplicate, and

AQUIOS STEM Single, 2-5

Forward Scatter (FS) versus Side Scatter (SS) Plot, 2-6

CD34-PE versus CD45-FITC Plot, 2-6

BEADS versus TIME Plot, 2-7

Side Scatter (SS) versus 7-AAD Plot, 2-7

Side Scatter (SS) versus CD45-FITC Plot, 2-8

Side Scatter (SS) versus CD34-PE Plot, 2-8

Side Scatter (SS) versus CD45-FITC Plot, 2-9

CD45 DIM Side Scatter (SS) versus Forward Scatter (FS) Plot, 2-9

LYMPHS Side Scatter (SS) versus Forward Scatter (FS) Plot, 2-10

Side Scatter (SS) versus CD45-FITC Plot, 2-10

Side Scatter (SS) versus CD34-PE Plot, 2-11

Side Scatter (SS) versus CD45-FITC Plot, 2-11

Side Scatter (SS) versus Forward Scatter (FS) Plot, 2-12

Side Scatter (SS) versus Forward Scatter (FS) Plot, 2-12

Side Scatter (SS) versus 7-AAD Plot, 2-13

CHAPTER 3: Quality Control, 3-1

Overview, 3-1

Quality Control Checks, 3-1

AQUIOS STEM Quality Control Workflow, 3-1

QC Materials, 3-2

Daily QC Overview, 3-2

QC Setup, 3-3

QC Process, 3-3

Flow-Check Fluorospheres - Single Tube Loader, 3-4

STEM Single (AutoLoader) - AQUIOS STEM CD34 L1 and L2 Control Cells, 3-7

Adding Reagents, 3-7

Adding and Using AQUIOS STEM CD34 Control Lots, 3-12

Adding New Lots of AQUIOS STEM CD34 L1 and L2 Control Cells using QR Code, 3-12

Adding New Lots of AQUIOS STEM CD34 L1 and L2 Control Cells Manually, 3-12

Starting AQUIOS STEM CD34 L1 and L2 Control Cell QC With Pre-Existing Lot, 3-15

QC Screen, 3-16

QC Reports, 3-18

AQUIOS STEM (Single Tube Loader) Flow-Check Fluorospheres QC Result Examples, 3-18

AQUIOS STEM Single (Auto Loader) - AQUIOS STEM CD34 Control Cells Level 1 & 2 QC Result Examples, 3-19

AQUIOS STEM Single (Auto Loader) - AQUIOS STEM CD34 Control Cells Level 1 & 2 QC Result Examples, 3-20

Interlaboratory Quality Assurance (IQAP), 3-24

Before Setting Up IQAP Export, 3-24

Setting Up IQAP Export, 3-25

CHAPTER 4: Sample Analysis, 4-1

Overview, 4-1

Test Description, 4-2

AQUIOS STEM Application Workflow, 4-2

Sample preparation, 4-3

Storage Conditions and Stability, 4-4

Non-Frozen Specimen, 4-4

Frozen Specimen Type, 4-4

Reagents, 4-4

AQUIOS STEM Testing Workflow, 4-4

Create a Request, 4-6

Load Sample in the Instrument, 4-8

Options for Running Specimens, 4-10

Logging In Controls, 4-11

Running Samples Using the Autoloader, 4-11

Running Samples Using the Single-tube Loader, 4-11

Running Screen, 4-12

CHAPTER 5: Data Review, 5-1

Overview, 5-1

Review Screen, 5-1

Review Screen Display Areas (left to right), 5-2

Graphic Options, 5-6

AQUIOS STEM Panel, 5-7

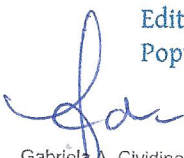
Action Toolbox, 5-9

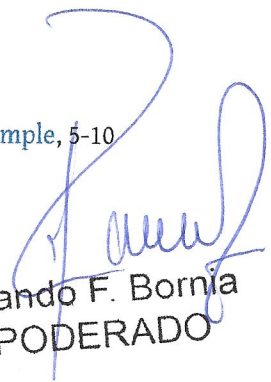
Data Review, 5-9

Review Data Displays, 5-9

Edit Regions for a Review Sample, 5-10

Population Statistics, 5-11


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Adjust Compensation Manually, 5-11

Result Screen, 5-15

Using the Result Screen to Select Data for Review, 5-15

Flags And Notifications, 5-16

Flags, 5-17

Notifications, 5-19

AQUIOS STEM Software Observations, 5-20

CHAPTER 6: Performance Characteristics , 6-1

Overview, 6-1

Linearity , 6-1

Limit of Blank/Limit of Detection/Limit of Quantitation, 6-2

Analytical Measuring Ranges, 6-3

Method Comparison, 6-4

Reference Interval, 6-6

Precision, 6-7

Using Control Cells, 6-7

Using Clinical Specimens, 6-7

Specificity, 6-8

Reagent Specificity, 6-8

Quality Control, 6-8

CHAPTER 7: Application Specifications, 7-1

Overview, 7-1

AQUIOS STEM Preparation, 7-1

AQUIOS STEM Sample Preparation, 7-1

AQUIOS STEM Throughput, 7-1

CHAPTER 8: Adjustment and Replacement Procedures, 8-1

Overview, 8-1

AQUIOS STEM Replacement Procedures, 8-1

Replacing the AQUIOS STEM Lysing Solution, 8-1

Replacing the AQUIOS STEM-Count Fluorospheres, 8-3

APPENDIX A: Reports, A-1

Overview, A-1

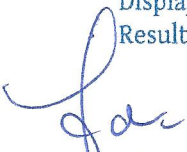
Reports, A-1

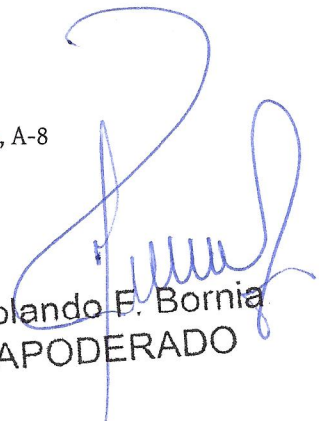
Report Description, A-8

Report Heading, A-8

Displays: Generating Reports, A-8

Result Table Heading, A-8


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Statistics: AQUIOS STEM Report, A-8

QC Report, A-8

QC Report Description, A-9

QC Result Report Heading, QC Instrument Report Heading, QC
Instrument Drift Report Heading, A-9

QC Result Displays & Statistics (Depend on Test Selected), A-9

QC Result First Table Heading, A-9

QC Result Second Table Heading, QC Instrument Second Table
Heading, QC Instrument Drift Second Table Heading, A-9

QC Reports, A-10

References

Index

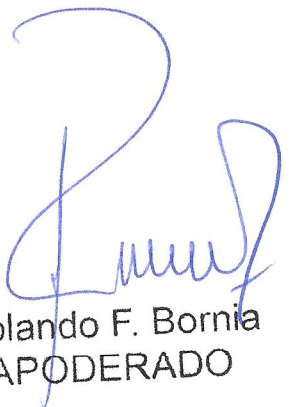
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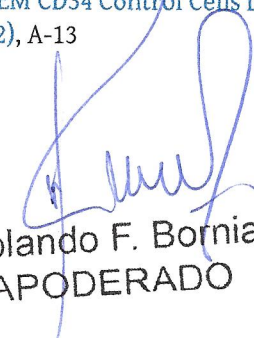
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Illustrations

- 2.1 Optical Filter Configuration, 2-2
- 2.2 FS versus SS Plot, 2-6
- 2.3 CD34-PE versus CD45-FITC Plot, 2-6
- 2.4 BEADS versus TIME Plot, 2-7
- 2.5 SS versus 7-AAD Plot, 2-7
- 2.6 SS versus CD45-FITC Plot, 2-8
- 2.7 SS versus CD34-PE Plot, 2-8
- 2.8 SS versus CD45-FITC Plot, 2-9
- 2.9 CD45 SS versus FS Plot, 2-9
- 2.10 LYMPHS SS versus FS Plot, 2-10
- 2.11 SS versus CD45-FITC Plot, 2-10
- 2.12 SS versus CD34-PE Plot, 2-11
- 2.13 SS versus CD45-FITC Plot, 2-11
- 2.14 SS versus FS Plot, 2-12
- 2.15 SS versus FS Plot, 2-12
- 2.16 SS versus 7-AAD Plot, 2-13
- 3.1 Results Tab Screen: Flow-Check Fluorospheres, 3-17
- 3.2 Results Tab: Flow-Check Fluorospheres Report Page 1, 3-18
- 3.3 Results Tab Screen: AQUIOS STEM CD34 Control Cells Level 1 (Run with AQUIOS STEM Single), 3-19
- 3.4 Results Tab Screen: AQUIOS STEM CD34 Control Cells Level 2 (Run with AQUIOS STEM Single), 3-19
- 3.5 Results Tab Screen: AQUIOS STEM CD34 Control Cells Level 1, Page 1 (Run with AQUIOS STEM Single), 3-20
- 3.6 Results Tab Screen: AQUIOS STEM CD34 Control Cells Level 1, Page 2 (Run with AQUIOS STEM Single), 3-21
- 3.7 Results Tab Screen: AQUIOS STEM CD34 Control Cells Level 2, Page 1 (Run with AQUIOS STEM Single), 3-22
- 3.8 Results Tab Screen: AQUIOS STEM CD34 Control Cells Level 2, Page 2 (Run with AQUIOS STEM Single), 3-23
- 3.9 QC Results Tab Screen: Export IQAP, 3-25
- 3.10 Export IQAP control data file, 3-25
- 4.1 Running Screen, 4-12
- 5.1 Review Screen: Display Areas, 5-2
- 5.2 Instrument Designation, 5-2

- 5.3 Auto Refresh, 5-2
- 5.4 Review Screen: Completed Runs List, 5-3
- 5.5 Review Screen: Sample Identifiers and Run Information Area, 5-3
- 5.6 Review Screen: Result Table Area (3 Wells), 5-4
- 5.7 Review Screen: Graphic Options Selection Menu, 5-4
- 5.8 Review Screen: Page Number, 5-4
- 5.9 Review Screen: Well#1 Page 1 (Mobilized Whole Blood), 5-7
- 5.10 Review Screen: Well#1 Page 2 (Mobilized Whole Blood), 5-8
- 5.11 Review Screen: Summary Page 1, 5-8
- 5.12 Action Toolbox, 5-9
- 5.13 Adjust Compensation, 5-13
- 5.14 Over Compensation, 5-14
- 5.15 Under Compensation, 5-14
- 6.1 Linearity: CD34+ cells/ μ L, 6-2
- 6.2 Linearity: CD45+ cells/ μ L, 6-2
- 6.3 Regression Analysis: CD34+ cells/ μ L, 6-5
- 6.4 Regression Analysis: CD34+ %, 6-5
- 6.5 Regression Analysis: CD45+ cells/ μ L, 6-5
- A.1 Report: STEM Panel - Apheresis - Well #1 Page 1, A-2
- A.2 Report: STEM Panel - Apheresis - Well #1 Page 2, A-3
- A.3 Report: STEM Panel - Apheresis - Well #1 Page 3, A-4
- A.4 Report: STEM Panel - Apheresis - Summary Page 1, A-5
- A.5 Report: STEM Panel - Apheresis - Summary Page 2, A-6
- A.6 Report: STEM Panel - Apheresis - Summary Page 3, A-7
- A.7 QC Results: Results View of AQUIOS STEM CD34 Control Cells Level 1, AQUIOS STEM Single, A-10
- A.8 QC Results: AQUIOS STEM CD34 Control Cells Level 1, AQUIOS STEM Single (Page 1), A-11
- A.9 QC Results: AQUIOS STEM CD34 Control Cells Level 1, AQUIOS STEM Single (Page 2), A-11
- A.10 QC Results: Results View of AQUIOS STEM CD34 Control Cells Level 2, AQUIOS STEM Single, A-12
- A.11 QC Results: AQUIOS STEM CD34 Control Cells Level 2, AQUIOS STEM Single (Page 1), A-13
- A.12 QC Results: AQUIOS STEM CD34 Control Cells Level 2, AQUIOS STEM Single (page 2), A-13


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Tables

1.1	System Parameters, 1-1
2.1	Parameter Results Provided by STEM Panel , STEM Duplicate, or STEM Single Analysis, 2-3
2.2	Equivalence Between Primary Region Name and Replicated Region Name, 2-5
3.1	AQUIOS STEM QC Workflow, 3-1
3.2	Handling AQUIOS STEM Reagent Caps, 3-7
3.3	General Table on QC Screens: Defined, 3-17
4.1	Test Descriptions, 4-2
4.2	Processing Samples Using the STEM Application, 4-3
4.3	Minimum Specimen Volume Required per Specimen Tube, 4-3
5.1	Review Screen: Summary Area Display (AQUIOS STEM, Mobilized Whole Blood), 5-5
5.2	Review Screen: Summary Area Display, Page Number 1 (AQUIOS STEM Panel, Mobilized Whole Blood), 5-6
5.3	Population Statistics Recommended Use, 5-11
5.4	AQUIOS STEM Specific Flags, 5-17
5.5	AQUIOS STEM Specific Notifications, 5-19
6.1	LoB, LoD and LLoQ Results, 6-3
6.2	Analytical Measuring Ranges, 6-3
6.3	Regression statistics for all specimen types combined, 6-4
6.4	Method Comparison study results of AQUIOS STEM system compared with predicate method, 6-4
6.5	Regression statistics by specimen type, 6-6
6.6	Reference Intervals, 6-6
6.7	AQUIOS STEM CD34 Control Cells Level 1, 6-7
6.8	AQUIOS STEM CD34 Control Cells Level 2, 6-7
6.9	Repeatability Precision with clinical specimens, 6-8

Introduction

Overview

This introduction contains the following information:

- [How to Use Your AQUIOS Manuals](#)
- [Before You Begin](#)
- [About this System Guide](#)
- [Conventions](#)
- [Symbols](#)
- [Graphics Icons](#)

How to Use Your AQUIOS Manuals

Your AQUIOS CL Flow Cytometry system includes the manuals listed below:

- The **AQUIOS CL Flow Cytometer Instructions For Use** manual provides information for the day-to-day running of your AQUIOS CL Flow Cytometer and AQUIOS system software. It also provides procedures for cleaning the instrument and replacement procedures. You can find detailed step-by-step procedures for daily startup for running and reviewing quality control (QC) data, running samples, analyzing data, printing reports, and shutting the instrument down. The Instructions for Use manual also contains information on safety, troubleshooting, error messages, and operation principles. It contains a glossary of terms, a list of abbreviations and acronyms, and the warranty information for the instrument.
- This **AQUIOS STEM System Guide** provides reference information and instructions for using the AQUIOS System with the STEM Test. Refer to the glossary of terms in the AQUIOS CL Flow Cytometer Instructions for Use.
- The **AQUIOS STEM Host Transmission** manual provides the information needed to program the transmission interface between the AQUIOS CL Flow Cytometer and the laboratory's host computer.

To quickly determine which manual to read for the information needed, refer to [Related Documents](#).

Before You Begin

IMPORTANT The AQUIOS STEM System Guide is not an inclusive manual. It is imperative that an Operator is familiar with the information in the AQUIOS CL Flow Cytometer Instructions for Use manual, and the AQUIOS STEM Reagent and Consumables Instructions for Use and is capable of performing basic operations.

About Your Cytometer Software

Your local Beckman Coulter representative will install AQUIOS System Software and AQUIOS STEM Software.

About this System Guide

This AQUIOS STEM System Guide provides reference information and instructions for using the AQUIOS STEM System.

Use this guide in conjunction with the AQUIOS CL Flow Cytometer Instructions for Use manual.

Use this guide with the applicable reagent Instructions for Use listed under [Consumables and Supplies](#). These Instructions for Use contain reagent-specific information not contained in this guide.

The information in the AQUIOS STEM System Guide is organized as follows:

[CHAPTER 1, Use and Function](#)

Provides the intended use of the AQUIOS CL Flow Cytometer system as well as information concerning system components (Cytometer, STEM Test, reagents and consumables) and are referred to as AQUIOS STEM System application. Limitations are also provided.

[CHAPTER 2, Operating Principles](#)

Contains a description of the principles used in AQUIOS STEM testing, and an overview of the analysis algorithm.

[CHAPTER 3, Quality Control](#)

Provides information on running QC samples to verify the performance of the instrument before analyzing non-QC samples.

[CHAPTER 4, Sample Analysis](#)

Provides information for storage conditions and stability for specimens and reagents, information on the preparation required to successfully run samples using AQUIOS STEM System reagents, running samples using the autoloader, and running samples using the Single-tube Loader.

[CHAPTER 5, Data Review](#)

Provides information on reviewing sample results, including flagged results.

[CHAPTER 6, Performance Characteristics](#)

Provides information on clinical performance characteristics such as expected values, reference

ranges, linearity, accuracy, precision, and the specificity of AQUIOS STEM monoclonal antibodies and quality control materials.

CHAPTER 7, Application Specifications

Provides information for sample preparation, throughput, and sample rate.

CHAPTER 8, Adjustment and Replacement Procedures

Provides information for adjustment or replacement procedures to maintain AQUIOS STEM functionality.

This manual also includes an appendix, references, and an index.

Conventions

This guide uses the following conventions:

- Throughout this manual, the AQUIOS STEM System application (Cytometer, STEM Test, reagents and consumables) may also be referred to as system components.
- **Blue** text indicates that you can select on the text to access related information.
- **Bold font** indicates a screen icon, menu item, or software option on the Workstation screen.
- *Italics font* indicates screen text displayed on the Workstation.
- The term 'select' is used to indicate either one or both of the following actions:
 - to tap or touch your finger to the touch screen of the computer
 - to click with a mouse
- Tabs in the software are blue when not selected and inactive. Tabs in the software turn green when selected and active.

IMPORTANT IMPORTANT is used for comments that add value to the step or procedure being performed. Following the advice in the IMPORTANT adds benefit to the performance of a piece of equipment or to a process.

NOTE NOTE is used to call attention to notable information that should be followed during use or maintenance of this equipment.

Symbols

Safety symbols alert you to potentially dangerous conditions. These symbols, together with text, apply to specific procedures and appear as needed throughout this guide.

Symbol	Warning Condition	Action
	Consider all materials (specimens, reagents, controls, and monoclonal antibodies) and areas these materials come into contact with as being potentially infectious.	Wear appropriate barrier protection and follow safe laboratory procedures when handling any material in the laboratory.

Graphics Icons

All graphics, including screens and printouts, are for illustration purposes only and must not be used for any other purpose.

CHAPTER 1

Use and Function

Overview

This chapter contains information about:

- [Intended Use](#)
- [System Components](#)
- [Limitations](#)

Intended Use

The AQUIOS STEM System, comprised of AQUIOS STEM Software for the AQUIOS CL Flow Cytometry System, AQUIOS STEM-Kit Reagents, AQUIOS STEM CD34 Control Cells and Flow-Check Fluorospheres, is an in vitro diagnostic medical device intended to be used by laboratory professionals for the detection of the parameters in the specimen types shown in [Table 1.1, System Parameters](#) on the automated AQUIOS CL Flow Cytometry System. This is a quantitative assay used for the identification and enumeration of the cell populations specified in [Table 1.1](#) in patients who are preparing for autologous or allogeneic hematopoietic progenitor cell transplantation, and in donors who undergo mobilization or collection schemes for autologous or allogeneic hematopoietic progenitor cell transplantations. Refer to [Table 1.1](#) for details of the supported specimen types and anticoagulants.

Table 1.1 System Parameters

Specimen Type	Anticoagulant						Kits/Parameters
	K ₂ EDTA	K ₃ EDTA	Heparin	Heparin ACD-A Mix	ACD-A	CPD	AQUIOS STEM Kit
Whole Blood (WB)	X	X	X				CD34 Percent CD34 Absolute Count CD45 Absolute Count
Mobilized Whole Blood (MB)	X	X	X				
Fresh or Thawed Bone Marrow (BM)	X	X	X	X			
Fresh or Thawed Apheresis Product (AP)				X	X		
Fresh or Thawed Cord Blood (CB)					X	X	

AQUIOS STEM-Kit reagents consist of a CD45-FITC/CD34-PE murine monoclonal antibody reagent, a corresponding negative control (CD45-FITC/CD34-CTRL), an absolute count reagent (AQUIOS STEM-Count Fluorospheres), a cell viability reagent (7-AAD), and a ready-to-use lysing reagent (AQUIOS STEM Lysing Solution).

AQUIOS STEM CD34 Control Cells are liquid preparations of stabilized human leukocytes for the verification of the parameters CD34 and CD45 as part of the AQUIOS STEM System. Each kit contains 2 levels of CD34 with approximately 10 CD34+ cells/ μ L (level 1) and approximately 30 CD34+ cells/ μ L (level 2).

AQUIOS CL Flow Cytometry system software may be run on an AQUIOS workstation for off-line analysis of results generated by the AQUIOS CL Flow Cytometer with the monoclonal antibody reagents listed above. The off-line analysis must be performed in accordance with the product labeling. The independent computer workstation must be approved to be used with the AQUIOS software.

NOTE An off-line analysis workstation cannot be used for acquisition.

Intended User

This product is intended for laboratory professional use.

System Components

AQUIOS STEM System

IMPORTANT [Contact us](#) if a product is damaged upon receipt.

The AQUIOS STEM system applies the principles of flow cytometry to analyze a stained and lysed sample to identify various cellular populations as determined by the specific monoclonal antibodies and fluorochromes used.

Automatic operation is initiated by adding requests and loading a cassette containing specimen tubes in the autoloader or a specimen tube in the Single-tube Loader. Samples are automatically processed according to these requests. The sample is stained and incubated, the red blood cells are lysed using the AQUIOS STEM Lysing Solution. The white blood cells are analyzed on the AQUIOS CL Flow Cytometry system with the AQUIOS STEM Tests.

The AQUIOS Smart Scheduler tracks requests as they proceed from sample preparation to analysis. All AQUIOS reagents are continuously monitored by the system to track reagent consumption and location changes. The acquired data is stored and provides immediate data access for laboratories.

AQUIOS STEM reagents use a unique barcode identity for tracking reagent type, lot number, container number, expiration dates, and remaining reagent levels. The reagent consumption is monitored by the system as the samples are processed.

Unique Load & Go Feature

The AQUIOS CL Flow Cytometer is a quantitative automated analyzer that performs the STEM diagnostic applications in a “no-wash” sample preparation process. Since this system is intended to be an automated analyzer with hands-off processing of samples from specimen introduction to results reports, it is referred to as a Load & Go flow cytometer. The AQUIOS System Software and AQUIOS STEM Tests and Quality Control Reagents do not require user verification of standardization of light scatter, and fluorescence intensities. AQUIOS CL instrument settings are monitored specifically for the AQUIOS STEM System by running Flow-Check Fluorospheres.

This “closed” system will only run tests preconfigured by Beckman Coulter and does not allow for user-designed protocols or panels.

AQUIOS STEM Test

The AQUIOS STEM Tests are used:

- with quality control reagents on an AQUIOS CL Flow Cytometry system with AQUIOS System Software and AQUIOS STEM Software for system quality control, and
- with AQUIOS STEM Kit Reagent and AQUIOS System Software with AQUIOS STEM Software for automated sample analysis.

The reagents used in the AQUIOS STEM System allow for automated sample preparation and analysis at room temperature without a negative effect on cell viability within the time window required for automated sample preparation and analysis.

For more information, refer to the associated Reagent Instructions for Use.

Consumables and Supplies

The AQUIOS CL Flow Cytometer is optimized to operate with AQUIOS reagents. The stated analytical characteristics and specifications cited in this manual can only be guaranteed by using AQUIOS reagents and the AQUIOS 96-Deep Well Plate.

STEM sample preparation is optimized to operate using barcoded 96-deep conical-shaped well plates. Each well holds up to 600 µL. The plates are made of virgin polypropylene.

Additionally, the AQUIOS reagents (with the exception of the AQUIOS Sodium Hypochlorite Solution and Flow-Check Fluorospheres) and the AQUIOS Deep Well Plate are labeled with bar codes for smart-track monitoring to help minimize potential errors. The system will only run with AQUIOS reagents and the AQUIOS 96-Deep Well Plate.

NOTE AQUIOS reagents are for use on the AQUIOS CL Flow Cytometer only. Do not dilute, aliquot, or freeze the reagents. The product should be used according to labeled instructions.

NOTE Do not use reagents beyond the expiration date printed on the associated labeling and always use good laboratory practices when handling these reagents.

NOTE The AQUIOS CL Flow Cytometer system tracks the AQUIOS STEM-Count on-board time and expiration date. Ensure enough stability time is remaining to complete the day's runs by reviewing the information in the reagents window after startup or when new reagents are added.

NOTE The AQUIOS CL Flow Cytometer system tracks the AQUIOS Cleaning Agent for the percent remaining and expiration date.

NOTE The AQUIOS CL Flow Cytometer system does not track the AQUIOS Sodium Hypochlorite Solution. You must track the expiration date of the AQUIOS Sodium Hypochlorite Solution upon use.

NOTE The AQUIOS CL Flow Cytometer system does not track the Flow-Check Fluorospheres for the percent remaining.

For more information, refer to the associated reagent Instructions for Use on the Beckman Coulter Web site at www.beckman.com or [Contact us](#).

Preparation

AQUIOS STEM Lysing Solution

The AQUIOS STEM Lysing Solution is a highly specific, ready to use and gentle lysing agent. The AQUIOS STEM Lysing Solution lyses red blood cells in samples sufficiently to perform monoclonal antibody panel analysis without interference from red blood cells and allows analysis without damage to white blood cells.

NOTE The AQUIOS STEM Lysing Solution does not contain fixatives.

AQUIOS STEM Lysing Solution is housed inside the Cytometer behind the reagent door (the larger of the two doors on the Cytometer front cover).

When the AQUIOS STEM Lysing Solution bottle is replaced, the system looks for a specific bar code to ensure that the correct reagent is being loaded and tracked.

NOTE To replace the AQUIOS STEM Lysing Solution, refer to [Replacing the AQUIOS STEM Lysing Solution](#).



Risk of erroneous results. To prevent erroneous results, ensure the lot number on the AQUIOS STEM Lysing Solution is the same as the lot number of the AQUIOS STEM Kit.

Monoclonal Antibodies

The AQUIOS STEM Kit comprises two separate murine monoclonal antibody panel reagents as well as a viability dye. Each murine monoclonal antibody is conjugated to a specific fluorochrome and specific for a different cell surface antigen:

- CD45-FITC/CD34-PE reagent
- CD45-FITC Isoclonic Control-PE reagent
- 7-AAD Viability Dye

Specific cell surface staining is accomplished by incubating samples of a biological specimen with the two-color CD45-FITC / CD34-PE reagent.

An additional test of the same sample is stained with CD45-FITC / Isoclonic Control-PE reagent to check the non-specific binding of the CD34-PE monoclonal antibody. 7-AAD Viability Dye, a nucleic

acid dye that binds to accessible base pairs (cellular DNA), is used to distinguish between viable and nonviable cells.

The test depends on the ability of a monoclonal antibody to bind to the surface of cells expressing discrete antigenic determinants. Specific cell staining is accomplished by incubating the sample with the monoclonal antibody reagents.

AQUIOS STEM-Count Fluorospheres

AQUIOS STEM-Count Fluorospheres is a fluorescent microsphere reagent for direct determination of the absolute counts of white blood cell subsets in biological specimens. For more information, refer to [Replacing the AQUIOS STEM-Count Fluorospheres](#).

Acquisition

AQUIOS Sheath Fluid

AQUIOS Sheath Fluid is a cyanide-free, isotonic buffered saline solution. It is used to rinse components between sample analysis, and provide a sheath stream to transport the cells in single file through the flow cell.

For more information, refer to Chapter 1, System Overview of the AQUIOS CL Flow Cytometer Instructions for Use manual.

Quality Control

AQUIOS STEM CD34 Control Cells

AQUIOS STEM CD34 Control Cells are liquid preparations of stabilized human leukocytes (lymphocytes, monocytes and granulocytes) and erythrocytes that have lysing, light scatter, antigen expression and antibody staining properties representative of those found in human whole blood specimens.

AQUIOS STEM CD34 Control Cells Level 1 and Level 2 are in vitro diagnostic medical devices intended to be used by laboratory professionals as process controls for the verification of the parameters CD34 and CD45 as part of the AQUIOS STEM System on the automated AQUIOS CL Flow Cytometry System. They provide positive cell controls that are processed in the same manner as a biological sample. They also verify the methods used for staining targeted cells, the lysing of red blood cells, and the analysis of samples by the AQUIOS CL Flow Cytometer.

NOTE When these controls are used, scan the barcode to ensure the correct control is being loaded and tracked. Select the test as a QC request to ensure you are tracking results via the Levey-Jennings charts.

For more information, refer to the associated reagent Instructions for Use.

Flow-Check Fluorospheres

Flow-Check Fluorospheres are an assayed suspension of fluorospheres (fluorescent microspheres) used for daily verification of a flow cytometer's optical alignment and fluidics system.

Limitations

1. Accurate and reproducible results will be obtained, provided the procedures used are in accordance with the AQUIOS CL Flow Cytometer Instructions for Use manual, the AQUIOS STEM System Guide, associated reagent Instructions for Use, and good laboratory practices.
2. When modifying the algorithm-generated results through user intervention (regions and quadrants), it is the user's responsibility to follow the instructions appropriately when adjusting the compensation and the region's algorithm generated results. Results require review by a qualified laboratory professional.
3. Results obtained with flow cytometry may be erroneous if the laser is misaligned or the gates and regions are improperly set.
4. Certain patients may present special problems due to altered or very low numbers of certain cellular populations.
5. Specimens must be maintained at the appropriate temperature prior to placement on the system. See [CHAPTER 4, Storage Conditions and Stability](#).

Material Safety Data Sheets (SDS/MSDS)

To obtain an SDS or MSDS for Beckman Coulter reagents used on the AQUIOS system:

- On the Internet, go to www.beckman.com:
 1. Select **Safety Data Sheets (SDS/MSDS)** from the Support menu.
 2. Follow the instructions on the screen.
 3. [Contact us](#) if you have difficulty locating the information.
- If you do not have Internet access, [contact us](#).

CHAPTER 2

Operating Principles

Overview

This chapter contains information about:

- Principles of AQUIOS STEM Tests
- Light Source Configuration
- CD34+HPC Enumeration Panels
- Analysis Algorithm Overview

Principles of AQUIOS STEM Tests

AQUIOS STEM tests are based on the ability of monoclonal antibodies to bind to the surface of cells expressing discrete, or a combination of discrete, antigenic determinants.

The flow cytometer measures light scatter, and the fluorescence of cells. This allows for the separation of the population of interest within the electronic window defined on various histograms, which correlates with different parameters.

A series of dual histograms are used in the gating stage. The fluorescence of the delimited cells is analyzed in order to distinguish the positively-stained events from the unstained ones.

The AQUIOS STEM Software establishes the gating regions for the negative control/CD45 sample in an identical manner as the gating regions are established for the CD34/CD45 samples.

The gating strategy allows detection of leukocytes which are further categorized into various parameters. Refer to Parameter Results in [Table 2.1](#) and [Table 2.2](#), for a listing of parameters.

The parameters, triggers, discriminators, and regions are specific to the test.

AQUIOS STEM Software has stop criteria for 100 CD34+ cells AND 75,000 CD45+ cells OR 300 seconds. In the case where cell concentration prevents the collection of 100 CD34+ cells, a notification will inform the user that less than 100 CD34+ cells are acquired.

75000 is the maximum number of events and 30000 cells/ μ L is the maximum WBC concentration.

AQUIOS STEM Software uses a total of 4 discriminators in order to ensure all CD34+ cells are captured: Forward Scatter, Side Scatter, Fluorescence 1 (CD45-FITC), and Fluorescence 2 (CD34-PE). An event is acquired if the value of only one parameter is above the defined discriminator.

CD34+HPC Enumeration Panels

AQUIOS STEM Tests

AQUIOS STEM Tests are using the AQUIOS STEM Kit reagents containing monoclonal antibodies for the simultaneous identification and enumeration of viable absolute count of CD34+ HPC/ μL , viable absolute count of CD45+/ μL , and percentage of viable CD34+ HPC.

Three AQUIOS STEM tests are available as part of the AQUIOS STEM menu:

- Stem Panel: Run tests in duplicate plus negative control (3 wells)
- Stem Duplicate: Run tests in duplicate (no negative control; 2 wells)
- Stem Single: Single test (1 well)

Refer to [Table 4.1](#) for a description of each test.

[Table 2.1](#) contains the parameter results generated when a STEM Single, STEM Duplicate, or STEM Panel is used for analysis.

Table 2.1 Parameter Results Provided by STEM Panel , STEM Duplicate, or STEM Single Analysis

STEM Panel	STEM Duplicate	STEM Single
Viable CD34+ HPC Count Well 1 (cells/ μL)	Viable CD34+ HPC Count Well 1 (cells/ μL)	Viable CD34+ HPC Count (cells/ μL)
Viable CD34+ HPC Count Well 2 (cells/ μL)	Viable CD34+ HPC Count Well 2 (cells/ μL)	Viable Leukocytes Count (cells/ μL)
AVG Viable CD34+ HPC Count (cells/ μL)	AVG Viable CD34+ HPC Count (cells/ μL)	Viable CD34+ HPC % (of Viable Leukocytes)
Viable CD34+ HPC % Diff (Well 1 vs Well 2)	Viable CD34+ HPC % Diff (Well 1 vs Well 2)	DF: Dilution Factor
Viable Leukocytes Count Well 1 (cells/ μL)	Viable Leukocytes Count Well 1 (cells/ μL)	Viable CD34+ HPC Count (cells/ μL) (x DF)
Viable Leukocytes Count Well 2 (cells/ μL)	Viable Leukocytes Count Well 2 (cells/ μL)	Viable Leukocyte Count (cells/ μL) (x DF)
AVG Viable Leukocytes Count (cells/ μL)	AVG Viable Leukocytes Count (cells/ μL)	HV: Harvest Volume (mL)
Viable CD34+ HPC Well 1 % (of Viable Leukocytes)	Viable CD34+ HPC Well 1 % (of Viable Leukocytes)	Viable CD34+ HPC Count (x DF x HV)
Viable CD34+ HPC Well 2 % (of Viable Leukocytes)	Viable CD34+ HPC Well 2 % (of Viable Leukocytes)	BW: Body Weight (kg)
AVG Viable CD34+ HPC % (of viable Leukocytes)	AVG Viable CD34+ HPC % (of viable Leukocytes)	Viable CD34+ HPC Count per kg (x DF x HV / BW)
DF: Dilution Factor	DF: Dilution Factor	CAL
AVG Viable CD34+ HPC Count (cells/ μL) (x DF)	AVG Viable CD34+ HPC Count (cells/ μL) (x DF)	

Table 2.1 Parameter Results Provided by STEM Panel , STEM Duplicate, or STEM Single Analysis (Continued)

STEM Panel	STEM Duplicate	STEM Single
AVG Viable Leukocyte Count (cells/ μ L) (x DF)	AVG Viable Leukocyte Count (cells/ μ L) (x DF)	
HV: Harvest Volume (mL)	HV: Harvest Volume (mL)	
AVG Viable CD34+ HPC Count (x DF x HV)	AVG Viable CD34+ HPC Count (x DF x HV)	
BW: Body Weight (kg)	BW: Body Weight (kg)	
AVG Viable CD34+ HPC Count per kg (x DF x HV / BW)	AVG Viable CD34+ HPC Count per kg (x DF x HV / BW)	
CAL	CAL	
Viable CD34+ HPC Count Negative Ctrl (cells/ μ L)		

NOTE Refer to [Table 5.3](#) for Population Statistics.

Analysis Algorithm Overview

The AQUIOS STEM algorithm is the software analysis component that works in conjunction with AQUIOS STEM Kit reagents to automatically identify and enumerate viable Leukocytes (CD45+ populations) and viable CD34+ HPC cells according to ISHAGE guidelines. The algorithm combines information from AQUIOS parameters (FS, SS and Fluorescence FL1-FL4 to automatically generate gates and regions to accurately identify populations of interests.

Introduction to Gating Strategy

Software algorithms automatically detect the subset populations of interest to calculate and report the results for the predefined tests. The software generates flags and notifications after analyzing samples.

The hallmark of the ISHAGE Guidelines is a sequential gating strategy that derives the number of CD34+ cells from viable leukocytes. While the starting point of the sequential ISHAGE gating strategy, i.e. viable leukocytes, facilitates the correct quantification of rare CD34+ cell populations, it leads to the fact that as an end point all enumerated CD34+ cells are automatically viable, and it can be difficult to directly calculate the percentage of viable CD34+ cells out of all CD34+ cells. In addition, it may be challenging to retrieve the total number of CD45+ leukocytes from the applied gating strategy in order to assess overall specimen viability.

In order to overcome this challenge, AQUIOS STEM Software employs an additional background gating strategy starting with all leukocytes, including dead cells. This “replicated” gating strategy follows the same gating logic as the classical ISHAGE gating, but enables for the direct enumeration of all cells, as well as a direct comparison of total vs viable cells for selected cell populations. The additional parameters following this gating logic are marked with double asterisks (**) as Population Statistics.

To maintain the consistency of region placement, certain regions are replicated in more than one plot. Refer to [Table 2.2](#) for the matching plots and regions (primary vs. replicated) for three STEM tests.

Table 2.2 Equivalence Between Primary Region Name and Replicated Region Name

Primary Regions Name	Plot / Figure	Replicated Region Name	Plot / Figure
LEUKS	Figure 2.6	WBC	Figure 2.11
LYMPHS		ALL LYMPH	
CD34 POS	Figure 2.7	ALL CD34POS	Figure 2.12
CD45 DIM	Figure 2.8	ALL CD45 DIM	Figure 2.13
!FS LYMPH	Figure 2.10	ALL FS LYMPH	Figure 2.15
!CD34+ HPC	Figure 2.10	!CD34+ HPC	Figure 2.9
		ALL CD34+ HPC	Figure 2.14
!VIABLE	Figure 2.5	!CD34 VIABILITY	Figure 2.16

Gating Strategy: AQUIOS STEM Panel, AQUIOS STEM Duplicate, and AQUIOS STEM Single

The gating strategy is the same for the three AQUIOS STEM tests. The graphs below ([Figure 2.2](#) through [Figure 2.16](#)) show the gating of a fresh peripheral mobilized whole blood stained with CD45-FITC, CD34-PE, and 7AAD. The order of the graphs is aligned with the sequential gating strategy.

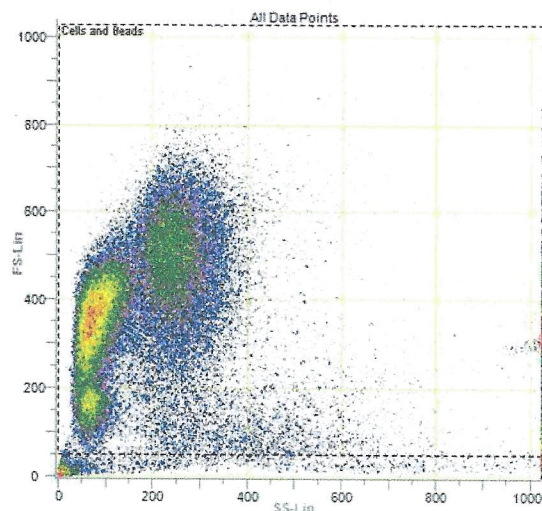
The first series of plots ([Figure 2.2](#) through [Figure 2.10](#)) show the identification and quantification of the viable cellular population.

The second series of plots ([Figure 2.11](#) through [Figure 2.16](#)) show the identification and quantification of the total (viable + non-viable) cellular population.

Forward Scatter (FS) versus Side Scatter (SS) Plot

The All Data Points gate is used to identify all cells of interest and eliminate debris. This FS/SS dot plot identifies the 'Cells and Beads' region consisting of leukocytes, and removes debris (lower left). Refer to [Figure 2.2](#).

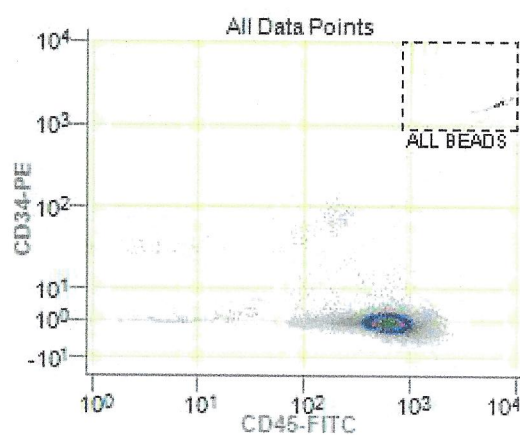
Figure 2.2 FS versus SS Plot



CD34-PE versus CD45-FITC Plot

The All Data Points gate is used to identify all cells of interest, and eliminate debris. This CD34-PE versus CD45-FITC dot plot identifies the 'ALL BEADS' region consisting all AQUIOS STEM-Count Fluorospheres. Refer to [Figure 2.3](#).

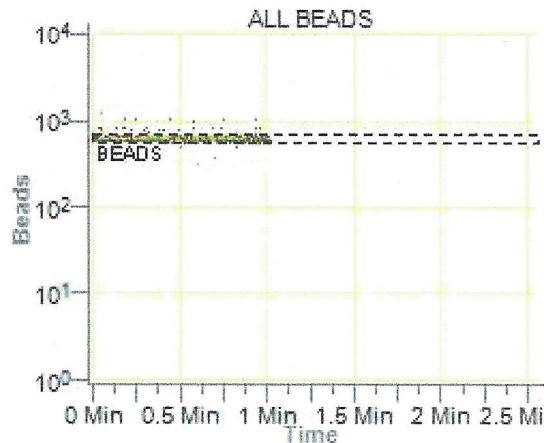
Figure 2.3 CD34-PE versus CD45-FITC Plot



BEADS versus TIME Plot

From the *ALL BEADS* region, a BEADS/TIME dot plot is created to accurately identify AQUIOS STEM-Count Fluorospheres single events needed for the absolute count calculation of cells. The duplicates are removed. Refer to [Figure 2.4](#).

Figure 2.4 BEADS versus TIME Plot

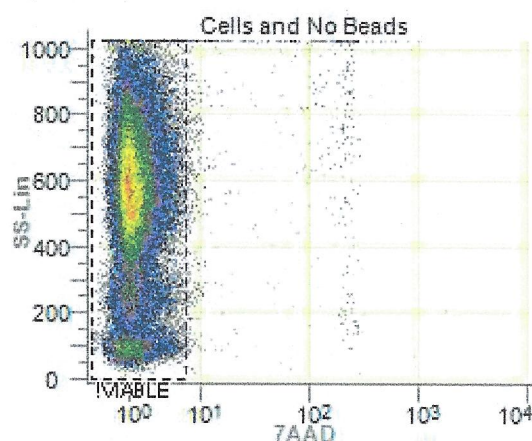


Side Scatter (SS) versus 7-AAD Plot

The *Cells and No Beads* region is defined as *Cells and Beads* AND NOT *All Beads*. This dot plot identifies the viable events *VIABLE* gate. The calculation of the ****Sample Viability %** parameter result (population statistic) is derived from this region. Refer to [Figure 2.5](#).

NOTE AQUIOS STEM CD34 Control Cells are analyzed with the same gating scheme as the actual sample material. However, for AQUIOS STEM CD34 Control Cells, since they are stabilized cells, the rectangular region '*VIABLE*' on this plot is enlarged to gate total events stained by 7-AAD. Refer to the AQUIOS STEM CD34 Control Cells Instructions for Use.

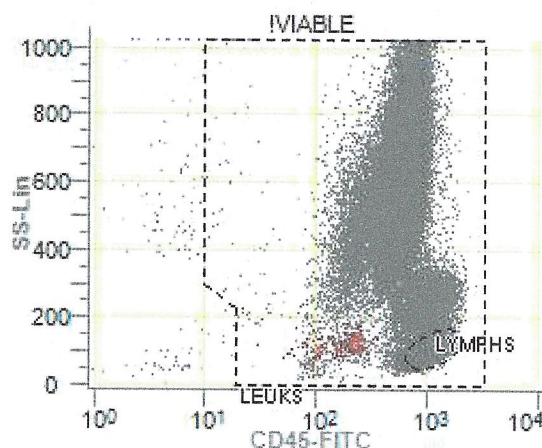
Figure 2.5 SS versus 7-AAD Plot



Side Scatter (SS) versus CD45-FITC Plot

From the *!Viable* region, a SS/CD45-FITC dot plot is created to define the viable Leukocytes *LEUKS* gate, and the viable Lymphocytes *LYMPHS* gate. The calculation of Viable Leukocytes Count (cells/ μ L) parameter result is derived from this region. The red events are CD34+HPC+ back-scattered from the *!CD34+ HPC* region. Refer to [Figure 2.6](#).

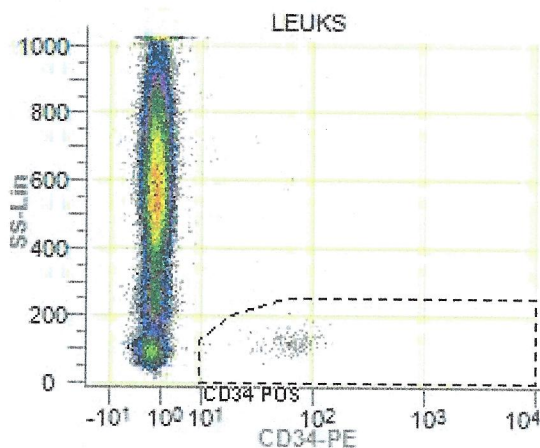
Figure 2.6 SS versus CD45-FITC Plot



Side Scatter (SS) versus CD34-PE Plot

From the *LEUKS* region, a SS/CD34-PE dot plot is created to define the viable CD34 positive cells *CD34 POS* gate. Refer to [Figure 2.7](#).

Figure 2.7 SS versus CD34-PE Plot



G.A.

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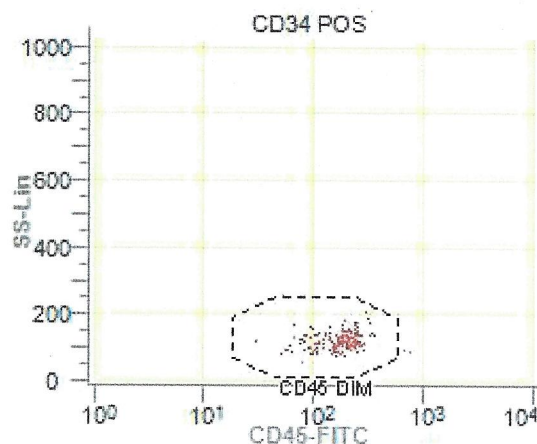
R.F.B.

Rolando F. Bornia
APODERADO

Side Scatter (SS) versus CD45-FITC Plot

From the *CD34 POS* region, a SS/CD45-FITC dot plot is created to distinguish the *CD34+HPC CD45 DIM* from the lymphocytes populations by their CD45 expression level. The *CD34+HPC* shows a lower expression of CD45 compared to Lymphocytes cells. Refer to [Figure 2.8](#).

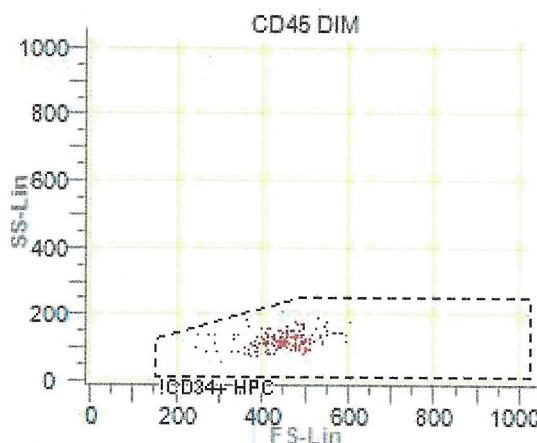
Figure 2.8 SS versus CD45-FITC Plot



CD45 DIM Side Scatter (SS) versus Forward Scatter (FS) Plot

From the *CD45 DIM* region, a SS/FS dot plot is created to identify a cluster of viable events *!CD34+ HPC* gate, meeting all the fluorescence and light scatter criteria of ISHAGE Guidelines for viable *CD34+ HPC*. The calculation of Viable *CD34+ HPC* Count (cells/ μ L) parameter result is derived from this region. The *!CD34+ HPC* region is linked to the *!FS LYMPH* region. Refer to [Figure 2.9](#).

Figure 2.9 CD45 SS versus FS Plot



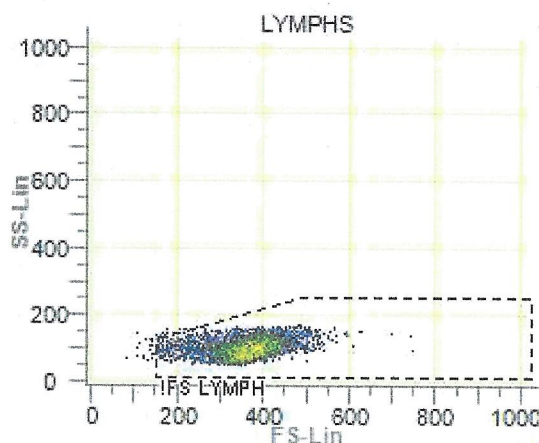
NOTE The Viable *CD34+ HPC* % (of Viable Leukocytes) parameter result is calculated as follows:

$$\frac{\text{Viable CD34 + HPC Count (cells}/\mu\text{L)}}{\text{Viable Leukocytes Count (cells}/\mu\text{L)}} = (\text{Viable CD34 + HPC\% (of Viable Leukocytes)})$$

LYMPHS Side Scatter (SS) versus Forward Scatter (FS) Plot

From the *LYMPHS* region, a SS/FS dot plot is created to identify a cluster of viable events *!FS LYMPH* gate, meeting all the fluorescence and light scatter criteria for viable Lymphocyte population. The *!FS LYMPH* region is linked to the *!CD34+ HPC* region. Refer to [Figure 2.10](#).

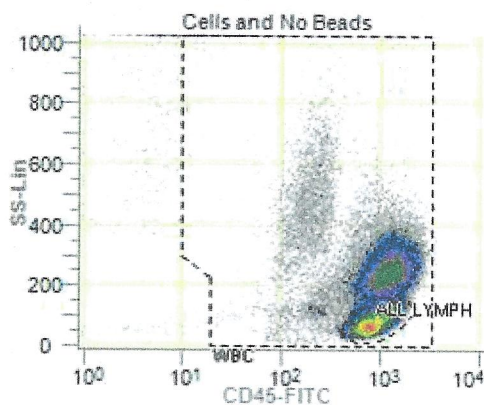
Figure 2.10 LYMPHS SS versus FS Plot



Side Scatter (SS) versus CD45-FITC Plot

The *Cells and No Beads* region is defined as *Cells and Beads* AND NOT *All Beads*. This dot plot identifies the total (viable + non-viable) leukocytes *WBC* gate, and the total (viable + non-viable) Lymphocytes *ALL LYMPH* gate. The calculation of the ****WBC Count (cells/ μ L)** parameter result (population statistic) is derived from this region. Refer to [Figure 2.11](#).

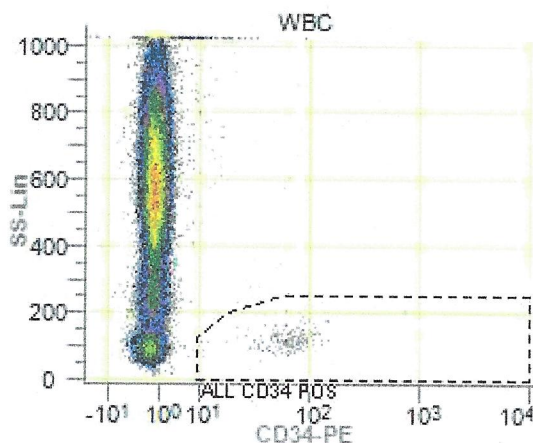
Figure 2.11 SS versus CD45-FITC Plot



Side Scatter (SS) versus CD34-PE Plot

From the WBC region, a SS/CD34-PE dot plot is created to define the total (viable + non-viable) CD34 positive cells *ALL CD34 POS* gate. Refer to [Figure 2.12](#).

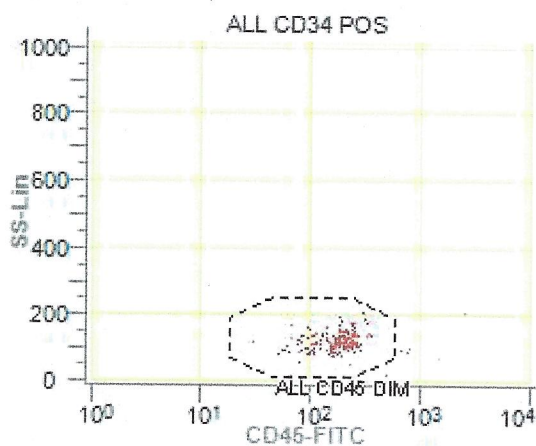
Figure 2.12 SS versus CD34-PE Plot



Side Scatter (SS) versus CD45-FITC Plot

From the *ALL CD34 POS* region, a SS/CD45-FITC dot plot is created to distinguish the total (live + non-viable) CD34+HPC *ALL CD45 DIM* gate from the total (live + non-viable) lymphocytes populations by their CD45 expression level. The CD34+HPC shows a lower expression of CD45 compared to Lymphocytes cells. Refer to [Figure 2.13](#).

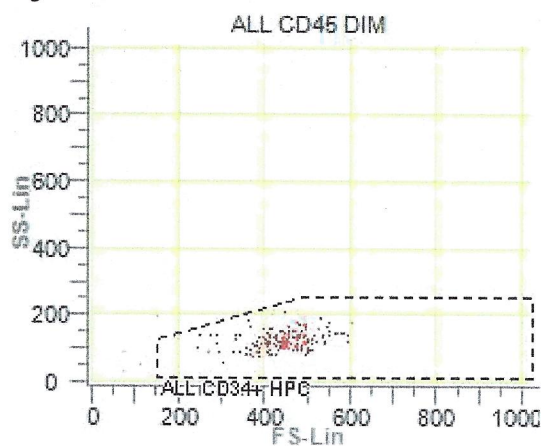
Figure 2.13 SS versus CD45-FITC Plot



Side Scatter (SS) versus Forward Scatter (FS) Plot

From the *ALL CD45 DIM* region, a SS/FS dot plot is created to identify a cluster of total (viable + non-viable) events *ALL CD34+ HPC* gate, meeting all the fluorescence and light scatter criteria of ISHAGE Guidelines for total (viable + non-viable) CD34+ HPC. The calculation of ****Total CD34+ HPC Count** (cells/ μ L) parameter result (population statistic) is derived from this region. Refer to [Figure 2.14](#).

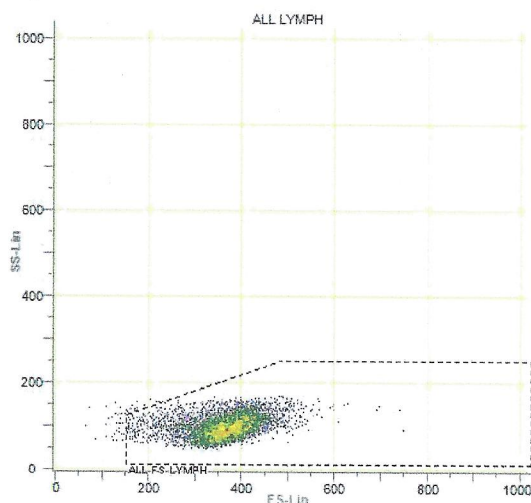
Figure 2.14 SS versus FS Plot



Side Scatter (SS) versus Forward Scatter (FS) Plot

From the *ALL LYMPH* region, a SS/FS dot plot is created to identify a cluster of total (viable + non-viable) events *ALL FS LYMPH* gate, meeting all the fluorescence and light scatter criteria for total (viable + non-viable) Lymphocyte population. Refer to [Figure 2.15](#).

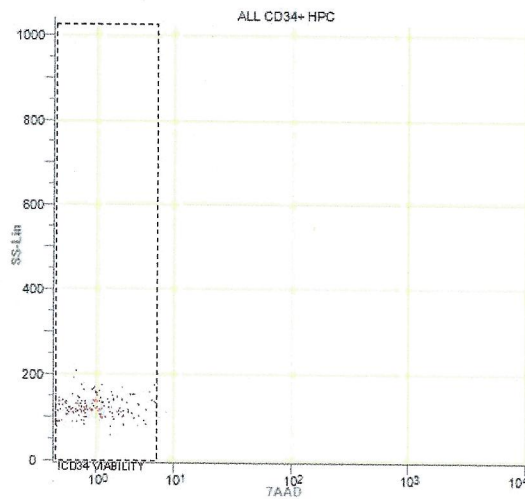
Figure 2.15 SS versus FS Plot



Side Scatter (SS) versus 7-AAD Plot

From the *ALL CD34+ HPC* region, a SS/7AAD dot plot is created to distinguish viable CD34+ HPC *!CD34 Viability* gate, out of the total (viable + non-viable) CD34+ HPC. The calculation of the ***CD34+ Viability%* (of total CD34+) parameter result (population statistic) is derived from this region. Refer to [Figure 2.16](#).

Figure 2.16 SS versus 7-AAD Plot





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CHAPTER 3

Quality Control

Overview

Perform daily QC samples to verify the performance of the instrument before analyzing non-QC samples. This includes both Flow-Check Fluorospheres and running AQUIOS STEM CD34 Control Cells. Daily Quality Control is a critical component to ensure the system's performance for the AQUIOS STEM Application.

This chapter contains information about:

- Quality Control Checks
- AQUIOS STEM Quality Control Workflow
- QC Materials
- Daily QC Overview
- QC Setup
- QC Screen

Quality Control Checks

AQUIOS STEM Quality Control Workflow

Table 3.1 AQUIOS STEM QC Workflow

Flow-Check Fluorospheres - Single Tube Loader	
Flow Check Fluorospheres - Alignment	Flow-Check Fluorospheres
Daily QC - AQUIOS STEM CD34 L1 and L2 Control Cells	
Add Reagents	AQUIOS STEM Lysing Solution
	AQUIOS STEM-Count Fluorospheres
	CD45-FITC/CD34-PE and 7-AAD Viability Dye
Load AQUIOS STEM CD34 L1 and L2 Control Cells	AQUIOS STEM CD34 Level 1 Control Cells
	AQUIOS STEM CD34 Level 2 Control Cells

The Quality Control workflow is as follows:

1. Run the Flow-Check Fluorospheres
2. Run the AQUIOS STEM CD34 Control Cells Level 1 and Level 2

The control data is automatically populated into the Levey-Jennings charts of the **QC Screen > Results**.

The AQUIOS system results are displayed and flagged based on the generated values. In general, the system displays fewer digits than that which is generated.

Results are rounded using standard rounding procedures. As a reminder, to round off decimals:

1. Find the place value you want (the 'rounding digit') and look at the digit to the immediate right of it.
2. If the digit to the right of the place value is less than 5, keep the original place value, and drop all digits to the right of the place value.
3. If the digit to the right of the place value is 5 or greater, add one to the place value, and drop all digits to the right of the place value.

For control results, if the assay range is, for example, 20-25, a result of 20 could be flagged as being out of range low, if the generated result is actually 19.9.

The same applies when comparing sample results to the normal and action ranges.

QC Materials

The following Beckman Coulter reagents are required to perform the daily QC for the AQUIOS STEM application:

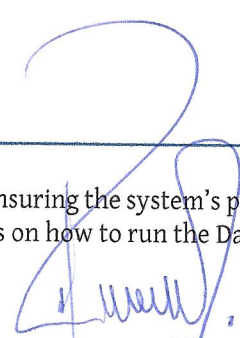
- AQUIOS STEM Kit
 - AQUIOS STEM Lysing Solution
 - AQUIOS STEM-Count Fluorosphere
 - AQUIOS STEM CD45-FITC/CD34-PE
 - AQUIOS STEM CD45-FITC / IsoClonic Control-PE
 - AQUIOS STEM 7-AAD Viability Dye
- AQUIOS STEM CD34 Control Cells
 - Level 1 (L1) Control Cells
 - Level 2 (L2) Control Cells
- Flow-Check Fluorospheres

Daily QC Overview

Daily Quality Control is a critical component of ensuring the system's performance for the AQUIOS STEM application. Refer to below for instructions on how to run the Daily QC procedures for the



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AQUIOS STEM application. Refer to Daily QC Procedure in the AQUIOS CL Flow Cytometer Instructions for Use manual to QC the AQUIOS CL instrument itself.

IMPORTANT When running QC, if a failure occurs, the system will issue a flag. Check the individual runs for STEM to determine which QC run failed and repeat that QC run.

QC Setup

CAUTION

Risk of erroneous results. When using AQUIOS STEM, each control cell vial is limited to 15 piercings. Cap-piercing beyond the allotted number is not recommended.

Before running the AQUIOS STEM CD34 Control Cells, verify that:

1. The Daily Startup was performed. Refer to Startup in Chapter 3, Daily Startup in AQUIOS CL Flow Cytometer Instructions for Use manual for details.
2. The Beckman Coulter reagents and the reagent levels are suitable and sufficient for the QC procedure. To verify reagent availability, select  on the Status Bar. To replace a reagent, refer to Replacing Reagents and Consumables in Chapter 11, Replacement Procedures in the AQUIOS CL Flow Cytometer Instructions for Use manual.
3. The control assay values have been previously registered into the system. Refer to Reagent Info Screen in Chapter 8, Setup in the AQUIOS CL Flow Cytometer Instructions for Use manual for more information. If the control lot number information has not been registered in the system, scan the control assay sheet before adding a QC request. Refer to Starting a New Lot of Controls in Chapter 11, Replacement Procedures in the AQUIOS CL Flow Cytometer Instructions for Use manual.
4. If a scan error occurs, readjust the barcode and re-scan.

QC Process

A plastic polypropylene 13x75 mm test tube is required to run the Flow-Check Fluorospheres. Beckman Coulter does not recommend or guarantee the use of a specific tube to produce quality results. If you need information on a tube, [contact us](#).



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Flow-Check Fluorospheres - Single Tube Loader



Risk of spill. Do not use the autoloader position to run the tube containing the Flow-Check Fluorospheres.



Risk of needle crash. Do not use a non-pierceable cap to close the tube.

Follow the steps below to Add a new lot of Flow-Check fluorospheres, otherwise skip to step 5.

1 Select **Setup** on the workstation main screen and then select **Reagent Info**.

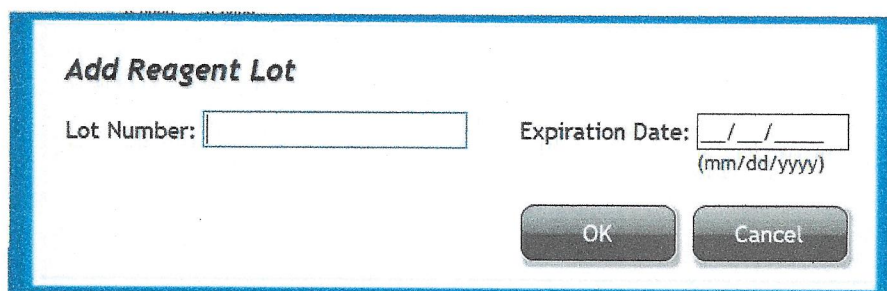
2 Select the following parameters on the screen:

- **Test:** FlowCheck_Alignment
- **Reagent/Sample:** Flow-Check

NOTE If the desired Lot already exists in the system, skip to step 5.

3 Select . On the **Add Reagent Lot** popup screen, input the lot number and expiration date.

IMPORTANT Verify input before selecting **OK**. Once saved in the system, The Lot number and Expiration Date cannot be edited. A table with the ranges for each field is displayed. You should accept the default ranges (but you have the option to modify if you want).



4 Select **OK**.

5 Select  to open the Single-tube door.

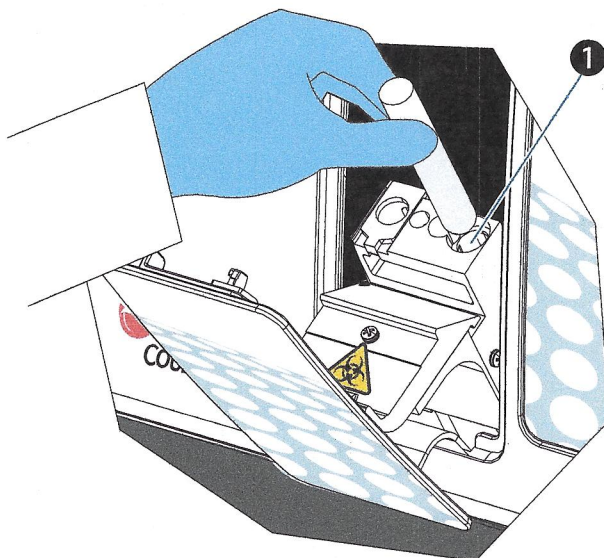
6 The message *Please press on the single tube door, and then wait for the system to release it is displayed.*

7 Open the door by pressing the top-middle part of the door in one single, solid motion.

NOTE If there is a tube present in the single tube loader, the message *Please remove any tubes from the Single-tube loader* is displayed. Remove the tube and select **OK**.

8 Gently invert the Flow-Check Fluorospheres bottle repeatedly to completely suspend (no visible pellet) fluorospheres and add >0.5 mL of undiluted Flow-Check Fluorospheres into a new plastic polypropylene 13x75 mm tube.

9 Place the 13x75 mm tube (without cap) in Position 1 of the single-tube loader.



10 On the **Sample Information Screen**, select **QC** radio button.

11 Enter **Flow Check** under **Sample ID** and select the following parameters,

- **Sample ID:** Flow Check
- **Test:** FlowCheck_Alignment
- **Type:** QC
- **Control:** Flow Check
- **Lot:** Select lot number

Sample Information + Request will be added

☐ Patient ☒ QC

Sample ID: Flow Check

Test: FlowCheck_Alignment

Type: QC

Control: Flow Check

Lot: 9435208

Lookup

12 Close the single-tube loader door. The request is automatically added.

13 Follow the sample preparation progression on the **Running** tab of the workstation main screen.

14 When the Flow-Check run is complete, view the results in the **Review** tab.

Select **stat** to open the Single-tube door to retrieve the control tubes.

15 Prior to running AQUIOS STEM CD34 Control Cells ensure Flow-Check HPCV and count meet specifications.

STEM Single (AutoLoader) - AQUIOS STEM CD34 L1 and L2 Control Cells

CAUTION

Risk of erroneous results. There are 15 tests per level of AQUIOS STEM CD34 Control Cells. Each cap should have no more than 15 piercings.

CAUTION

Make sure to correctly resuspend the cellular suspension by performing several manual mixing steps per inversion (6-7 times). Visually verify that there is no visible pellet of cells remaining in the tube.

NOTE The Control Cells qualify the system for use with all specimen types as outlined in [Table 1.1](#).

IMPORTANT Use the Type 1 cassette (13x75mm) for AQUIOS STEM CD34 Control Cells Level 1 and Level 2.

IMPORTANT QC test failure or failure to run QC tests (Flow-Check Fluorospheres and AQUIOS STEM CD34 L1 and L2 Control Cells) will result in a *Missing QC* flag being triggered for the patient test.

AQUIOS STEM CD34 Control Cells Level 1 and Level 2 are in vitro diagnostic medical reagents intended to be used by laboratory professionals as process controls for the verification of the parameters CD34 and CD45 as part of the AQUIOS STEM System on the automated AQUIOS CL Flow Cytometry System. Refer to [Table 1.1, System Parameters](#) for a list of supported specimen types.

Adding Reagents

Refer to [Table 3.1, AQUIOS STEM QC Workflow](#).

CAUTION

Risk of losing on-board samples. Replacing reagents and opening the reagent door while operating the Cytometer puts on-board samples at risk. Replacing reagents while the system is running should be performed as quickly as possible to avoid flagged results due to over lysing and over incubation.

1 Select Open Reagent Door. The open reagent door prompt will appear.

2 Press the reagent door to open it.

Table 3.2 Handling AQUIOS STEM Reagent Caps

Reagent	Cap Action
AQUIOS STEM Lysing Solution	Remove cap before loading into system.
AQUIOS STEM-Count Fluorospheres	Replace regular cap with screw cap with hole.
Monoclonal Antibodies & 7AAD Viability Dye Reagents	Replace shipping caps with pierceable caps.

 CAUTION

Risk of instrument damage. For the monoclonal antibodies and the 7AAD viability dye reagents, ensure the shipping caps have been replaced with the pierceable caps provided with the reagent packaging. For the AQUIOS STEM Lysing Solution, remove the cap before loading into the system. For the AQUIOS STEM-Count, the regular cap and seal foil have to be replaced with a screw cap with hole before loading into the system. (see further instructions below and in reagent IFU). Otherwise, the probe can be damaged.

IMPORTANT AQUIOS STEM-Count Fluorospheres should be vortexed for 10 to 12 seconds before placing in the carousel.

IMPORTANT When prompted to re-mix AQUIOS STEM-Count Fluorospheres, remove the screw cap with hole from the bottle and replace it with the standard cap before vortex mixing. After mixing, replace the standard cap with the screw cap with hole before returning to the instrument.

At the end of the day, remove the AQUIOS STEM-Count Fluorospheres bottle from the system and replace the screw cap with hole with the standard cap. Dry the inner surface of the screw cap with hole with low lint tissue paper before storing in the kit box. Store the kit box at 2-8°C until the next use.

IMPORTANT An additional label on the side of the bottle allows the association between AQUIOS STEM Lysing Solution and the kit lot number.

- 3** Add the required reagents to the reagent carousel, refer to [Table 3.1, AQUIOS STEM QC Workflow](#), and insert an AQUIOS 96-deep well plate in the correct orientation. Make sure reagent levels and number of unused wells are sufficient for the number of runs requested. If needed, add or replace with new reagents as appropriate before proceeding to analysis.

Refer to Heading , [AQUIOS STEM Replacement Procedures](#) in [CHAPTER 8, Adjustment and Replacement Procedures](#).

- a.** Place the vials of CD45-FITC /CD34-PE and 7AAD viability dye reagents in the carousel. Mount the carousel containing the vials of monoclonal antibody reagents on the carousel platform inside the reagent compartment.

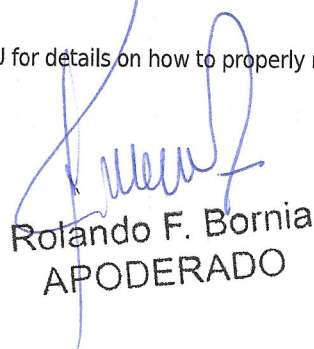
NOTE When loading the carousel into the instrument, be sure to place it on the wheel and gently turn it until it locks into position on the wheel.

- b.** Remove the cap and place the AQUIOS STEM Lysing Solution bottle in any of the three available positions in the reagent compartment. Make sure the bar code label face outward.
- c.** Before testing or when a reminder pops up to remind mixing, with the original white cap on, mix the bottle of AQUIOS STEM-Count Fluorospheres thoroughly. Remove the original white cap and the aluminum heat seal (when applicable), and replace the original white cap with the screw cap with hole that is provided with the kit. Place the AQUIOS STEM-Count Fluorospheres in the bottle holder with the adapter. Make sure the barcode labels face outward.

NOTE Refer to the appropriate reagent IFU for details on how to properly mix reagents.



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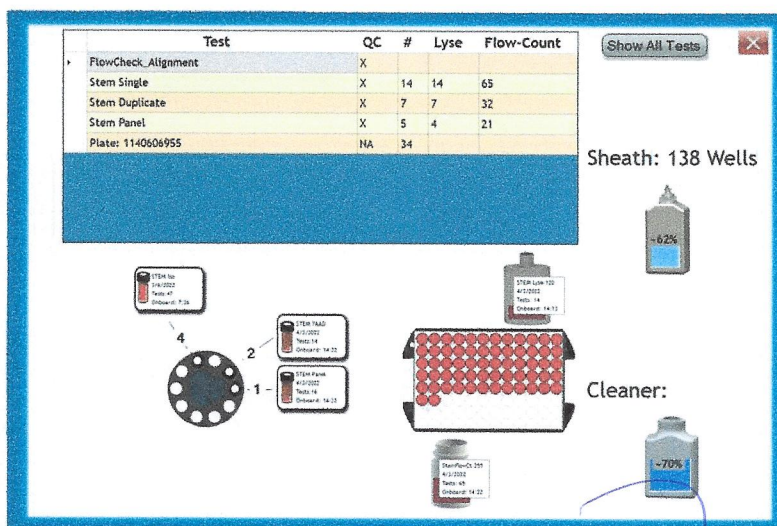
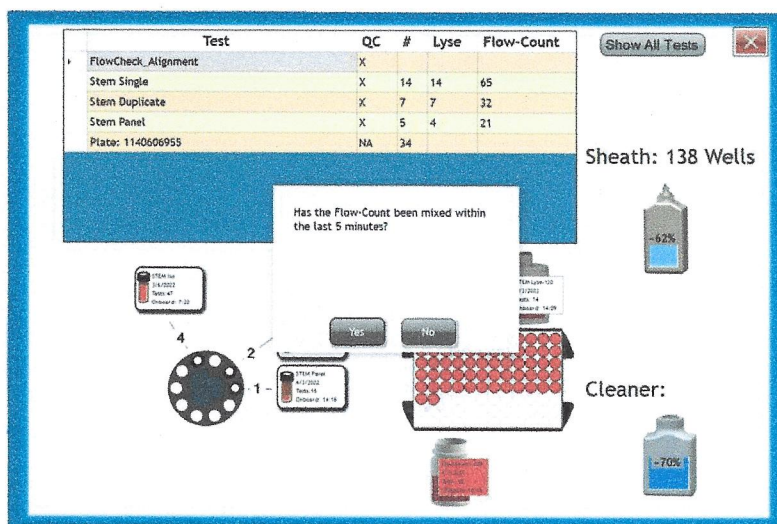


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- 4 Close the reagent door. The instrument scans the reagent barcodes.

A window appears to ask if Flow-Count Fluorospheres have been mixed. Select **Yes** if Flow-count Fluorospheres were mixed. Select **No** if Flow-count Fluorospheres were not mixed and open the reagent door to mix the beads.

NOTE For the AQUIOS STEM application you are using AQUIOS STEM-Count Fluorospheres, not Flow-Count Fluorospheres even though the message says Flow-Count Fluorospheres.



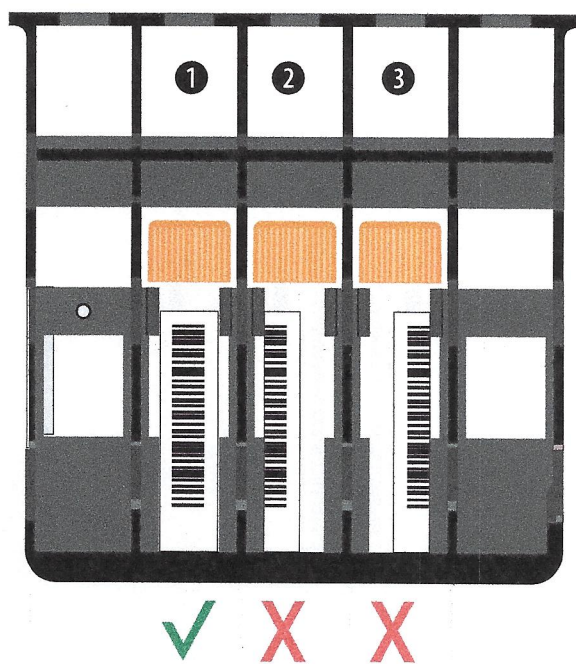
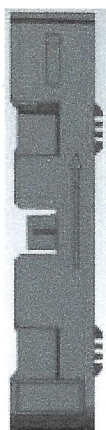
-
- 5 Use a pre-existing lot or add a new lot of AQUIOS STEM CD34 L1 and L2 Control cells and add a request.
- Refer to [Starting AQUIOS STEM CD34 L1 and L2 Control Cell QC With Pre-Existing Lot](#) to use a pre-existing lot.
 - Refer to [Adding New Lots of AQUIOS STEM CD34 L1 and L2 Control Cells using QR Code](#) to automatically add a lot with a barcode.
 - Refer to [Adding New Lots of AQUIOS STEM CD34 L1 and L2 Control Cells Manually](#) to manually add a lot.
-
- 6 If you select Pause for QC, once QC samples have completed analysis, the autoloader remains paused if QC fails so that the problem can be corrected before running subsequent samples. If QC passes, the autoloader continues processing additional cassettes in the autoloader following the list of samples to run in the Request folder.
-
- 7 Gently roll/invert the control reagent to mix the product in a manner similar to the handling of a whole blood specimen (mixing with vortex or a rotator is not recommended).
-


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- 8 Insert control tubes into cassette #1 in the proper configuration with the barcode facing outward.

NOTE Refer to AQUIOS CL Flow Cytometer IFU, Chapter 5, for details on how to properly insert tubes into the cassette.



- 9 Place the cassette onto the cassette loading area (above autoloader).
- 10 Follow the sample preparation progression on the **Running** tab of the workstation main screen.

- 11 After the control tubes have ejected from the cytometer, the cassette will be moved to the unloading area below the autoloader. Remove and store the control tubes properly until next use.

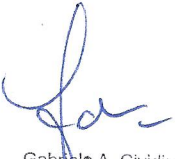
Adding and Using AQUIOS STEM CD34 Control Lots

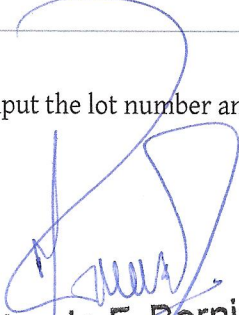
Adding New Lots of AQUIOS STEM CD34 L1 and L2 Control Cells using QR Code

- 1 Select  on the right side of the workstation main screen and the *Barcode Reagents* screen will appear.
- 2 After the system scanner light turns on, scan the QR code for the L1 and L2 control cells on the corresponding assay sheets.
- 3 Select **OK** on the *Barcode Reagents* screen.

Adding New Lots of AQUIOS STEM CD34 L1 and L2 Control Cells Manually

- 1 Select **Setup** on the workstation main screen.
- 2 Select **Reagent Info** tab on the left side of the main screen.
- 3 Select the following parameters:
 - **Test:** STEM Single.
 - **Reagent/Sample:** STEM CD34 – Level 1 or STEM CD34 – Level 2
- 4 Select . On **Add Reagent Lot** popup screen, input the lot number and expiration date.


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IMPORTANT Verify input before selecting **OK**. Once saved in the system, it cannot be edited.

Add Reagent Lot

Lot Number: Expiration Date:
(mm/dd/yyyy)

5 Select **OK**.

6 Select **Edit**. The *In Edit Mode* screen is displayed.

Test:

Reagent/Sample:

Lot Number: 

Expiration: CAL Factor:
(mm/dd/yyyy)

Note: Percents must be entered as decimal. Example 20% = .2

Result	Min	Max
CD34+ Leukocytes Percent		
CD34+ Count/uL		
CD45+ Count/uL		



7 Using the assay sheet, enter assay values for the following **MIN** and **MAX** parameters as shown in the example of assay sheet shown below:

- Percent Positive CD34+

NOTE For Percent Positive, ensure that the values within the parentheses from the assay sheet are used. For example, ("0.0020").

- Absolute Number

NOTE From CD34+ and CD45+.

IVD

AQUIOS STEM CD34 Control Cells

Table of Expected Results

REF C43667

LOT	11300063
	2021-08-07



Level 1

	Percent Positive Cell ^a	Min ^b	Max ^b	Absolute Number (cells / μ L)	Min	Max
CD34+	0.21 (.0021)	0.14 (.0014)	0.28 (.0028)	12.9	7.7	18.1
CD45+				6250	5250	7250

^a - based on leukocytes

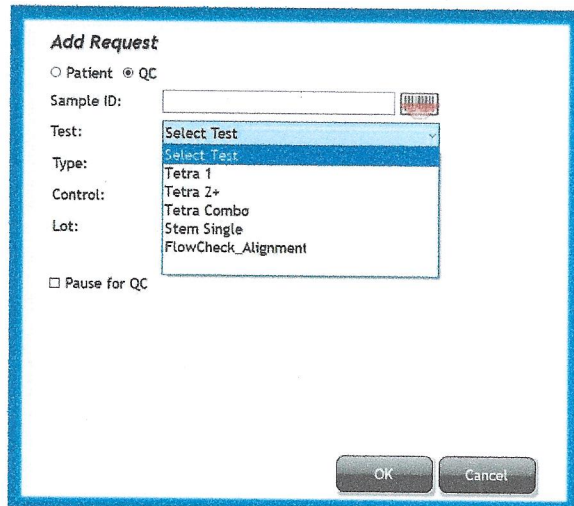
^b - in case of manual entry, values must be entered as shown in parentheses

IMPORTANT: The Expiration date is displayed as YYYY-MM-DD. If entering the Lot and Expiration information manually, the expiration date must be entered in the software in the following format: MM/DD/YYYY.

8 Select **Save**.

Starting AQUIOS STEM CD34 L1 and L2 Control Cell QC With Pre-Existing Lot

- 1 Select  on the workstation main screen and then select  .
The *Add Request* screen appears.



- 2 Select **QC**.

- 3 Select the test **STEM Single** .

- 4 Select the  icon on the **Add Request** screen. After the system scanner light turns on scan the barcode on the control cell vial.

NOTE Screen will automatically switch from **Patient** to **QC** if the lot number already exists in the system.

- 5 **Sample ID** field will automatically populate with the control lot number on the vial when scanned.

NOTE Refer to AQUIOS CL Instructions for Use for more information on barcodes.

- 6 Verify and confirm the following parameters:

- **Test:** .
- **Type:** QC
- **Control:** STEM CD34 – Level 1 or STEM CD34 – Level 2
- **Lot:** Confirm the lot number

- 7 If you select Pause for QC, once QC samples have completed analysis, the autoloader remains paused if QC fails so that the problem can be corrected before running subsequent samples. If QC passes, the autoloader continues processing additional cassettes in the autoloader following the list of samples to run in the Request folder.

QC Screen

The Results tab on the QC screen tracks the changes over time in HPCV (Half Peak coefficient of variation) for FS, FL1, FL2, FL3, FL4 and FL5 parameters using Flow-Check Fluorospheres. This data reflects performance and stability of the instrument over the specified period.

NOTE Under **Test**, switch between **FlowCheck_Alignment** for Flow-Check results and **Stem Single** for Control Cells results.



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Figure 3.1 Results Tab Screen: Flow-Check Fluorospheres

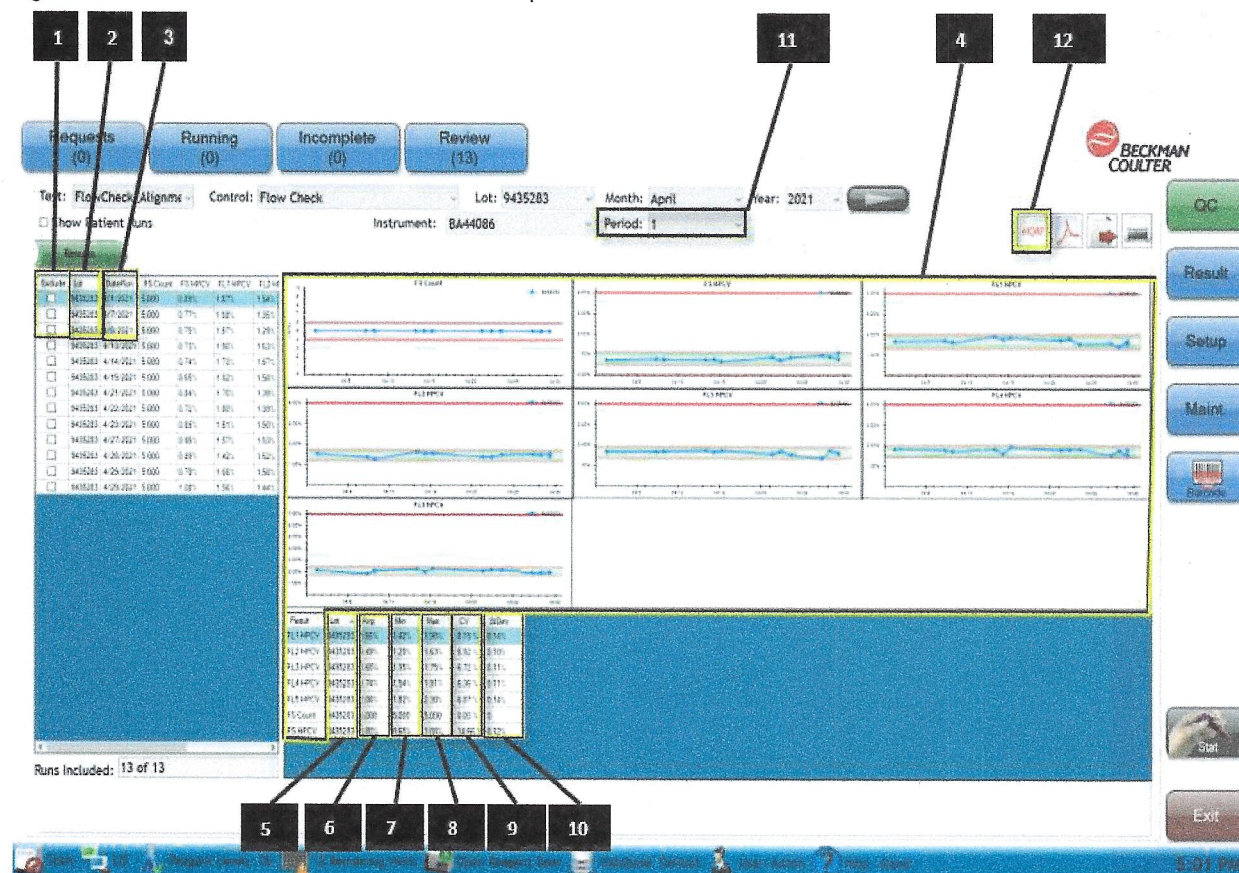


Table 3.3 General Table on QC Screens: Defined

1	Exclude Checkbox: Use the checkbox to eliminate this run from the QC range calculation and select  .	7	Min: The lowest value of all the non-excluded runs listed.
2	Lot: Control reagent lot number used for the specified QC run.	8	Max: The highest value of all the non-excluded runs listed.
3	Date run: The date on which the selected QC run was performed.	9	CV: The coefficient of variation of all the non-excluded runs listed (Standard Deviation/Average) x 100.
4	Results: The QC results quantitatively for the selected QC run. The results displayed depend on the selected test.	10	StDev: The standard deviation of all the non-excluded runs listed.
5	Lot: The lot numbers of the control reagent for all of the runs listed.	11	Period: Select the number of months to display in each graph.
6	Average: The average of all the non-excluded runs listed.	12	elQAP: Refer to Setting Up IQAP Export .

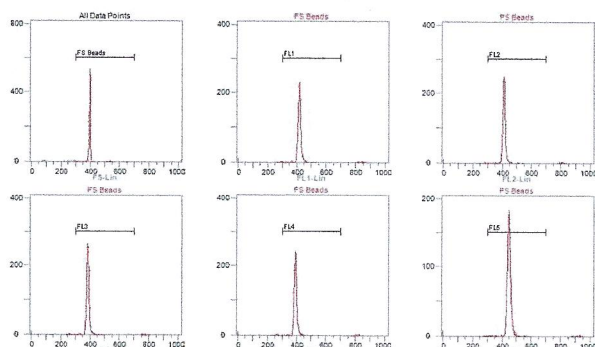
NOTE Summary statistics are listed at the bottom of the graphs. Use the vertical scroll bar to access all statistics. The customer can move the region.

QC Reports

AQUIOS STEM (Single Tube Loader) Flow-Check Fluorospheres QC Result Examples

Figure 3.2 Results Tab: Flow-Check Fluorospheres Report Page 1

Sample ID: 89352285090 Test: FlowCheck_Alignment v1.0
Run Date: 11 Jun 2021 08:10:01 Analysis Date: 11 Jun 2021 08:10:01
User: Admin Collect Date:
Specimen Type: Control Patient Name: Flow Check
Patient ID: Lot: 9435283 Gov. ID:
Status: Location:
Gender: Date Of Birth:
Physician: Physician Code:
Instrument Serial #: BA44086
Run Flags:
Run Notifications:
Comments:



Result	Value	Flag	Normal Range	Action Range
FS Count	5,000			4,000-6,000
FS Mean	399.25			
FS HPCV	0.78%			0.01%-4.00%
FL1 Mean	419.99			
FL1 HPCV	1.71%			0.01%-4.00%
FL2 Mean	412.61			
FL2 HPCV	1.56%			0.01%-4.00%
FL3 Mean	386.97			
FL3 HPCV	1.64%			0.01%-4.00%
FL4 Mean	395.90			
FL4 HPCV	1.81%			0.01%-4.00%
FL5 Mean	450.41			
FL5 HPCV	2.09%			0.01%-7.00%

Signature:

NOTE The region can be manually adjusted in order to capture all the fluorospheres.

AQUIOS STEM Single (Auto Loader) - AQUIOS STEM CD34 Control Cells Level 1 & 2 QC Result Examples

Figure 3.3 Results Tab Screen: AQUIOS STEM CD34 Control Cells Level 1 (Run with AQUIOS STEM Single)

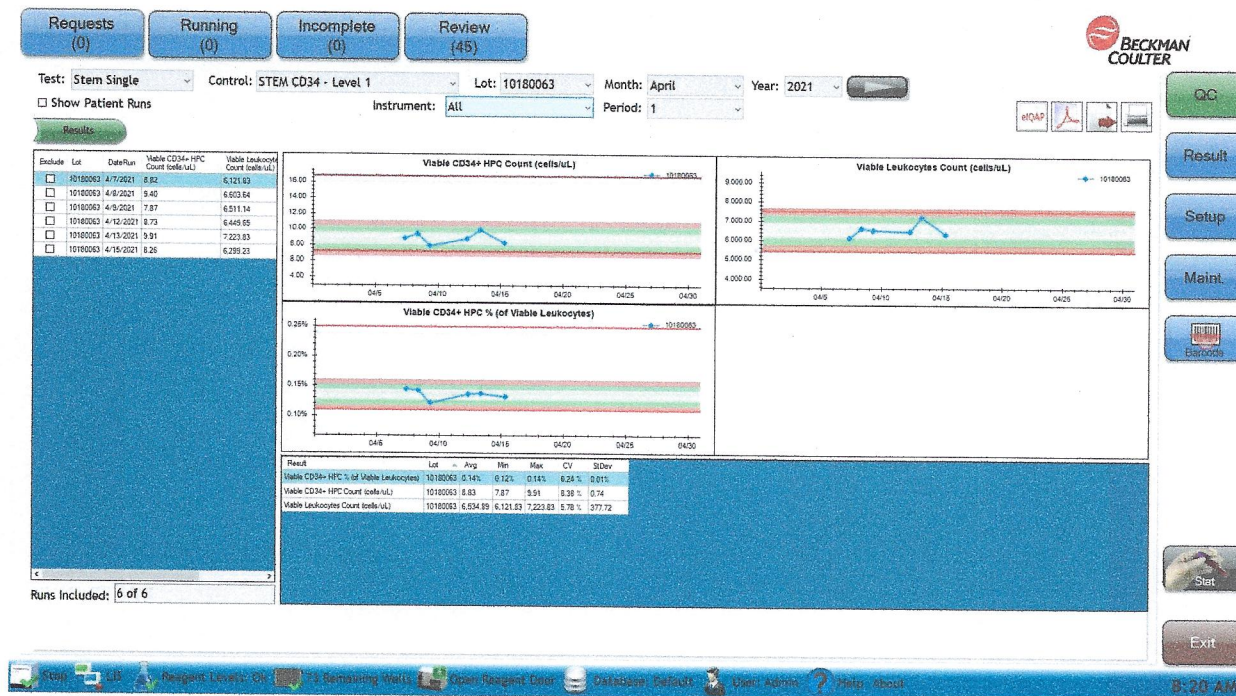


Figure 3.4 Results Tab Screen: AQUIOS STEM CD34 Control Cells Level 2 (Run with AQUIOS STEM Single)

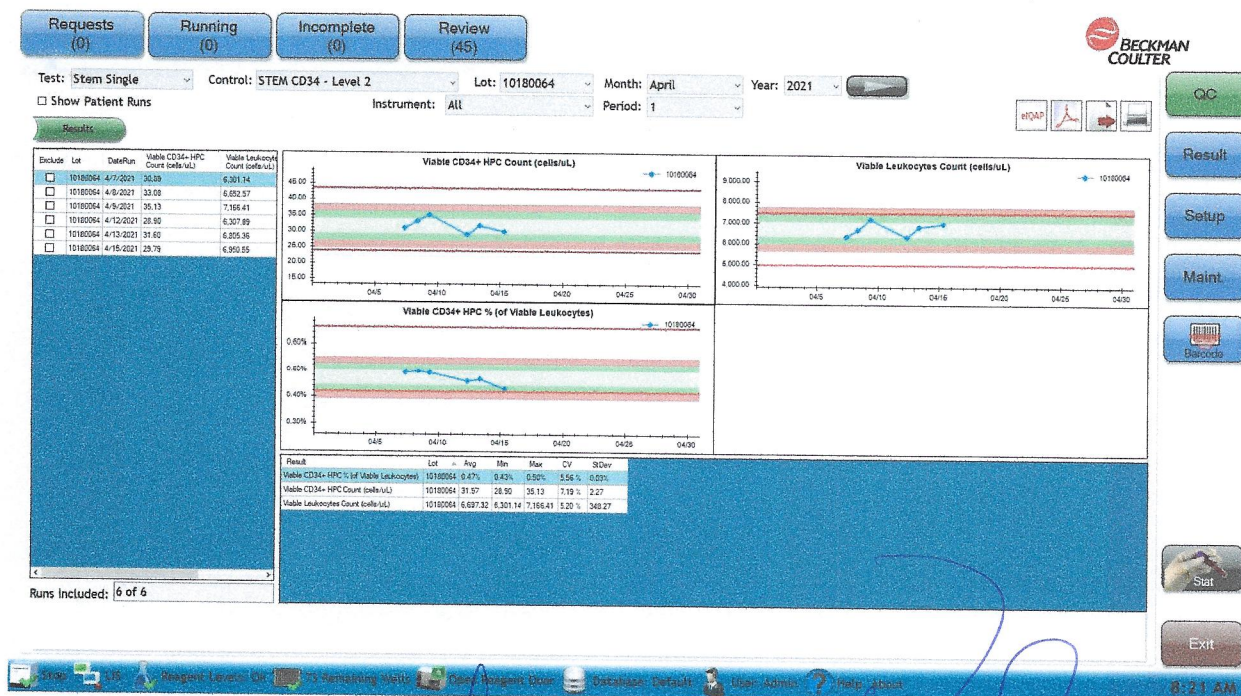


Figure 3.6 Results Tab Screen: AQUIOS STEM CD34 Control Cells Level 1, Page 2 (Run with AQUIOS STEM Single)

Sample ID: 10180063 Test: Stem Single v1.0
Run Date: 18 Mar 2021 09:16:45 Analysis Date: 18 Mar 2021 09:16:45

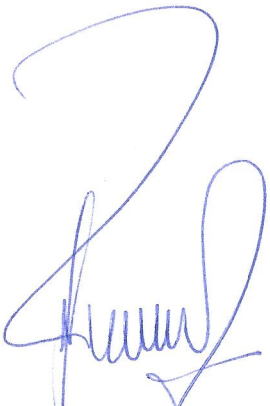
Result	Value	Flag	Normal Range	Action Range
Viable CD34+ HPC Count (cells/uL)	12.12			7.20-16.80
Viable Leukocytes Count (cells/uL)	6,526.36			5,451.00-7,527.00
Viable CD34+ HPC % (of Viable Leukocytes)	0.19%			0.11%-0.25%
DF: Dilution Factor	0.00			
Viable CD34+ HPC Count (cells/uL) (x DF)	0.00			
Viable Leukocyte Count (cells/uL) (x DF)	0.00			
HV: Harvest Volume (mL)	0.00			
Viable CD34+ HPC Count (x DF x HV)	0.00			
BW: Body Weight (kg)	0.00			
Viable CD34+ HPC Count per kg (x DF x HV / BW)				
CAL	989			

Statistic	Value	Flag	Normal Range	Action Range
**CD34+ Viability % (of total CD34+)	100.00%			
**Total CD34+ HPC Count (cells/uL)	12.12			
**WBC Count (cells/uL)	6,526.36			
**Sample Viability % (of WBC)	100.00%			
**DF: Dilution Factor	0.00			
**Total CD34+ HPC Count (cells/uL) (x DF)	0.00			
**WBC Count (cells/uL) (x DF)	0.00			
**Viable Events	76,508			
**Viable Leukocytes Events	76,495			
**Viable CD34+ HPC Events	142			
**Single Beads Events	11,592			

Signature:



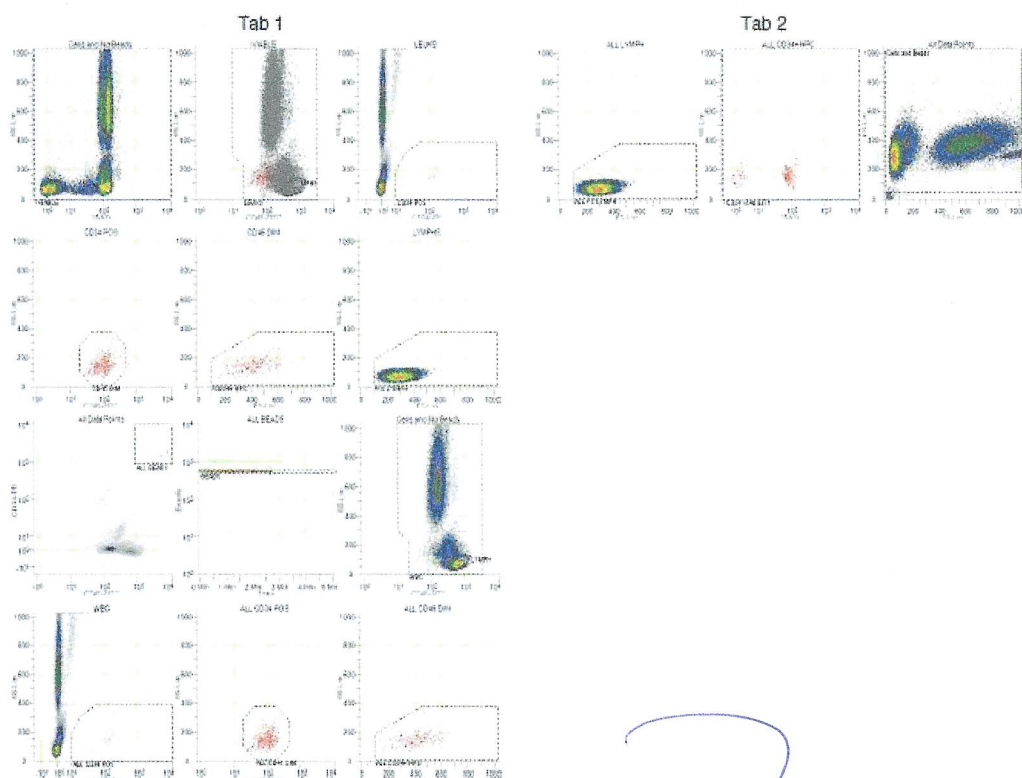
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Figure 3.7 Results Tab Screen: AQUIOS STEM CD34 Control Cells Level 2, Page 1 (Run with AQUIOS STEM Single)

Sample ID:	10180064	Test:	Stem Single v1.0
Run Date:	18 Mar 2021 09:23:47	Analysis Date:	18 Mar 2021 09:23:47
User:	Admin	Collect Date:	
Specimen Type:	Blood Control	Patient Name:	STEM CD34 - Level 2
Patient ID:	Lot: 10180064	Gov. ID:	
Status:		Location:	
Gender:		Date Of Birth:	
Physician:		Physician Code:	
Instrument Serial #:	BA44086	Harvest Volume (mL):	0
Report:	Well 1	Weight (kg):	0
		Dilution:	0
Run Flags:			
Run Notifications:			
Comments:			



** Population Statistics

Page #1 of 2


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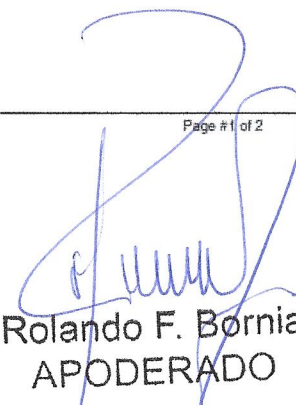

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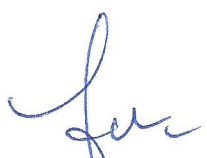
Figure 3.8 Results Tab Screen: AQUIOS STEM CD34 Control Cells Level 2, Page 2 (Run with AQUIOS STEM Single)

Sample ID: 10180064 Test: Stem Single v1.0
Run Date: 18 Mar 2021 09:23:47 Analysis Date: 18 Mar 2021 09:23:47

Result	Value	Flag	Normal Range	Action Range
Viable CD34+ HPC Count (cells/uL)	37.63			23.90-43.50
Viable Leukocytes Count (cells/uL)	6,585.61			4,978.00-7,466.00
Viable CD34+ HPC % (of Viable Leukocytes)	0.57%			0.42%-0.66%
DF: Dilution Factor	0.00			
Viable CD34+ HPC Count (cells/uL) (x DF)	0.00			
Viable Leukocyte Count (cells/uL) (x DF)	0.00			
HV: Harvest Volume (mL)	0.00			
Viable CD34+ HPC Count (x DF x HV)	0.00			
BW: Body Weight (kg)	0.00			
Viable CD34+ HPC Count per kg (x DF x HV / BW)				
CAL	989			

Statistic	Value	Flag	Normal Range	Action Range
**CD34+ Viability % (of total CD34+)	100.00%			
**Total CD34+ HPC Count (cells/uL)	37.63			
**WBC Count (cells/uL)	6,585.61			
**Sample Viability % (of WBC)	100.00%			
**DF: Dilution Factor	0.00			
**Total CD34+ HPC Count (cells/uL) (x DF)	0.00			
**WBC Count (cells/uL) (x DF)	0.00			
**Viable Events	76,492			
**Viable Leukocytes Events	76,477			
**Viable CD34+ HPC Events	437			
**Single Beads Events	11,485			

Signature:



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Interlaboratory Quality Assurance (IQAP)

The Interlaboratory Quality Assurance Program (IQAP) is a Beckman Coulter program available to you through enrollment that complements and enhances your laboratory's in-house quality control. IQAP lets you submit your control recovery data to Beckman Coulter and in return, receive a personalized report that summarizes your results and compares them to those of your peer group (pool).

Before Setting Up IQAP Export

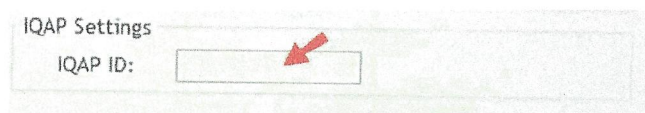
Before you export an IQAP file, you must register your AQUIOS instrument with IQAP. The IQAP group will assign an IQAP ID number for your AQUIOS.

- 1 Using an internet connected computer, navigate to website,
<https://qspweb.beckmancoulter.com>
and follow the instructions on the website to create an account and register your instrument.

- 2 On the AQUIOS main screen, select .

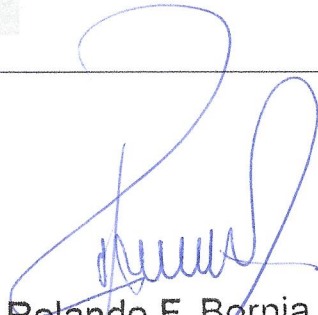
- 3 On the Setup screen, select .

- 4 On the System Setup screen, enter your IQAP ID number and select .



The screenshot shows a section titled "IQAP Settings" with a label "IQAP ID:" followed by a text input field. A red arrow points to the input field.


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Setting Up IQAP Export

1 On the QC Results Tab Screen select .

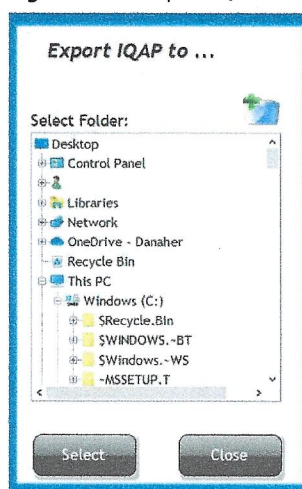
NOTE Use the eIQAP button to export IQAP control data files.

Figure 3.9 QC Results Tab Screen: Export IQAP



2 Choose a location to export (save) the IQAP control data file.

Figure 3.10 Export IQAP control data file



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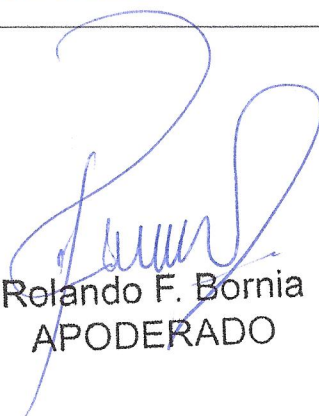
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- 3 Make a note of the location of the saved IQAP control data file, you will need to know the file location when you upload it to the IQAP website.

Refer to the Cytometry Interlaboratory Quality Assurance Program Procedure Manual for instructions for uploading your control data files. See [Related Documents](#).



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CHAPTER 4

Sample Analysis

Overview

IMPORTANT Before performing an analysis using the AQUIOS STEM application, ensure you are thoroughly familiar with the operating procedures in the AQUIOS CL Flow Cytometer Instructions for Use manual.

This chapter contains the following sections:

- Test Description
- AQUIOS STEM Application Workflow
- Sample preparation
- Storage Conditions and Stability
- AQUIOS STEM Testing Workflow
- Create a Request
- Load Sample in the Instrument
- Options for Running Specimens
- Logging In Controls
- Running Samples Using the Autoloader
- Running Samples Using the Single-tube Loader



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Test Description

Three AQUIOS STEM tests are available in the AQUIOS STEM application:

- Stem Panel: Run test in duplicate plus negative control (3 wells)
- Stem Duplicate: Run test in duplicate, no negative control (2 wells)
- Stem Single: Run test in single, no negative control (1 well)

Refer to [Table 4.1, Test Descriptions](#) for the list of AQUIOS STEM kit reagents necessary for each test.

Table 4.1 Test Descriptions

Test Name	Reagent					Test Description
	CD45-FITC / CD34-PE	7-AAD Viability Dye	CD45-FITC / Isoclonic Control	Lysing Solution	STEM-Count Fluorospheres	
Stem Panel	X	X	X	X	X	Run tests in duplicate plus negative control (3 wells)
Stem Duplicate	X	X		X	X	Run tests in duplicate , no negative control (2 wells)
Stem Single	X	X		X	X	Single test (1 well)

AQUIOS STEM Application Workflow

When running samples using the AQUIOS STEM application with Single, Duplicate, and Panel tests, each test goes through four stages:

- Preparing** The specimen, monoclonal antibodies, and 7AAD viable dye are aspirated, dispensed and then mixed in the designated well of the 96-deep well plate. Refer to [Table 4.2](#).
- Incubating** An approximate 15-minute incubation allows proper staining of the specimen by the monoclonal antibodies. Refer to [Table 4.2](#).
- Lysing** The lysing system is dispensed into the well containing the stained specimen to lyse the RBCs and preserve the WBCs. Refer to [Table 4.2](#).
- Analyzing** The AQUIOS STEM-Count Fluorospheres are added to the prepared sample into the well and the mixture is passed through the flow cell to obtain the sample results. Refer to [Table 4.2](#).

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Table 4.2 Processing Samples Using the STEM Application

PREPARING	INCUBATING	LYSING	ANALYZING
1. User loads specimen^a. 2. Specimen is mixed and aspirated from the collection tube. 3. Specimen is dispensed into a microtiter plate well. 4. Antibodies are added to the well. 5. Suspension is mixed.	1. About 15 minutes.	1. AQUIOS STEM Lysing Solution is added to the well. 2. Solution is mixed. 3. Lysing, including incubation, for about 15 minutes.	1. AQUIOS STEM Kit STEM-Count Fluorospheres are added into the well. 2. Solution is mixed. 3. Sample is aspirated. 4. Sample is analyzed by flow cytometry up to 5 minutes.

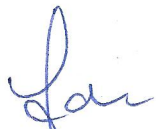
a. When using the autoloader, specimens are automatically mixed. When using the Single-tube Loader, mix the collection tube as instructed before loading the specimen tube. (Refer to Chapter 5 in the AQUIOS CL Flow Cytometer Instructions for Use manual for details.)

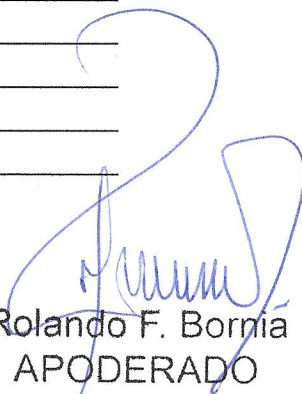
Sample preparation

- Retain fresh specimens in blood collection tubes at recommended temperature depending on the specimen type, between 18°C and 25°C (64.4°F and 77°F) or between 2°C and 8°C (35.6°F and 46.4°F).
- Fresh samples are ideally analyzed as soon as possible after drawn, refer to [Storage Conditions and Stability](#) for storage conditions for each sample type.
- Make sure each patient specimen tube to be loaded complies with the minimum running volume. When using the autoloader, ensure that the specimen tube has a barcode on it before loading it to the system. Refer to [Table 4.3](#). Refer to AQUIOS CL Instructions for Use for complete list of specimen tubes for the Autoloader and Single-tube loader.

Table 4.3 Minimum Specimen Volume Required per Specimen Tube

Specimen Tube Size	Minimum Volume
13 mm x 75 mm	750 µL
13 mm x 100 mm	750 µL
16 mm x 100 mm	1000 µL
10.25 mm x 50 mm	650 µL
Sarstedt 13 mm x 75 mm	750 µL
Sarstedt 13 mm x 90 mm	750 µL
Sarstedt 11 mm x 66 mm	750 µL
Sarstedt 15 mm x 92 mm	1500 µL
Sarstedt 13 mm x 65 mm	750 µL


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Storage Conditions and Stability

Non-Frozen Specimen

Fresh samples are ideally analyzed as soon as possible after drawn, but no later than described below.

- Normal whole blood samples are stable for up to 20 hours if stored between 18-25°C (64-77°F).
- Mobilized whole blood samples are stable for up to 20 hours if stored between 18-25°C (64-77°F).
- Cord blood samples are stable for up to 24 hours if stored between 18-25°C (64-77°F).
- Apheresis samples are stable for up to 24 hours if stored between 2-8°C (35-46°F).
- Bone marrow samples are stable for up to 24 hours if stored between 2-8°C (35-46°F).

For best staining results, the following rules should be applied:

- Viable Leukocytes below 30000 Cells/ μ L
- Viable CD34+ HPC cells below 1000 Cells/ μ L

Frozen Specimen Type

Frozen samples should be processed within 15 minutes after thawing and kept on ice.

Beckman Coulter recommends using the Single Tube Loader function to analyze thawed samples.

Frozen samples should not be rerun.

In case of rerun, a new aliquot should be thawed.

Reagents

Refer to the appropriate package inserts for information on reagent stability.

- AQUIOS Cleaning Agent
- AQUIOS Sodium Hypochlorite Solution
- AQUIOS Sheath Solution
- AQUIOS STEM Kit Reagents
- AQUIOS STEM CD34 Control Cells
- Flow-Check Fluorospheres

AQUIOS STEM Testing Workflow

1 Perform AQUIOS Startup.

Refer to the AQUIOS CL Flow Cytometer Instructions for Use manual, as needed. Make sure AQUIOS CL Startup is completed and acceptable. Refer to Chapter 3, Daily Startup in the AQUIOS CL Flow Cytometer Instructions for Use manual.

- 2 Load AQUIOS STEM Kit reagents. The application specific reagents are automatically scanned by the system once they are loaded in their respective holders.

CAUTION

Risk of losing on-board samples. Replacing reagents and opening the reagent door while operating the Cytometer puts on-board samples at risk. Replacing reagents while the system is running should be performed as quickly as possible to avoid flagged results due to over lysing and over incubation.

CAUTION

Risk of instrument damage. For the monoclonal antibodies and the 7AAD viability dye reagents, ensure the shipping caps have been replaced with the pierceable caps provided with the reagent packaging. For the AQUIOS STEM Lysing Solution, remove the cap before loading into the system. For the AQUIOS STEM-Count, the regular cap and seal foil have to be replaced with a screw cap with hole before loading into the system. (see further instructions below and in reagent IFU). Otherwise, the probe can be damaged.

IMPORTANT AQUIOS STEM-Count Fluorospheres should be vortexed for 10 to 12 seconds before placing in the carousel.

IMPORTANT When prompted to re-mix AQUIOS STEM-Count Fluorospheres, remove the screw cap with hole from the bottle and replace it with the standard cap before vortex mixing. After mixing, replace the standard cap with the screw cap with hole before returning to the instrument.

Make sure AQUIOS STEM kit reagents were loaded and scanned correctly.

- Place the vials of CD45-FITC /CD34-PE and 7AAD viability dye reagents in the carousel.

NOTE When using STEM Panel test, you must also place a vial of CD45-FITC/ Isoclonic Control in the carousel. Refer to [Table 4.1, Test Descriptions](#).

- Mount the carousel containing the vials of monoclonal antibody reagents on the carousel platform inside the reagent compartment

NOTE When loading the carousel into the instrument, be sure to place it on the wheel and gently turn it until it locks into position on the wheel.

- Remove the cap and place the AQUIOS STEM Lysing Solution bottle in any of the three available positions in the reagent compartment. Ensure the bar code label faces outward.
- Before testing or when a reminder pops up to remind mixing, with the original white cap on, mix the bottle of AQUIOS STEM-Count Fluorospheres thoroughly. Remove the original white cap and the aluminum heat seal (when applicable), and replace the original white cap with the screw cap with hole that is provided with the kit. Place the AQUIOS STEM-Count Fluorospheres in the bottle holder with the adapter. Make sure the bar code label faces outward.

NOTE Refer to the appropriate reagent IFU for details on how to properly mix reagents.

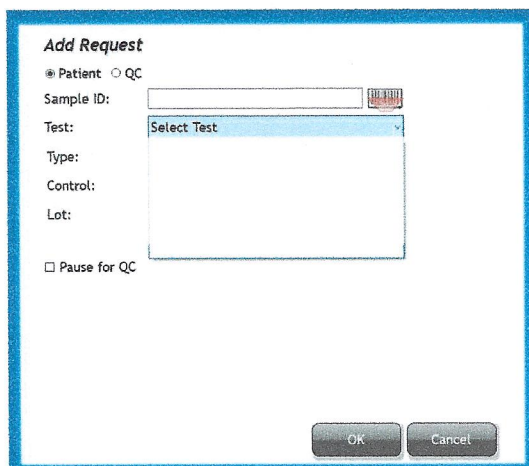
- Insert an AQUIOS 96-deep well plate in the correct orientation. Make sure reagent levels and number of unused wells are sufficient for the number of runs requested. If needed, add or replace with new reagents as appropriate before proceeding to analysis.

At the end of the test day, remove the STEM-Count bottle from the system and replace the screw cap with hole with the standard cap. Dry the inner surface of the screw cap with hole with low lint tissue paper before storing in the kit box. Store the kit box at 2-8°C until the next use. Store the AQUIOS STEM Lysing Solution bottle at room temperature.

- 3 Ensure Quality Control checks have been completed and are acceptable within 24 hours using AQUIOS STEM CD34 Control Cells Level 1 and level 2. Refer to Chapter 4, Quality Control in the AQUIOS CL Flow Cytometer Instructions for Use manual as needed

Create a Request

- 1 Select  on the workstation main screen and then select . The *Add Request* screen appears.



- 2 Select **Patient**.

- 3 Select the  icon on the **Add Request** screen. After the system scanner light turns on scan the barcode on the control cell vial.

NOTE It is possible to manually populate the Sample ID field.

NOTE Refer to AQUIOS CL Instructions for Use for more information on barcodes.

4 Select an AQUIOS STEM test.

Three AQUIOS STEM tests are available: Stem Single, Stem Duplicate or Stem Panel.

Add Request

☒ Patient ☐ QC

Sample ID:

Test: **Select Test**

Specimen Type: **Select Test**

Patient Name:

Patient ID:

Status:

Location:

Gender: **Select** Date of Birth:

Physician Name:

Physician Code:

OK Cancel

5 Select the Specimen Type.

Five specimen types are available:

- Apheresis
- Bone Marrow
- Cord Blood
- Mobilized Blood
- Whole Blood

Add Request

☒ Patient ☐ QC

Sample ID:

Test: **Stem Panel**

Specimen Type: **Select Type**

Patient Name:

Patient ID:

Status:

Location:

Gender: **Select** Date of Birth:

Physician Name:

Physician Code:

Harvest Vol. (mL): Weight (kg): Dilution:

OK Cancel

-
- 6 Enter Harvest Volume, Patient Weight and Dilution Factor information.

 CAUTION

Risk of erroneous results. If no values are entered for these parameters, the instrument will default them to 0. This will cause some calculations in the results page to equal 0. Input "1" for Harvest Volume, Weight, and Dilution if these fields would have otherwise been left blank.

The harvest volume (**Harvest Vol. (mL)**) of the sample, the patient weight (**Weight (kg)**) and the dilution factor of the tested sample (**Dilution**) are available as shown above in the **Add Request** screen. The values can be integer or with decimals, the maximum number of digits is 5.

- **Harvest Vol. (mL)** should be expressed in milliliter unit.
- **Weight (Kg)** should be expressed in Kilogram unit.
- If the **Dilution** of the sample is 1:10, the entered value will be 10 (Note: 1:10 equals 1 part of sample plus 9 parts of diluent).
- Enter additional information if necessary, in the Add Request screen: Collect Date, Patient Name, Status, etc.

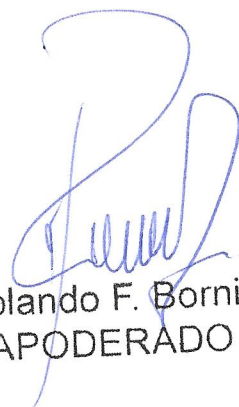
-
- 7 When finished entering information on the **Add Request** screen, select **OK**.
-

Load Sample in the Instrument

-
- 1 Gently roll/invert the sample tube to mix the product (mixing with vortex or a rotator is not recommended).



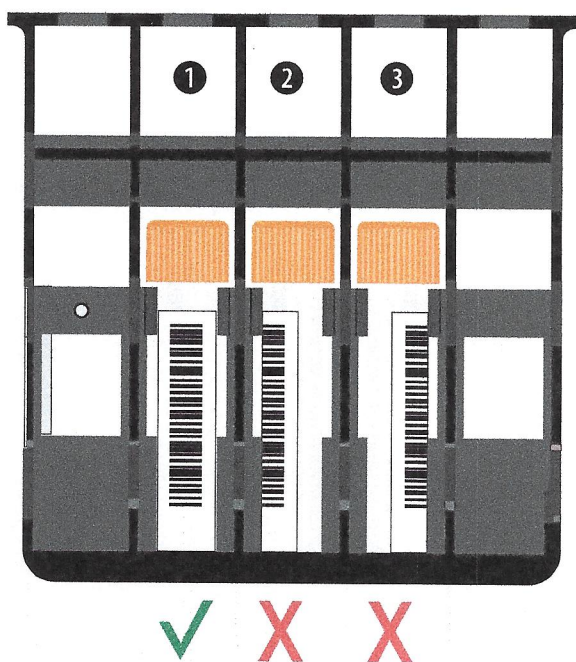
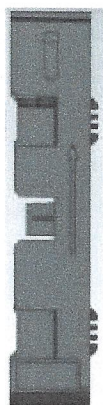
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- 2 Insert sample tubes into a cassette that matches the tube size in the proper orientation with the barcode facing outward.

NOTE Refer to AQUIOS CL Flow Cytometer IFU, Chapter 5, for details on how to select the appropriate cassette and properly insert tubes into the cassette.



- 3 Place the cassette onto the cassette loading area (above autoloader).
- 4 Follow the sample preparation progression on the **Running** tab of the workstation main screen.

- 5 After the sample tubes have ejected from the cytometer, the cassette will be moved to the unloading area below the autoloader. Remove the sample tube and store properly if it might be used again. Refer to [Storage Conditions and Stability](#)

Options for Running Specimens

WARNING

Risk of personal injury or contamination:

- If not properly shielded while using the instrument, it is possible to become injured or contaminated. To prevent possible injury or biological contamination, you must wear proper laboratory attire, including gloves, a laboratory coat, and eye protection.
- Operating the instrument while the waste level sensor is disconnected can cause biological contamination. To prevent biological contamination, do not operate the instrument while the waste level sensor is disconnected.

CAUTION

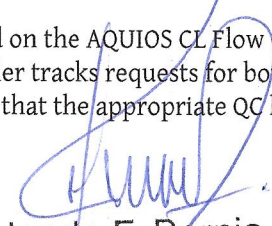
Risk of clogging or erroneous results if samples contain clots, fibrin strands, or cellular debris, or if samples are lipemic. Use good laboratory practices and follow your laboratory procedures for specimen handling and/or inspection prior to placing on the system.

Specimen tubes can be loaded in the autoloader or the Single-tube Loader. The Single-tube Loader functions as a stat loader. A higher priority is given to a specimen tube loaded into the Single-tube Loader; therefore, it will be processed ahead of the specimen tubes loaded in an autoloader cassette.

For the AQUIOS STEM application, the autoloader has continuous loading capability with up to 15 runs (15 specimens in Single, 7 in Duplicate, and 5 in Panel) in order to avoid overincubation with the lysing reagent. The specimens are automatically processed according to the unprocessed stack cassette position (bottom to top) at the top of the autoloader holder and according to the sample position within a cassette (position 1 to 5). Place the cassette that you want to run first at the bottom of the unprocessed stack and place the specimen you want to run first in position one (1) of the cassette. Refer to Running Samples Using the Autoloader in Chapter 5, Sample Processing in the AQUIOS CL Flow Cytometer Instructions for Use manual.

The AQUIOS Tetra tests can be simultaneously loaded on the AQUIOS CL Flow Cytometry system with AQUIOS STEM Tests. The AQUIOS Smart Scheduler tracks requests for both tests as they proceed from sample preparation to analysis. Ensure that the appropriate QC has been run for the


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AQUIOS Tetra tests prior to loading patient samples. Ensure that the appropriate and sufficient AQUIOS Tetra reagents are loaded. Refer to AQUIOS Tetra System Guide for more information.

NOTE Wait until the AQUIOS instrument displays green light on autoloader and status bar to process additional samples.

Logging In Controls

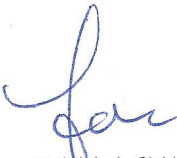
For detailed information on Logging In Controls, refer to Chapter 11, Replacement Procedures in the AQUIOS CL Flow Cytometer Instructions for Use manual.

Running Samples Using the Autoloader

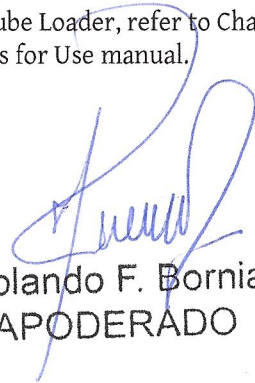
For detailed information on Running Samples Using the Autoloader, refer to Chapter 5, Sample Processing, in the AQUIOS CL Flow Cytometer Instructions for Use manual.

Running Samples Using the Single-tube Loader

For detailed information on Running Samples Using the Single-tube Loader, refer to Chapter 5, Sample Processing in the AQUIOS CL Flow Cytometer Instructions for Use manual.



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Running Screen

The Running screen (Figure 4.1) tracks any samples currently being processed by the Cytometer. The sample workflow is displayed on the screen (**Running**) as the sample progresses from one stage to the next (from Preparing to Analyzing). The **Details** portion of the screen provides visibility and the specifics of each stage, including timing.

Figure 4.1 Running Screen



For more information about the Running Screen, refer to Appendix A in the AQUIOS CL Flow Cytometer Instructions for Use manual.

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Overview

This chapter contains information about:

- Review Screen
- Data Review
- Adjust Compensation Manually
- Result Screen
- Flags And Notifications

The AQUIOS Workstation provides the user with the ability to review both QC data and completed patient tests.

The review process provides the user with the ability to review data based on the Review/Editor and Administrator rights function to edit completed runs. The following are the items which can be edited:

- Sample information
- Gate and Region Placement
- Compensation

Review Screen

IMPORTANT There is a risk of reporting incorrect results. Data displays used to arrive at the test result for light scatter patterns, antibody staining profiles, and all gates and boundaries should be reviewed by a laboratory professional when interpreting the data. If results are suspect, follow your laboratory's procedures to resolve.

For a more detailed explanation of this screen and its components, refer to Chapter 6, Data Review in the AQUIOS CL Flow Cytometer Instructions for Use manual.

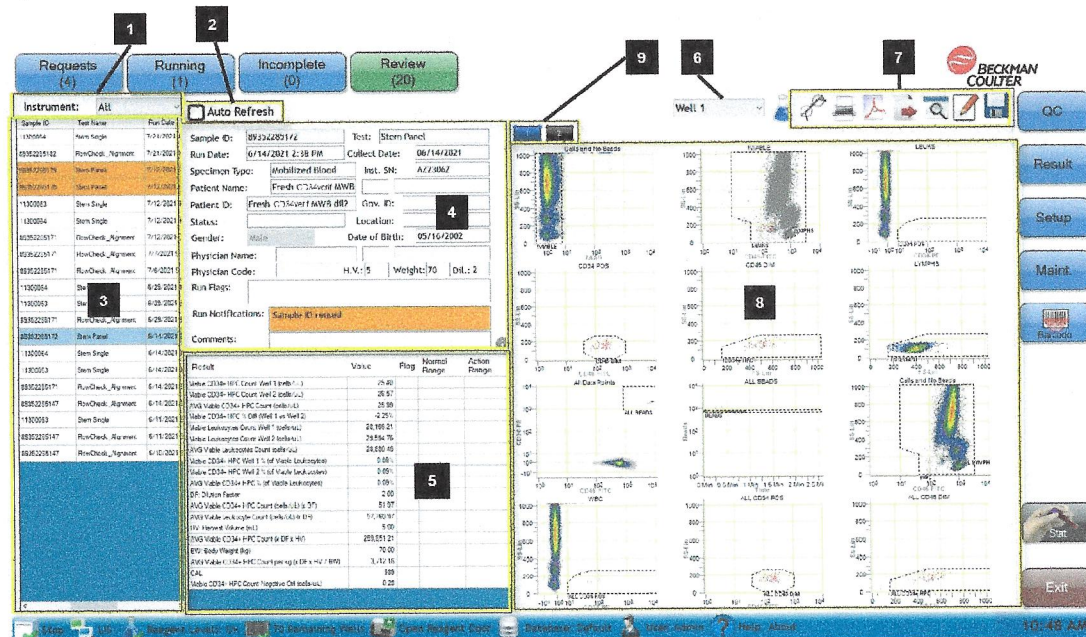
The Review screen displays analyzed samples that were previously run and that are currently pending review and/or transmission. The Review screen can be customized using a drop down menu with results from each well (Well#1, Well#2 or Control) or with a pre-defined graph combinations of the 3 wells (Panel test) or 2 wells (Duplicate test) called Summary. The access to the different well is dependent of the Test option selected. These screens allow you to review, edit, and save changes to regions, gates, compensation and/or patient information prior to transmitting results to the LIS. For easy editing, you can zoom any of these displays as needed. Also, the results can be printed or exported as a PDF, as a Flow Cytometry Standard listmode (.lmd) or native format (.crd) file. Both sample history changes and reagent information are available for review. All the displays can be zoomed in for easier editing.

The following Review screen (Figure 5.1) illustrates the different display areas associated with a typical Review screen. This is an example; individual results vary.

NOTE The Review Screen can be enabled to automatically refresh to display the last completed run.

NOTE If results for a run are auto-transmitted, they will not appear under the Review Tab. In this case, you will need to reference these results under the Results Tab. Refer to Results Screen.

Figure 5.1 Review Screen: Display Areas



1. Instrument Designation
2. Auto Refresh
3. Completed Run List
4. Sample Identifiers and Run Information Area
5. Result Table Area
6. Graphic Options Selection (drop-down box)
7. Action Toolbar
8. Selected Graphic Display
9. Pages

Review Screen Display Areas (left to right)

Figure 5.2 Instrument Designation

Instrument: All

Allows for selection of data based on the instrument that was used to collect the data. This is important when multiple instruments are networked. This feature allows the Operator to view data generated by other instruments from any networked Workstation.

Figure 5.3 Auto Refresh

☒ Auto Refresh

Automatically refreshes to display the last completed run.

Figure 5.4 Review Screen: Completed Runs List

Sample ID	Test Name	Run Date
11300064	Stem Single	7/21/2021 1
89352285182	FlowCheck_Alignment	7/21/2021 1
89352285179	Stem Panel	7/12/2021 3
89352285178	Stem Panel	7/12/2021 3
11300063	Stem Single	7/12/2021 1
11300064	Stem Single	7/12/2021 1
89352285171	FlowCheck_Alignment	7/12/2021 9
89352285171	FlowCheck_Alignment	7/7/2021 9:1
89352285171	FlowCheck_Alignment	7/6/2021 9:1
11300064	Stem Single	6/29/2021 1
11300063	Stem Single	6/29/2021 9
89352285171	FlowCheck_Alignment	6/29/2021 9
89352285172	Stem Panel	6/14/2021 2
11300064	Stem Single	6/14/2021 1
11300063	Stem Single	6/14/2021 1
89352285171	FlowCheck_Alignment	6/14/2021 9
89352285147	FlowCheck_Alignment	6/14/2021 9
11300063	Stem Single	6/11/2021 8
89352285147	FlowCheck_Alignment	6/11/2021 8
89352285147	FlowCheck_Alignment	6/10/2021 8

This area presents completed runs that are awaiting review and release. The last run completed is located at the top of the list. The runs are identified by:

- Sample ID
- Test Name
- Run Date
- Patient ID
- Patient Name
- ID

Any test that generated one or more Notification is highlighted in orange.

Any test that resulted in the generation of one or more Flags is highlighted in red.

Any test having both notification and flags is highlighted in red.

Samples not highlighted have no flags or notifications.

NOTE Use the horizontal scroll bar to see all fields.

Figure 5.5 Review Screen: Sample Identifiers and Run Information Area

Sample ID:	89352285172	Test:	Stem Panel
Run Date:	6/14/2021 2:38 PM	Collect Date:	06/14/2021
Specimen Type:	Mobilized Blood	Inst. SN:	AZ23062
Patient Name:	FreshCD34verifMWB		
Patient ID:	FreshCD34verifMWB df12	Gov. ID:	
Status:		Location:	
Gender:	Male	Date of Birth:	05/16/2002
Physician Name:			
Physician Code:		H.V.: 5	Weight: 70
		Dil.: 2	
Run Flags:			
Run Notifications:	Sample ID reused		
Comments:			

This area provides the sample information that was entered when the test request was generated. It also provides the information regarding when the test was run and displays any Flag or Notification messages generated during the run. Refer to [Flags And Notifications](#).

Next to the comments field is . Select this to see details about your sample, such as population statistics (non-IVD results). If a result is modified, the comment field is available for documentation regarding why the modification was performed.


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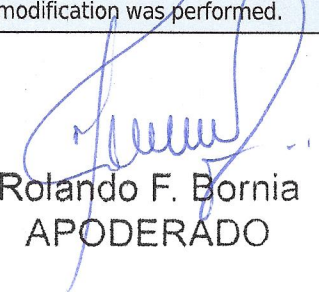

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Figure 5.6 Review Screen: Result Table Area (3 Wells)

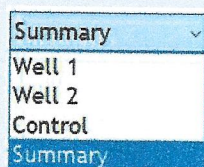
Result	Value	Flag	Normal Range	Action Range
Viable CD34+ HPC Count Well 1 (cells/uL)	25.40			
Viable CD34+ HPC Count Well 2 (cells/uL)	26.57			
AVG Viable CD34+ HPC Count (cells/uL)	25.99			
Viable CD34+ HPC % Diff (Well 1 vs Well 2)	-2.25%			
Viable Leukocytes Count Well 1 (cells/uL)	28,166.21			
Viable Leukocytes Count Well 2 (cells/uL)	29,594.76			
AVG Viable Leukocytes Count (cells/uL)	28,880.48			
Viable CD34+ HPC Well 1 % (of Viable Leukocytes)	0.09%			
Viable CD34+ HPC Well 2 % (of Viable Leukocytes)	0.09%			
AVG Viable CD34+ HPC % (of Viable Leukocytes)	0.09%			
DF: Dilution Factor	2.00			
AVG Viable CD34+ HPC Count (cells/uL) (x DF)	51.97			
AVG Viable Leukocyte Count (cells/uL) (x DF)	57,760.97			
HV: Harvest Volume (mL)	5.00			
AVG Viable CD34+ HPC Count (x DF x HV)	259,851.21			
BW: Body Weight (kg)	70.00			
AVG Viable CD34+ HPC Count per kg (x DF x HV / BW)	3,712.16			
CAL	989			
Viable CD34+ HPC Count Negative Ctrl (cells/uL)	0.28			

This area provides the results generated from the test run, in tabular format. Refer to [Quality Control Checks](#) for information on how results are rounded.

NOTE Parameters listed depend on the Test option requested: 1 well, 2 wells or 3 wells (as shown in [Figure 5.6](#)).

NOTE Results can be shown or hidden. Refer to Test Setup in Chapter 8 Setup in the AQUIOS CL Flow Cytometer Instructions For Use manual.

Figure 5.7 Review Screen: Graphic Options Selection Menu



Graphic options are accessed by selecting the desired view from a drop-down menu.

Results from each well (Well#1, Well#2 or Control) or one pre-defined graph combinations (Summary) are accessed by selecting the desired view from a drop-down menu:

- Well #1
- Well #2
- Control
- Summary

On [Figure 5.7](#) and [Table 5.1](#), the graphic options drop-down box specifies **Summary**.

Figure 5.8 Review Screen: Page Number



Allows you to switch between page 1 and page 2 to review all the graphics.

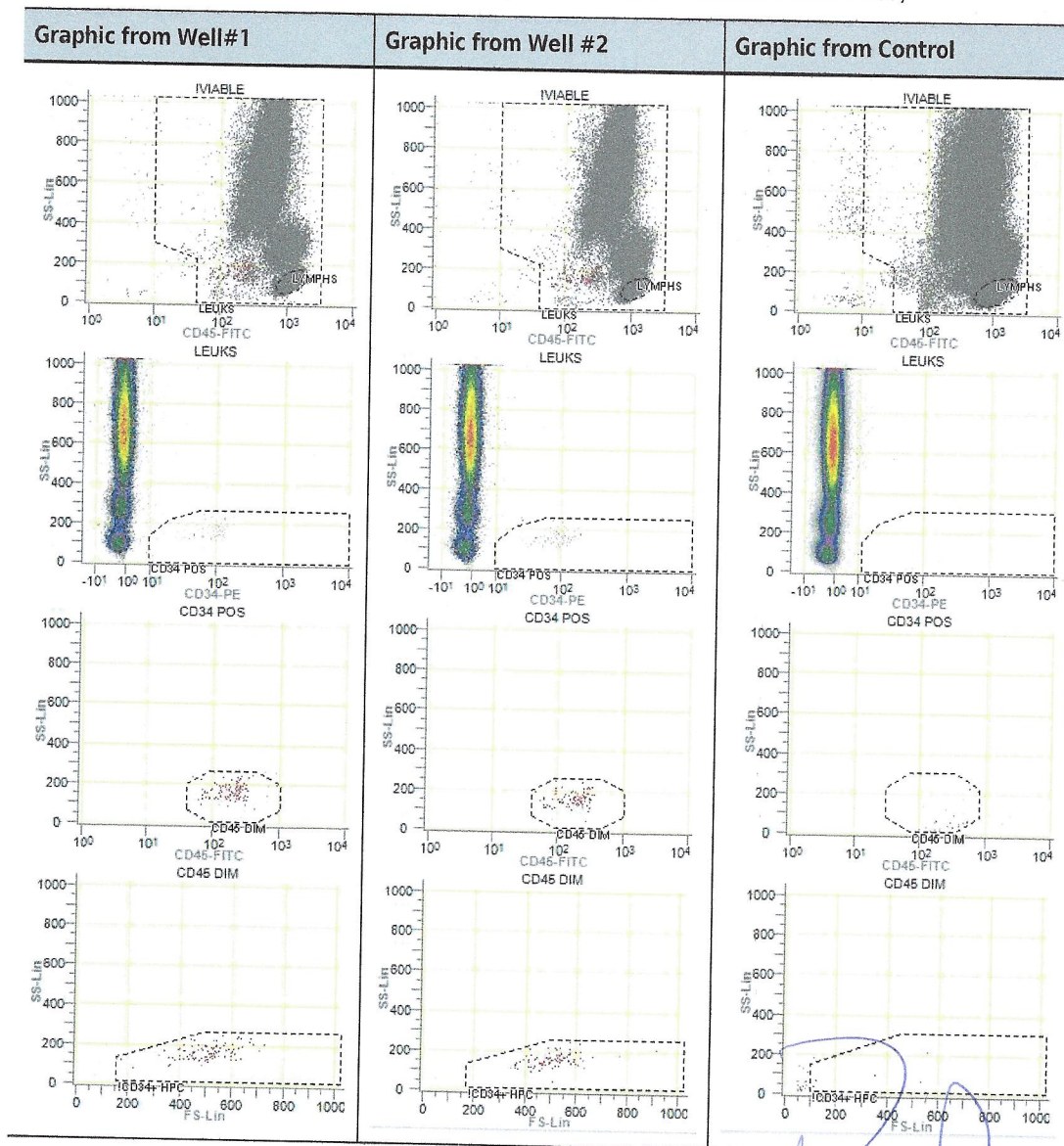
[Table 5.2](#) shows examples of graphics displayed on Page 1 and on Page 2.

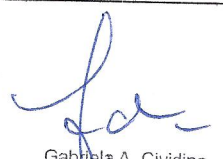
NOTE Graphics shown are dependent upon the AQUIOS STEM test selected.

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Table 5.1 Review Screen: Summary Area Display (AQUIOS STEM, Mobilized Whole Blood)




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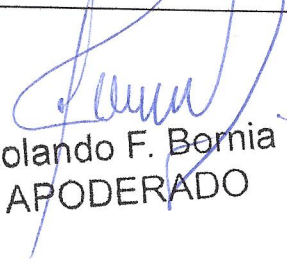
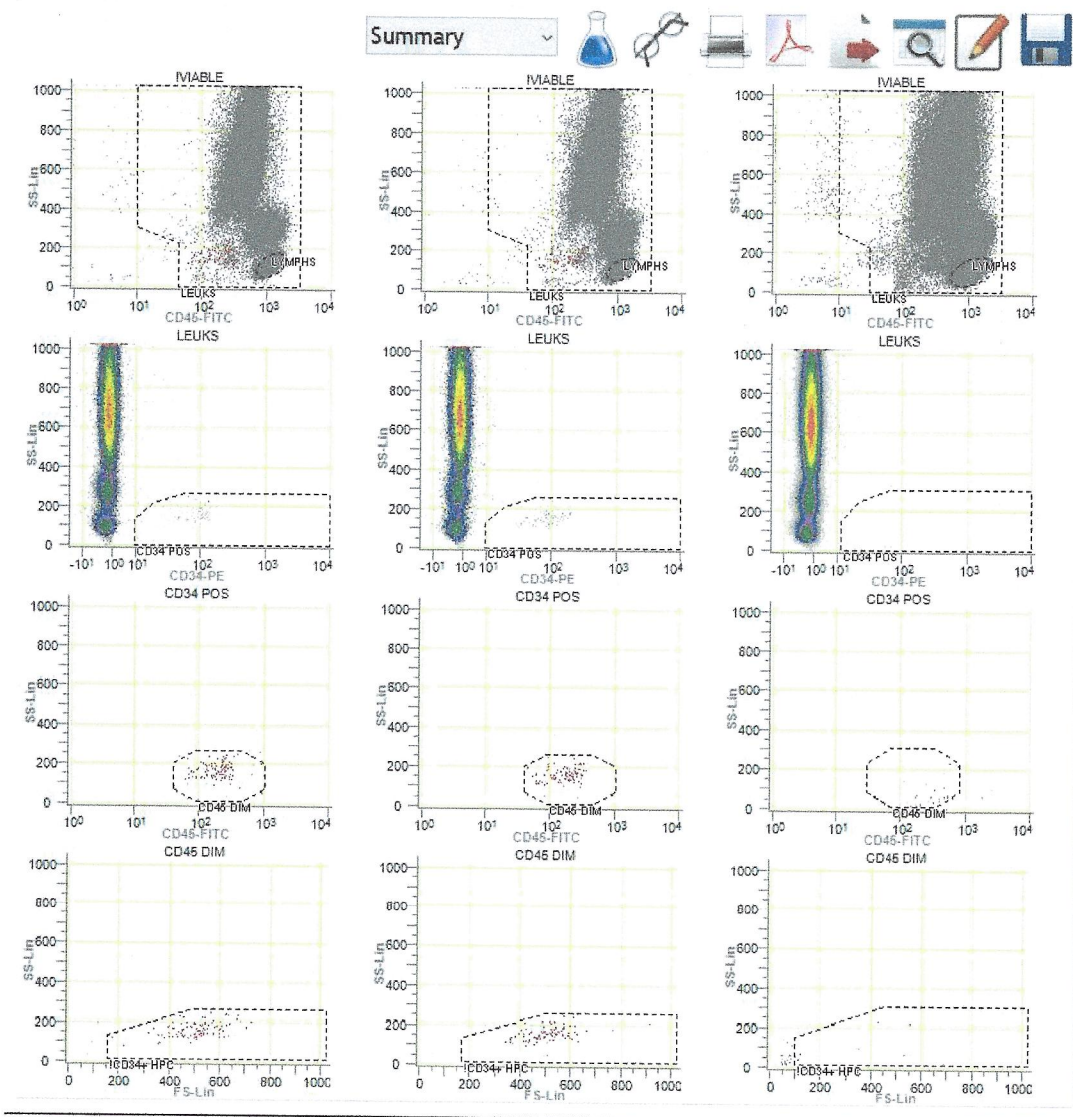

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Table 5.2 Review Screen: Summary Area Display, Page Number 1 (AQUIOS STEM Panel, Mobilized Whole Blood)

Graphics from Page1



Graphic Options

The following Review screens illustrate the different graphic options available for each individual patient result. There are 2 graphic options, one is for each tested well separately (such as Well #1, Well #2, and Control if the STEM Panel analysis option is used), and the other is combined wells Summary. These are examples only. Results may vary.

NOTE When a sample is selected for review, the Summary Review screen appears for that sample. Select the Well #1, Well #2 or Control option from the drop-down box.

Figure 5.10 Review Screen: Well#1 Page 2 (Mobilized Whole Blood)

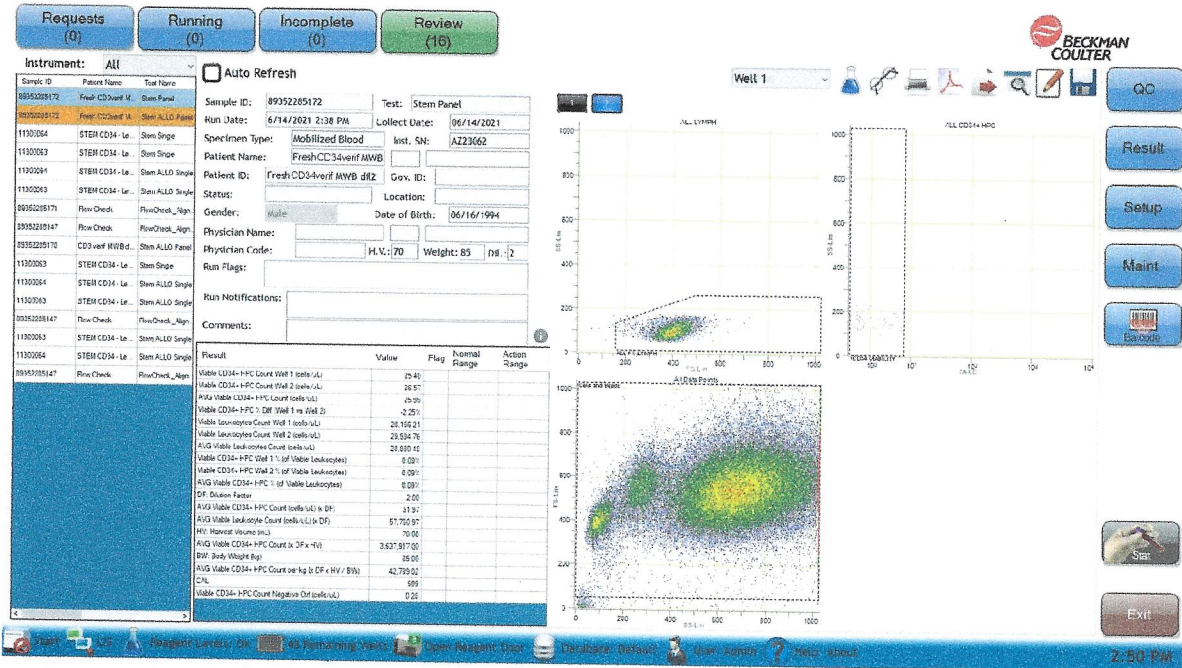
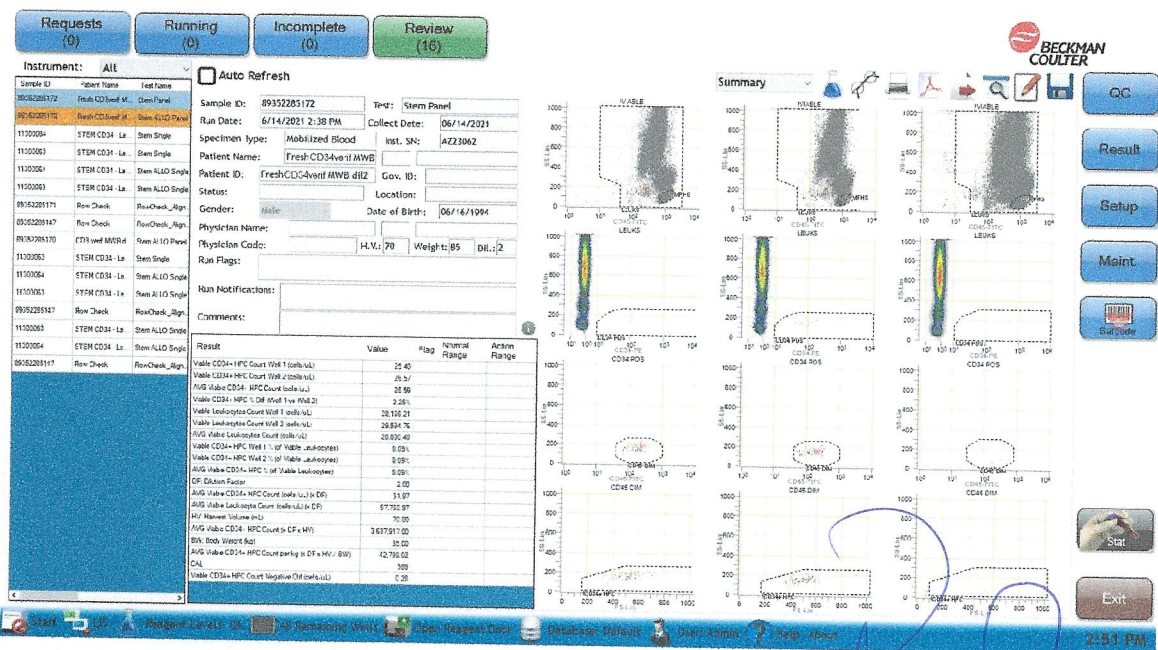


Figure 5.11 Review Screen: Summary Page 1



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Action Toolbox

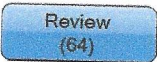
Use the Action Toolbox (Figure 5.12) on the  screen to review, edit, and save changes to both regions and/or patient information prior to transmitting results to the LIS. Also, the results can be printed or exported in a PDF or CRD or LMD format (CRD and LMD files can be exported from the Review screen only). Both the sample history changes and the reagent information are available for review. All the displays can be zoomed in for easier editing. Refer to Chapter 6, Data Review in the AQUIOS CL Flow Cytometer Instructions for Use manual.

Figure 5.12 Action Toolbox



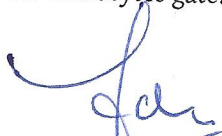
Data Review

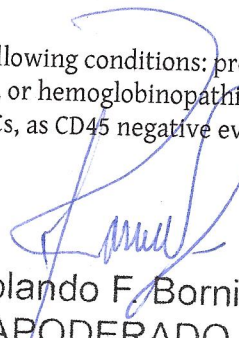
Review Data Displays

IMPORTANT There is a risk of reporting incorrect results. Data displays used to arrive at the test result for light scatter patterns, antibody staining profiles, and all gates and boundaries should be reviewed by a laboratory professional when interpreting the data. If results are suspect, follow your laboratory's procedures to resolve.

Data review should include the following:

1. Review the light scatter.
 - a. Verify any population of interest is resolved as much as possible from other populations that are present (within biological constraints).
2. Review the antibody staining patterns.
 - a. Verify overall expected staining patterns are observed (the fluorescence staining correlates to the antibody used in sample preparation).
 - b. Verify abnormally dim or negative sample staining patterns are reviewed to ensure agreement with clinical presentation and other diagnostic data.
3. Review Gate and Region boundaries.
 - a. Verify gates and regions encompass any populations of interest and exclude any undesired events.
 - b. All red blood cells may not be lysed under the following conditions: presence of nucleated red blood cells, abnormal protein concentration, or hemoglobinopathies. Use of CD45 as a gating condition for leukocytes ensures that RBCs, as CD45 negative events, are not included in the leukocytes gate.


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Edit Regions for a Review Sample

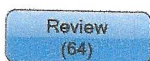
NOTE The viable region is automatically extended to capture all the 7AAD- cells.

IMPORTANT Do NOT move the regions for control runs.

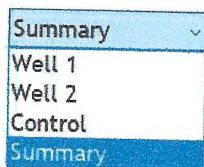
IMPORTANT Sample ID, Test, Run Date, and Serial # cannot be edited.

IMPORTANT Administrator, Reviewer, or Editor role required. Editing or adjusting regions is not a routine adjustment.

- 1 Select **Review**



- 2 Select the sample of interest from the Review Screen Completed Run List. Select the run to edit from the menu below.



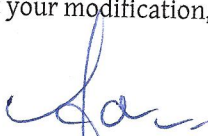
- 3 Select . The Edit action toolbox appears, and the fields for Sample ID, Test and Run Date and Instrument Serial Number turn grey to indicate that this is information that cannot be changed.

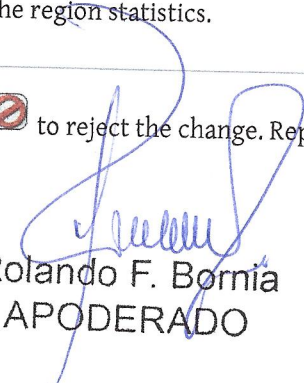
- 4 Select any other field to add or change patient information.

- 5 Select the plot that you want to edit.
- Double-click the graph to enlarge.
 - Select on the region you want to edit.

- 6 Once adjustment is done, select  to refresh the region statistics.

- 7 If you need to correct your modification, select  to reject the change. Repeat the steps above.


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- 8 Select  to save the changes to the file.

Population Statistics

The statistics presented in the [Table 5.3](#) are used as indicators of pre-analytical sample handling issues and to assist in troubleshooting instrument performance issues.

Table 5.3 Population Statistics Recommended Use

Population Statistics	Recommended Use
CD34+ Viability % (of total CD34+)	Can be used as numeric aid for the direct assessment of CD34+ viability out of all CD34+ cells.
Sample Viability % (of WBC)	Provides a numeric aid for the direct assessment of overall sample viability out of all CD45+ white blood cells.
Total CD34+ HPC Count (cells/ μ L)	Can be used as numeric aid for the direct assessment of all CD34+ cells (both viable and non-viable).
WBC Count (cells/ μ L)	Can be used as numeric aid for the direct assessment of all CD45+ white blood cells (both viable and non-viable).

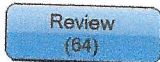
Adjust Compensation Manually

IMPORTANT Adjustment to compensation may be required in rare cases. Circumstances may include:

- At installation when compensation is performed the first time.
- After service is performed.
- If after reviewing a run, the operator determines that compensation needs to be adjusted.

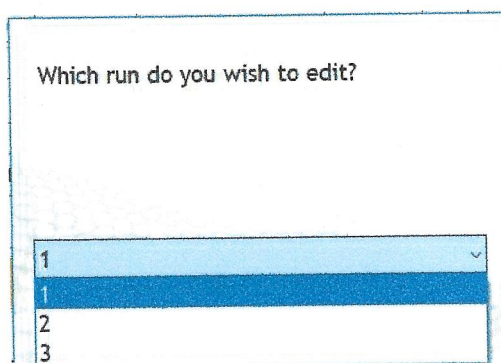
IMPORTANT Compensation may only be adjusted by an Administrator, Reviewer, or Editor

If it is determined that compensation needs to be adjusted, follow the steps described below:

- 1 Select .
- 2 Select the sample of interest from the Review Details List.
- 3 Select . The Edit action toolbox appears.

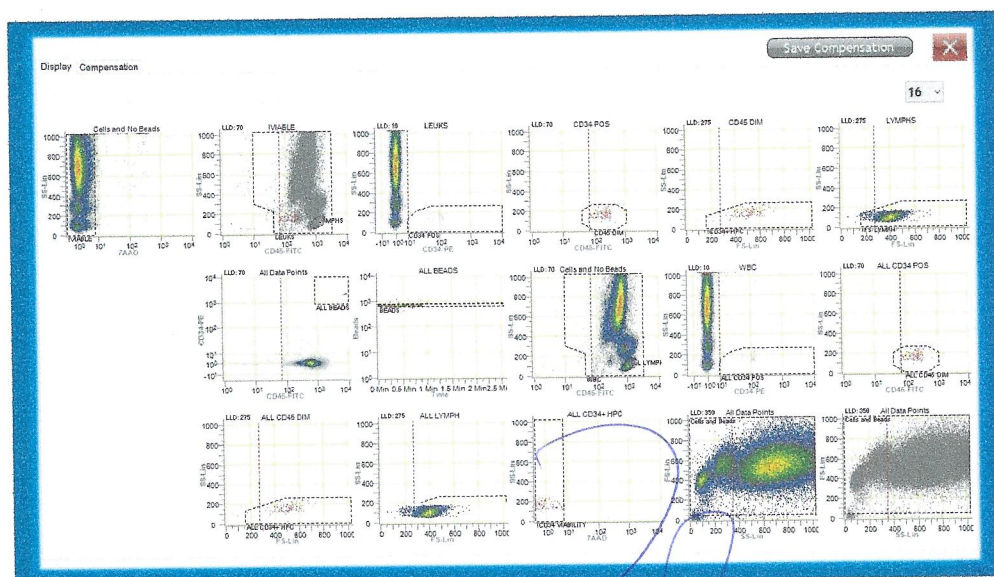
4 Select .

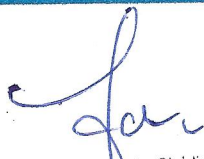
5 Select the run to edit from the menu below. 1 is Well#1, 2 is Well#2 and #3 is Control:



6 Select  to edit compensation or select  to cancel the adjust compensation action.

7 Adjust from Display tab as show below:




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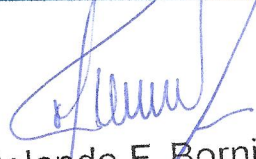

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Figure 5.14 Over Compensation

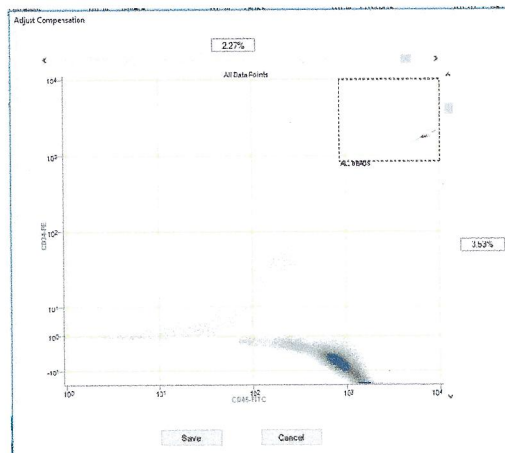
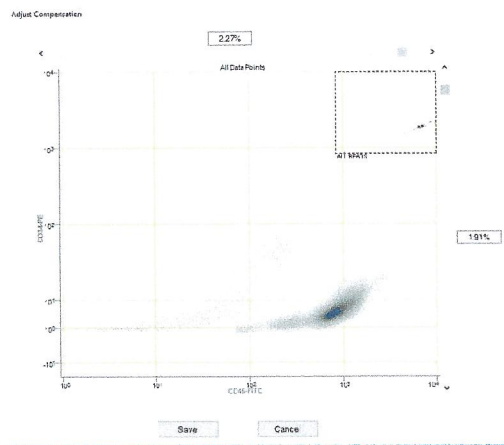


Figure 5.15 Under Compensation

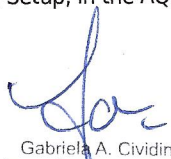


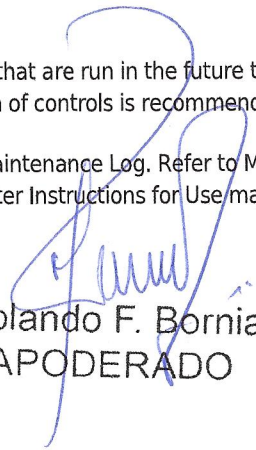
d. Select .

- 8 Select , select to save the changes to Future Runs or to cancel the changes.

NOTE Selecting Future Runs only applies to all tests that are run in the future that use this compensation. After selecting Future Runs, re-run of controls is recommended.

NOTE Compensation changes are recorded in the Maintenance Log. Refer to Maintenance Screen in Chapter 8, Setup, in the AQUIOS CL Flow Cytometer Instructions for Use manual.


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9 Select:



NOTE To revert to the previous compensation, go to the previous run and resave the compensation.

Result Screen

NOTE For a more detailed explanation of this screen and its components, refer to Chapter 6, Data Review in the AQUIOS CL Flow Cytometer Instructions for Use manual.

The Result screen provides a search menu to navigate through the results database. The Search criteria is entered under  and the results for the query are displayed under .

NOTE Results can also be accessed and viewed through  or .

To review the status of a sample, refer to the **Review Option** icons below (under the action toolbox).

NOTE Once the Review Option is selected, the sample is removed from the Review screen but it continues to be accessible through the Result screen.



indicates that the sample was reviewed.

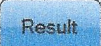


indicates that the sample was reviewed and rejected.



indicates that the sample was not reviewed.

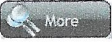
Using the Result Screen to Select Data for Review

Once you have selected , you will have access to the following options:

- Search results by the following criteria:
 - Sample ID
 - Patient ID
 - Gov. ID
 - Patient Name
 - Test

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- Instrument Start Date
- Instrument End Date
- QC Results
- Reviewed Only
- Clear search criteria.
- Export results to .crd, .lmd, .pdf or .csv file.
- Do advanced searches using .
- Fields to be displayed as columns in View Results screen.
- Exclude run from View Results screen.
- Load a Query request.
- Append to a current search.
- Save a query result.

For detailed instructions for using any of these options, refer to Chapter 6 in the AQUIOS CL Flow Cytometer Instructions manual.

Flags And Notifications

CAUTION

Beckman Coulter Inc. does not claim to identify every abnormality in all samples. Beckman Coulter suggests using all available options to optimize the sensitivity of instrument results. Options include:

- **Flags**
- **Notifications**

The AQUIOS System Software generates a set of algorithm flags and notifications. The AQUIOS STEM Tests also generate flags and notifications that are specific to the AQUIOS STEM application.

The flag and notification messages appear on the Review and Result screen. Samples with flags are highlighted in red, while samples with notifications are highlighted in orange.

All results with flags or notifications are automatically sent to the review tab for further review. Only samples with no flags or notifications can be setup for automatic transmission. A laboratory professional should review all results, regardless of flags and notifications, prior to data release. To setup automatic transmission, refer to the **Auto Transmit** heading in Chapter 8 in the AQUIOS CL Flow Cytometer Instructions for Use manual.

- For the list of AQUIOS System Software flags, notifications, and specific result notifications, refer to Chapter 6 in the AQUIOS CL Flow Cytometer Instructions for Use manual.
- For the list of AQUIOS STEM specific flags and criteria, refer to [Table 5.4](#). For AQUIOS STEM specific notifications and criteria, refer to [Table 5.5](#).

Flags

A Flag indicates an issue that affects the results, follow the Recommended User Action in the table below.

NOTE Bleach is defined as high-quality, fragrance-free, gel-free bleach (5 to 6% solution of sodium hypochlorite - available chlorine).



Risk of chemical injury from bleach. To avoid contact with the bleach, use barrier protection, including protective eyewear, gloves, and suitable laboratory attire. Refer to the Safety Data Sheet for details about chemical exposure before using the chemical.

Table 5.4 AQUIOS STEM Specific Flags

Flag	Definition	Recommended User Action
Missing QC	Occurs if the Setup option QC Tracking was enabled and QC was not run successfully.	1. Confirm the Setup Option QC Tracking was set as expected. 2. Perform Daily QC procedure. 3. Reject, Re-Request from the Review Options menu. 4. If the problem persists, contact us.
General Error	An error occurred that did not fall into one of the categories below.	1. Run a Bleach Cycle followed by a Flush Cycle. 2. Reject, Re-Request from the Review Options menu. 3. If the problem persists, contact us.
High Count Rate	Based on events/second.	1. Confirm the sample WBC concentration that is within Beckman Coulter recommendation. Refer to Principles of AQUIOS STEM Tests. 2. Run a Bleach Cycle followed by a Flush Cycle. 3. Reject, Re-Request from the Review Options menu. 4. If the problem persists on the same sample, the sample is limited to run the application. Reject the sample. 5. If the problem persists, contact us.
Over Incubation	Sample staining incubation time exceeded.	1. Run a Bleach Cycle followed by a Flush Cycle. 2. Reject, Re-Request from the Review Options menu. 3. If the problem persists, contact us.
Over Lyse Incubation	Lyse incubation time exceeded.	1. Run a Bleach Cycle followed by a Flush Cycle. 2. Reject, Re-Request from the Review Options menu. 3. If the problem persists, contact us.
Clog or Bubble	The system detected unstable sample flow while analyzing the sample.	1. Run a Bleach Cycle followed by a Flush Cycle. 2. Reject, Re-Request from the Review Options menu. 3. If the problem persists, contact us.

Table 5.4 AQUIOS STEM Specific Flags

Flag	Definition	Recommended User Action
Control Range Failure	Only applies to daily QC control samples. Control results are outside of the acceptable ranges.	1. Run a Bleach Cycle followed by a Flush Cycle. 2. Check the controls expiration date. 3. Check if the controls blood level is sufficient. 4. Repeat Quality Control. 5. If the problem persists, contact us.
AQUIOS STEM-Count Mix Time Expired	Time since last mixing of flow counts exceeded (6 hours).	1. Mix the AQUIOS STEM-Count Fluorospheres, refer to the AQUIOS STEM Kit Instructions for Use. 2. Reject, Re-Request from the Review Options menu.
General algorithm Error	Algorithm did not complete the analysis of current sample.	1. Reject, Re-Request from the Review Options menu. 2. If the problem persists, contact us.
Not Enough Events	Not enough data points in the sample.	1. Verify that there is sufficient specimen in the tube. 2. Reject, Re-Request from the Review Options menu. 3. If the problem persists, contact us.
Bead Events Error	Number of events in the "fluorospheres" region is too low or too high.	1. Check the volume of AQUIOS STEM-Count Fluorospheres. 2. Run a Bleach Cycle followed by a Flush Cycle. 3. Reject, Re-Request from the Review Options menu. Mix the AQUIOS STEM-Count Fluorospheres before the repeated run.
Laser Power Error	Insufficient laser power.	1. Select Result Rejected from the Review Options Menu. 2. Perform a Shutdown per CHAPTER 7 in the AQUIOS CL Flow Cytometer Instructions For Use. 3. Perform a startup of the Startup per CHAPTER 3 in the AQUIOS CL Flow Cytometer Instructions For Use. 4. Review maintenance log and if the problem persists, contact us.
Vacuum Low	Insufficient vacuum.	1. Select Result Rejected from the Review Options Menu. 2. Perform a Shutdown per CHAPTER 7 in the AQUIOS CL Flow Cytometer Instructions For Use. 3. Perform a startup of the Startup per CHAPTER 3 in the AQUIOS CL Flow Cytometer Instructions For Use. 4. Review maintenance log and if the problem persists, contact us.
Power Supply Error	Detected by measuring the power supply voltages.	1. Select Result Rejected from the Review Options Menu. 2. Perform a Shutdown per CHAPTER 7 in the AQUIOS CL Flow Cytometer Instructions For Use. 3. Perform a startup of the Startup per CHAPTER 3 in the AQUIOS CL Flow Cytometer Instructions For Use. 4. Review maintenance log and if the problem persists, contact us.

Table 5.4 AQUIOS STEM Specific Flags

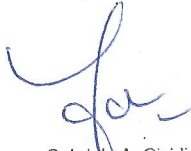
Flag	Definition	Recommended User Action
Onboard Expiration	A reagent has exceeded the maximum allowed time on board the system.	1. Replace onboard expired reagent with a non-expired reagent. 2. Reject, Re-Request from the Review Options menu. 3. If the problem persists, contact us.
Expired reagent	Based on barcode expiration dates (open, on-board, and closed vial), The reagent is run after the expiration date has passed.	1. Replace expired reagent with a non-expired reagent. 2. Reject, Re-Request from the Review Options menu. 3. If the problem persists, contact us.

Notifications

Notifications are generated to convey an abnormal cell distribution or population which may be specimen specific. Follow the Recommended User Action in the table below.

Table 5.5 AQUIOS STEM Specific Notifications

Notification	Definition	Recommended User Action
High CD34 count in control run	CD34 counts in the negative control run is above the requirements: 1. Average of CD34 cells is less than 50 cells/μL , IsoClonic Control of CD34 shall be less than or equal to 5 cells/μL 2. Average of CD34 cells is greater or equal to 50 cells/μL , IsoClonic Control of CD34 shall be less than or equal to 10% of the average of CD34 cells count.	1. Review the gating of CD34+HPC, CD45+ and fluorospheres from the Review screen. 2. Adjust the gating if determined to be necessary. 3. If the problem persists after gate adjustment, lab professionals shall evaluate the results based on their assessment and standard practice in lab. NOTE Notification is not removed if the count goes back to normal range after adjusting the gating.
Action Range	Result was outside the user defined action range.	1. Follow your laboratory's policies and procedures for out-of-range results for the specific Action Range.


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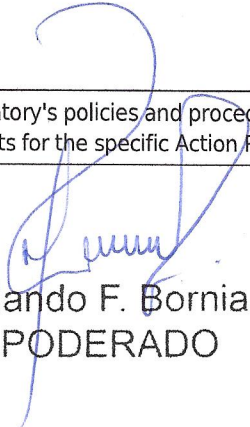

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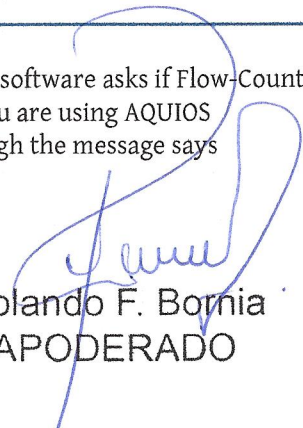
Table 5.5 AQUIOS STEM Specific Notifications

Notification	Definition	Recommended User Action
Sample ID Reused	Only patient runs are identified with this notification. This occurs when: 1. The Sample ID for this specimen run has been used in a prior run (patient or control) within the last 24 hours. 2. There is a duplicate Sample ID in the Running tab for this run.	1. Ensure this is a re-run of a previous run. 2. Check Sample ID of the specimen to ensure it is correct for the specimen.
User Modified	The demographics or the gating for this run were modified by a user.	1. Review the changes and determine if run is to be rejected and/or re-run (Rejected, Re-Request option) or accepted (Reviewed).
Less than 100 CD34+ events acquired	Less than 100 CD34+ events acquired	1. This notification is for informational use only, no further action is required. Lab professionals shall evaluate the results based on their assessment and standard practice in laboratory.

AQUIOS STEM Software Observations

While running QC for AQUIOS STEM CD34 L1 and L2 Control Cells, the software asks if Flow-Count Fluorospheres have been mixed. For the AQUIOS STEM application you are using AQUIOS STEM-Count Fluorospheres, not Flow-Count Fluorospheres even though the message says Flow-Count Fluorospheres.


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Performance Characteristics

Overview

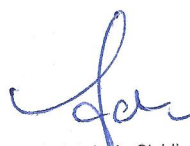
The performance characteristics presented below were collected on the AQUIOS CL Flow Cytometry System with AQUIOS System software and AQUIOS STEM application with no modification of the algorithm generated results.

This chapter contains the following information:

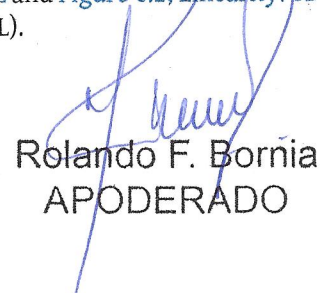
- Linearity
- Method Comparison
- Reference Interval
- Precision
- Specificity
- Quality Control

Linearity

Three replicates were made at each of 13 dilutions for CD34+ and CD45+. Ranges for CD34+ and CD45+ were established by staining an Apheresis sample with AQUIOS STEM Kit reagents, and analyzing by flow cytometry using AQUIOS system software. Statistical determination of linearity was performed using the guideline CLSI EP06-Ed2 Nov 2020, Evaluation of Linearity of Quantitative Measurement Procedures. See [Figure 6.1, Linearity: CD34+ cells/μL](#) and [Figure 6.2, Linearity: CD45+ cells/μL](#). Values are expressed in terms of absolute count (cells/μL).



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Figure 6.1 Linearity: CD34+ cells/ μ L

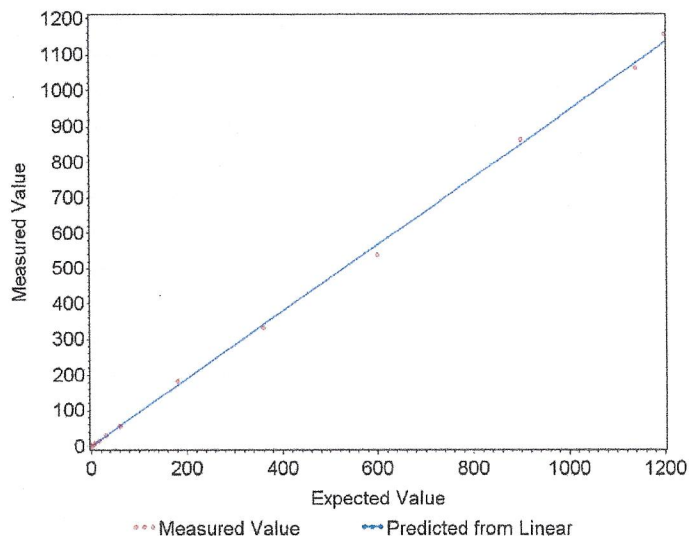
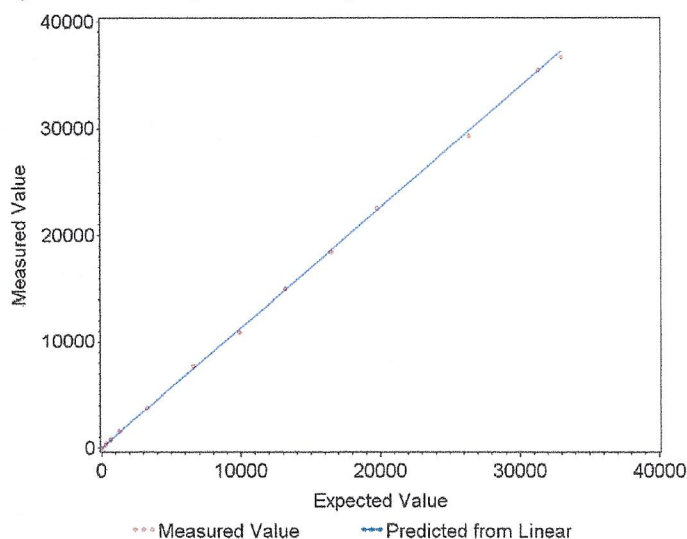


Figure 6.2 Linearity: CD45+ cells/ μ L



Limit of Blank/Limit of Detection/Limit of Quantitation

Limit of Blank (LoB) is the highest measurement result that is likely to be observed (with a stated probability or type I error) for a blank sample per the CLSI EP17-A3 guideline, Protocols for Determination of Limits of Detection and Limits of Quantitation.

Limit of Detection (LoD) is the lowest number of cells in a sample that can be detected with (stated) probability, although perhaps not quantified as an exact value, per the CLSI-EP17-A3 guideline, Protocols for Determination of Limits of Detection and Limits of Quantitation.

Lower Limit of Quantitation (LLoQ) is the lowest number of cells in a sample that can be quantitatively determined with stated acceptable precision and trueness, under stated

experimental conditions per the CLSI EP17-A3 guideline, Protocols for Determination of Limits of Detection and Limits of Quantitation.

Table 6.1 LoB, LoD and LLoQ Results

Analyte	LoB	LoD	LLoQ	Upper 95% Confidence Limit of LLoQ
CD34c	0.49	1.49	2.00	4.00
CD45c	31.33	35.33	36.00	36.00

Analytical Measuring Ranges

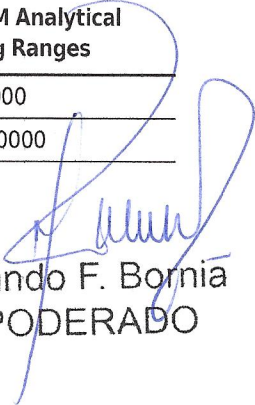
The Analytical Measuring Ranges provided indicate the AQUIOS STEM System's analytical capabilities to enumerate CD34+ cells and CD45+ cells. The AQUIOS STEM Analytical Measuring Ranges are derived from Linearity and Lower Limit of Quantitation values:

- **Linearity:** Ranges over which results are directly proportional to the amount of analyte in a sample, per the CLSI EP06-Ed2 Nov 2020, Evaluation of Linearity of Quantitative Measurement Procedures.
- **Lower Limit of Quantitation:** The lowest amount of cell number in a sample that can be quantitatively determined with stated acceptable precision and trueness, under stated experimental conditions per the CLSI EP17-A3 guideline, Protocols for Determination of Limits of Detection and Limits of Quantitation.

Table 6.2 Analytical Measuring Ranges

Parameters	Units	AQUIOS STEM Analytical Measuring Ranges
CD 34+	cells/ μ L	4-1000
CD 45+	cells/ μ L	500-30000


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Method Comparison

The comparability of AQUIOS STEM System was assessed by comparing the results with the predicate method using the estimation of difference as described in CLSI EP9-A3 Method Comparison and Bias Estimation Using Patient Samples. For viable CD34+ stem cells (count and %) and CD45+ cells (count). The comparator method is the stemCXP System. A total of 442 specimens were collected from a multi-center clinical study, including 161 Whole Blood, 53 Mobilized Whole Blood, 101 Bone Marrow, 97 Apheresis Product, and 30 Cord Blood.

Table 6.3 Regression statistics for all specimen types combined

Specimen Type	Parameter	N*	Correlation	Slope	Intercept
Overall	Viable CD34+ (cells/uL)	289	0.990	1.00	0.04
	% viable CD34+ of viable CD45+	442	0.966	0.92	0.01
	Viable CD45+ (cells/uL)	440	0.991	1.00	161.57

* CD34+ and CD45+ counts below LLOQ have been excluded from the respective analyses

Table 6.4 Method Comparison study results of AQUIOS STEM system compared with predicate method

Parameter	N*	Percentile	Level	Bias	95% Confidence Limit of Bias
Viable CD34+ (cells/uL)	289	25th	3.00	0.06	-0.87 – 1.00
		50th	25.75	0.06	-0.54 – 0.66
		75th	98.50	0.06	-2.25 – 2.37
% viable CD34+ of viable CD45+	442	25th	0.05	0.01	-0.10 – 0.12
		50th	0.22	-0.00	-0.08 – 0.07
		75th	0.86	-0.05	-0.13 – 0.02
Viable CD45+ (cells/uL)	440	25th	5701.00	169.78	94.31 – 245.26
		50th	9104.50	173.50	92-73 – 254.27
		75th	16486.00	181.55	-39.43 – 402.54

* CD34+ and CD45+ counts below LLOQ have been excluded from the respective analyses


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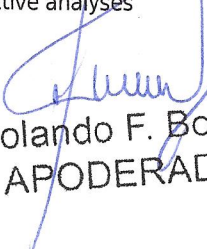

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Figure 6.3 Regression Analysis: CD34+ cells/ μ L

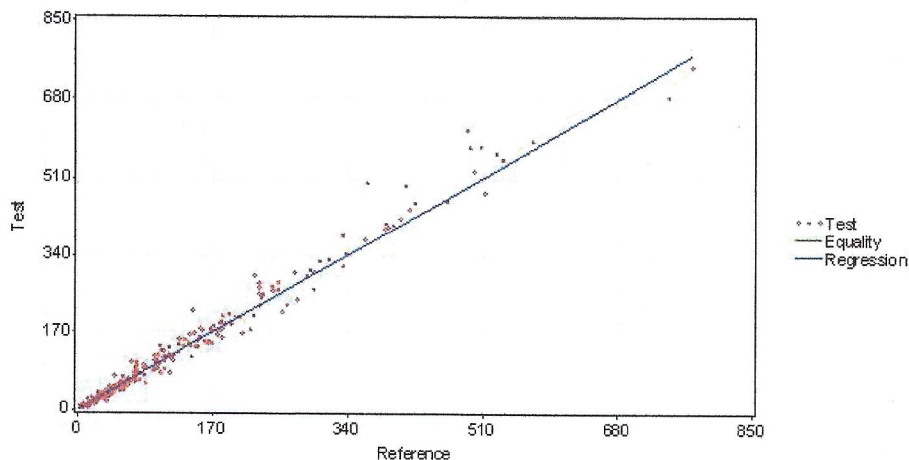


Figure 6.4 Regression Analysis: CD34+ %

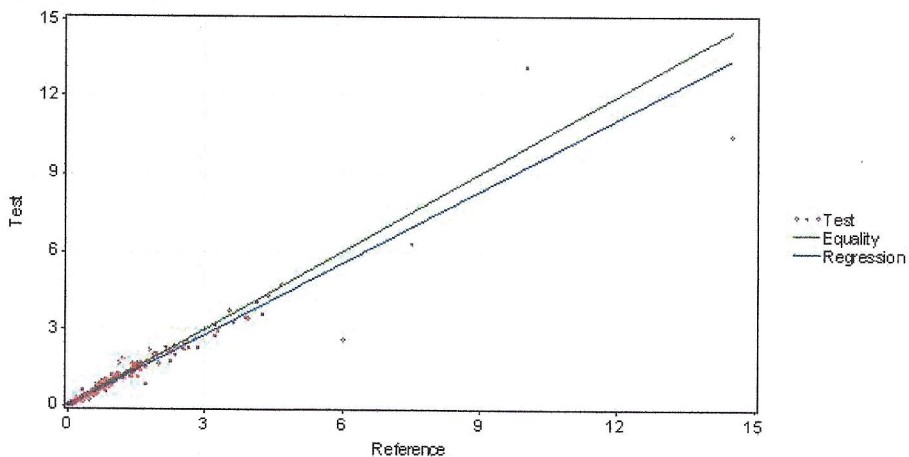
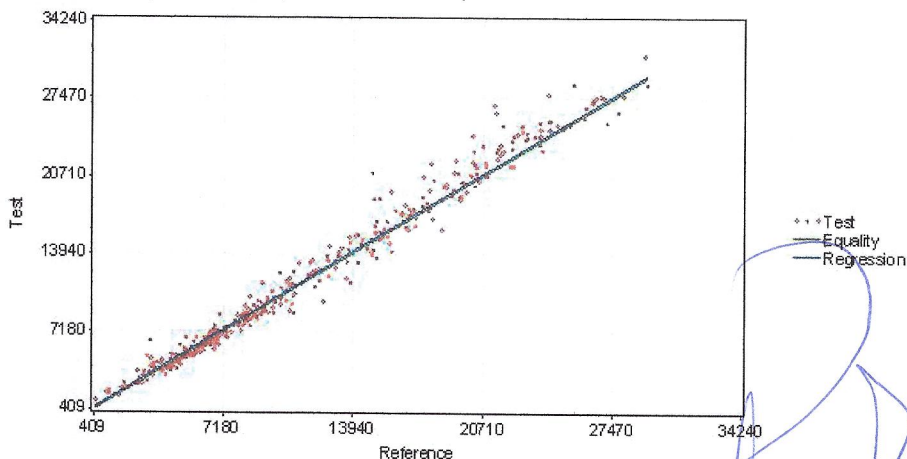


Figure 6.5 Regression Analysis: CD45+ cells/ μ L



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6-5

Table 6.5 Regression statistics by specimen type

Specimen Type	Parameter	N*	Correlation	Slope	Intercept
Peripheral blood	Viable CD34+ (cells/uL)	64 (normal: 18, mobilized: 46)	0.996	0.94	0.47
	% viable CD34+ of viable CD45+	214 (normal: 161, mobilized: 53)	0.999	0.99	80.95
	Viable CD45+ (cells/uL)	213 (normal: 161, Mobilized: 52)	0.994	0.97	-0.01
Bone Marrow	Viable CD34+ (cells/uL)	98	0.982	1.00	1.66
	% viable CD34+ of viable CD45+	101	0.942	0.90	241.61
	Viable CD45+ (cells/uL)	100	0.988	1.03	0.05
Apheresis	Viable CD34+ (cells/uL)	97	0.991	1.04	-2.07
	% viable CD34+ of viable CD45+	97	0.995	1.06	8.05
	Viable CD45+ (cells/uL)	97	0.972	0.96	-0.00
Cord Blood	Viable CD34+ (cells/uL)	30	0.990	0.89	0.28
	% viable CD34+ of viable CD45+	30	0.980	0.95	319.15
	Viable CD45+ (cells/uL)	30	0.978	0.96	-0.01

Reference Interval

A total of 120 normal Whole Blood specimens from apparently healthy adult donors were collected from 3 geographically diverse sites in order to assess the reference interval using AQUIOS STEM System. The selection of donors is consistent with guidelines stated in CLSI EP28-A3C Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory.

Data analysis was performed in accordance to CLSI EP28-A3c. Non-parametric calculation of the 95% upper and lower reference limits for CD34 and CD45, with calculation of 90% confidence intervals were summarized in the table below. These values are intended to be representative only. Each laboratory must establish its own.

Table 6.6 Reference Intervals

Parameter	Units	N	Mean	Lower Limit (90% confidence bounds)	Upper Limit (90% confidence bounds)
CD34+	Absolute viable count (cells/uL)	120	2.75	0.88 (0.54 – 1.02)	6.16 (5.33 – 10.80)
% CD34+	% viable CD34+ of viable CD45+	120	0.05	0.01 (0.01 – 0.02)	0.09 (0.08 – 0.14)
CD45+	Absolute viable count (cells/uL)	120	6203.35	3746.91 (2660.36 – 4363.74)	8901.82 (8262.02 – 9883.23)

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Precision

Using Control Cells

The imprecision performance of the AQUIOS STEM System was demonstrated using AQUIOS STEM Control Cells (Level 1 and Level 2). One of three sites ran Control Cells in duplicate, twice a day for 20 days. The other two sites ran Control Cells in triplicate, twice a day for 5 days. Absolute count and percentage of CD34+ cells and absolute count of CD45+ cells were measured.

Data analysis was performed in accordance with EP05-A3 and summarized below in Table 6.7 and Table 6.8.

Table 6.7 AQUIOS STEM CD34 Control Cells Level 1

Name	N	Mean	Repeatability		Between Runs		Between Days		Between Sites		Reproducibility	
			SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
CD34+	140	8.71	1.206	13.85	0.000	0.00	0.305	3.50	0.286	3.28	1.276	14.66
% CD34+	140	0.14	0.019	13.71	0.000	0.00	0.004	2.94	0.01	6.90	0.022	15.62
CD45+	140	6173.88	203.567	3.30	0.000	0.00	69.142	1.12	266.13	4.31	342.119	5.54

Table 6.8 AQUIOS STEM CD34 Control Cells Level 2

Name	N	Mean	Repeatability		Between Runs		Between Days		Between Sites		Reproducibility	
			SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Name	N	Mean	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
CD34+	140	28.85	2.203	7.64	0.375	1.30	0.091	0.32	0.000	0.00	2.236	7.75
% CD34+	140	0.46	0.030	6.56	0.000	0.00	0.000	0.00	0.016	3.40	0.034	7.39
CD45+	140	6311.97	216.117	3.42	105.999	1.68	80.976	1.28	304.309	4.82	396.363	6.28

Using Clinical Specimens

In order to demonstrate the repeatability precision performance of the AQUIOS STEM System for clinical specimens, a total of 63 samples per intended use with a mix of specimen and anticoagulant types were collected from multiple clinical sites. Each clinical sample was analyzed with minimum three, maximum five replicates, and the absolute count and percentage of CD34+ cells and absolute count of CD45+ cells were measured.

Data analysis was performed in accordance with CLSI H26-A2. Mean, standard deviation and coefficient of variations were calculated for each specimen. Profiles for CD34 and CD45 were created based on the relationship between means and %CV. Percent CV was estimated at percentiles and relevant medical decision levels (5, 10, 20 CD34+ cells/ μ L).


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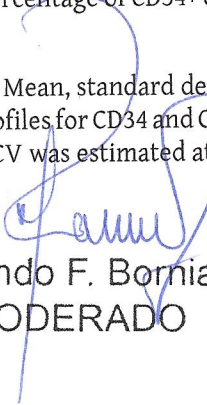

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Table 6.9 Repeatability Precision with clinical specimens

Parameter	Percentile	Mean	%CV
Viable CD34+ (cells/uL)	25th	14.57	7.55
	50th	24.12	6.67
	75th	84.77	4.89
% viable CD34+ of viable CD45+	25th	0.07	10.88
	50th	0.28	7.03
	75th	1.09	4.59
Viable CD45+ (cells/uL)	25th	5873.96	2.28
	50th	9576.57	2.30
	75th	21054.44	2.35

Specificity

Reagent Specificity

The CD45 antigen is expressed on every type of hematopoietic cell except mature erythrocytes and their immediate progenitors.^{8, 9} It has not been detected in differentiated nonhematopoietic tissue.^{8, 9, 10, 11}

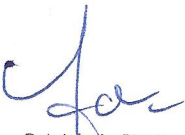
The CD34 antigen is expressed on virtually all hematopoietic precursor cells including multipotent stem cells.

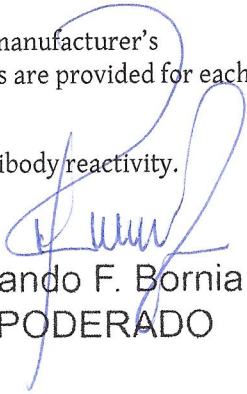
CD34 epitopes have been separated into three classes based upon sensitivity to neuraminidase and to *Pasteurella haemolytica* glycoprotease.⁴² The CD34 antibody recognizes a class III epitope of the CD34 molecule.⁴⁴

Quality Control

Ensure that controls and Flow-Check Fluorospheres are run according to manufacturer's recommendations as listed in the instrument manuals. Target value ranges are provided for each lot of CD34 Control Cells, Level 1 and Level 2.

Before samples are analyzed, assayed controls need to be run to verify antibody reactivity.


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Application Specifications

Overview

This chapter contains the following information:

- AQUIOS STEM Preparation
- AQUIOS STEM Throughput

AQUIOS STEM Preparation

All samples are prepared and analyzed onboard using a 96-deep well plate.

AQUIOS STEM Sample Preparation

Refer to [Table 4.1](#) for test descriptions and reagents used accordingly.

The following description applies to the AQUIOS STEM Single test (= 1 well from the 96-Deep Well Plate).

The test uses 43 µL of samples stained with 13 µL of each reagent (monoclonal antibodies and viability dye). After 15 minutes of incubation, the sample is lysed using 430 µL Lysing Reagent, then AQUIOS STEM-Count is added after the lyse incubation of approximately 15 minutes. The sample is then mixed and aspirated for analysis.

For AQUIOS STEM Duplicate or AQUIOS STEM Panel, 2 or 3 wells will be used respectively

AQUIOS STEM Throughput

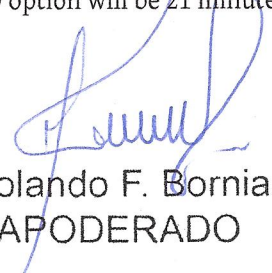
Time from loading a specimen to result for the first sample is approximately 45 minutes for single (1 well) option, 52 minutes for duplicate (2 well) option, and 59 minutes for panel (3-well) option.

Each additional well results take 7 minutes, so results for single (1 well) option will be 7 minutes, whereas duplicate (2 well) option will be 14 minutes, and panel (3 well) option will be 21 minutes for final result.

NOTE AQUIOS STEM System uses a flow rate of 70 µL/minute.



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Adjustment and Replacement Procedures

Overview

This chapter contains the following information:

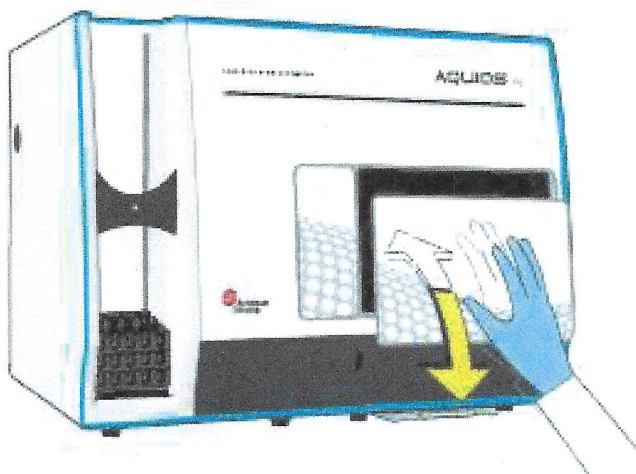
- AQUIOS STEM Replacement Procedures

AQUIOS STEM Replacement Procedures

Replacing the AQUIOS STEM Lysing Solution

NOTE You should discard a reagent bottle (on board) that is expiring and use a new reagent bottle to avoid errors.

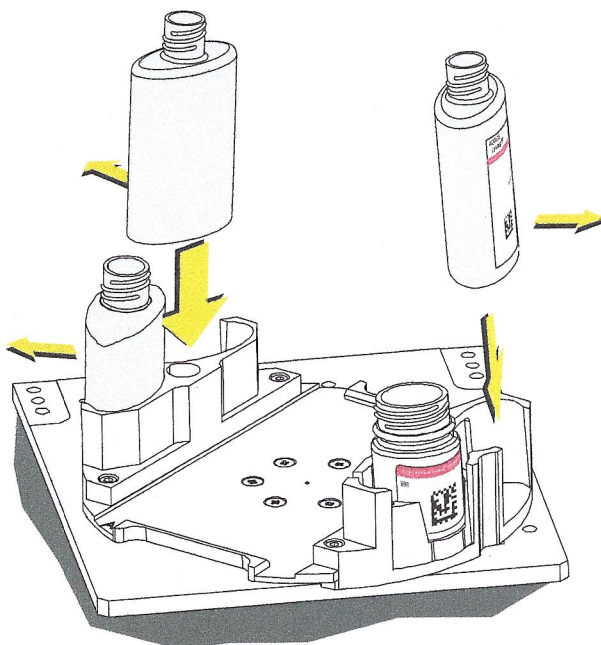
- 1 Select  on the status bar. When prompted, open the reagent door by pressing the top middle part of the door in one single, solid motion.



- 2 Remove the empty AQUIOS STEM Lysing Solution bottle.
- 3 Remove the caps on the new AQUIOS STEM Lysing Solution bottle before loading.

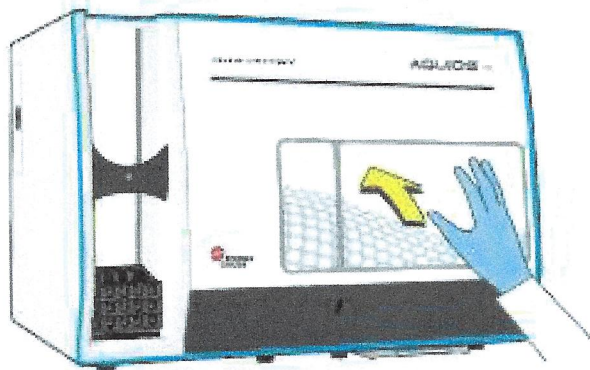
NOTE These caps are not pierceable.

- 4 Place the new bottles in the appropriate holders with the barcodes facing outwards. The AQUIOS STEM Lysing Solution bottles are interchangeable and can be placed in any of the three available positions.



NOTE Remove all reagents having invalid barcode reading before proceeding.

- 5 Close the reagent door. The reagents and plate are scanned, then the Reagent Levels screen appears.

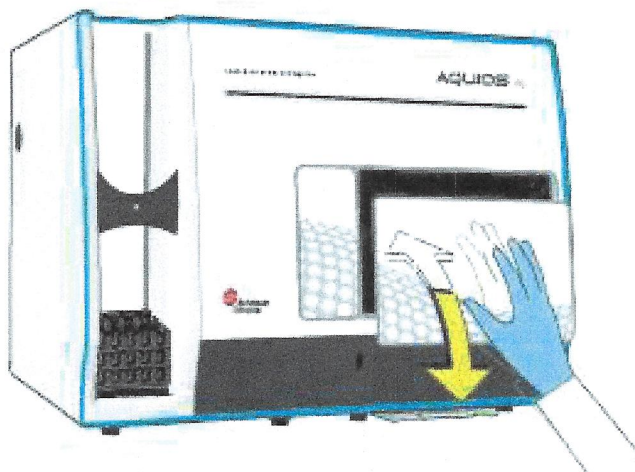


- 6 Close the Reagent Levels screen and the Main screen appears.

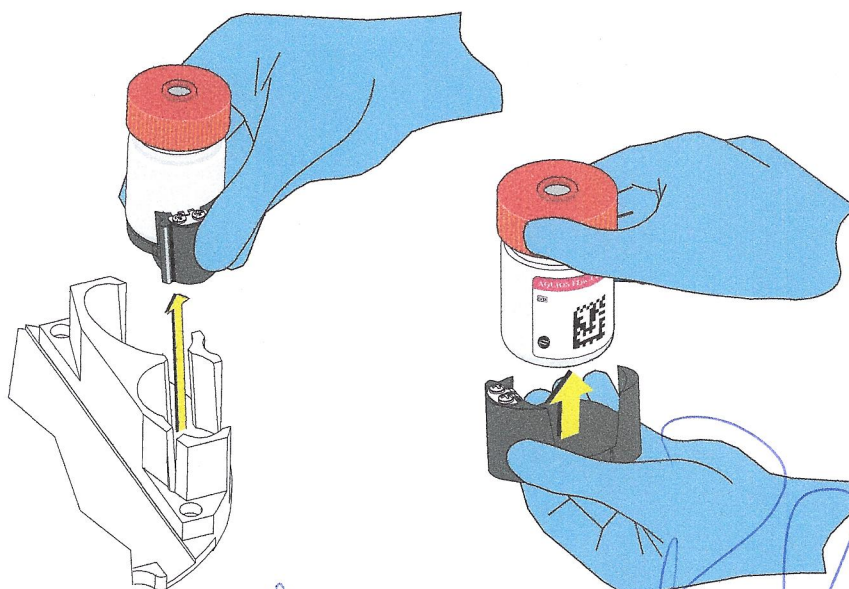
Replacing the AQUIOS STEM-Count Fluorospheres

IMPORTANT Do not use the AQUIOS Flow-Count Fluorospheres reagent in replacement of the AQUIOS STEM-Count Fluorospheres. The system will not start.

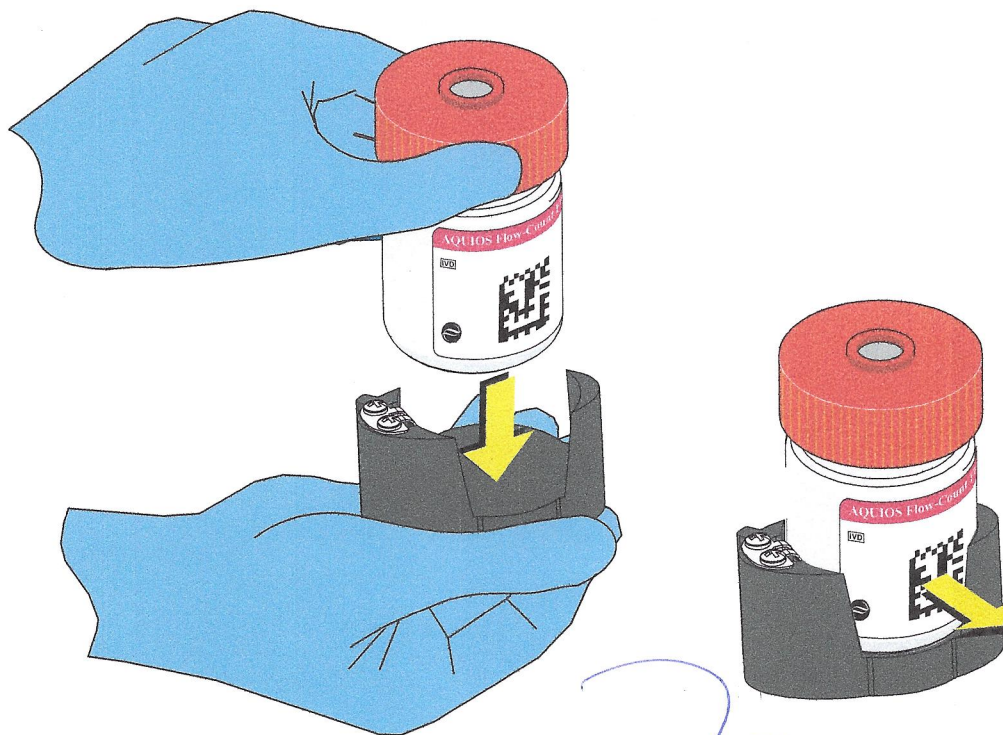
- 1 Select  on the status bar. When prompted, open the reagent door by pressing the top middle part of the door in one single, solid motion.



- 2 Remove the empty AQUIOS STEM-Count Fluorospheres bottle, pull out the bottle and adapter as a single unit. Hold the adapter in one hand and pull out the AQUIOS STEM-Count Fluorospheres bottle with the other hand.

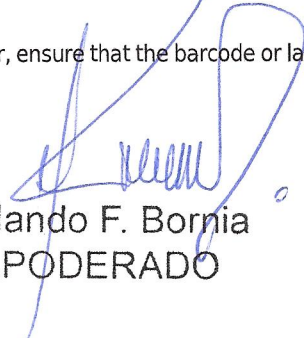


- 3 Properly mix the new AQUIOS STEM-Count Fluorospheres bottle (vortex 10 to 12 seconds is required).
 - 4 Remove the cap on the new AQUIOS STEM-Count Fluorospheres bottle, and completely remove the aluminum seal before loading.
NOTE This cap and aluminum seal are not pierceable.
- IMPORTANT** Place the specific holder for AQUIOS STEM-Count Fluorospheres in the instrument prior to placing the AQUIOS STEM-Count Fluorospheres bottle in the holder.
- 5 Place the screw cap with hole on the AQUIOS STEM-Count Fluorospheres bottle.
 - 6 Place the new AQUIOS STEM-Count Fluorospheres bottle in the adapter with the barcode facing outward and ensure that there is no space between the bottom of the AQUIOS STEM-Count Fluorospheres bottle and the adapter. The fit will be snug.

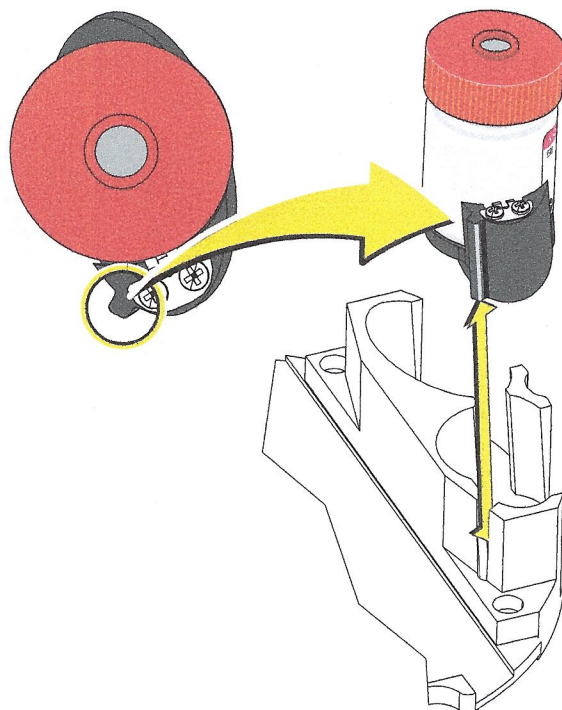


NOTE If you need to rotate the bottle in the holder, ensure that the barcode or label is not scratched by the securing metal spring.

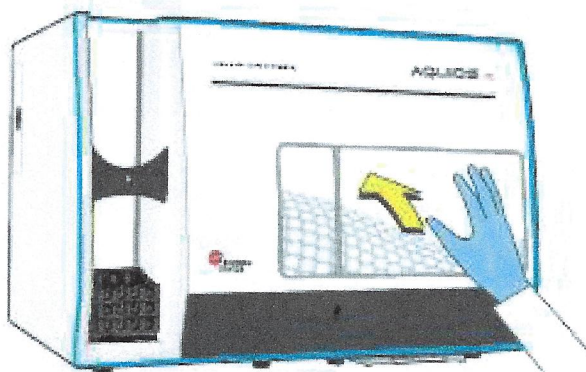

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- 7 Place the adapter into the AQUIOS STEM-Count Fluorospheres holder. The adapter can only be inserted one way, the key in the adapter must fit in the groove of the holder as shown.



- 8 Close the reagent door. The reagents and plate are scanned, and the Reagent Levels screen appears.

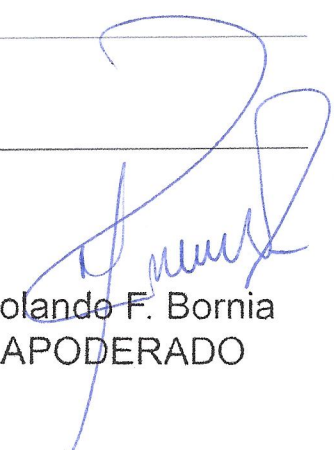


NOTE On the Reagent Levels screen, if a sample is running, the AQUIOS STEM-Count Fluorospheres column displays the number of tests scheduled to have AQUIOS STEM-Count Fluorospheres added in parentheses. AQUIOS STEM-Count Fluorospheres information will also be available on the Reagent Levels screen including name, date, and number of tests remaining.

9 Close the Reagent Levels screen and the Main screen appears.



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Overview

This appendix contains the following information:

- [Reports](#)
- [QC Report](#)

Reports

Reports can be printed or saved (PDF) from the Review or the Result screens. The report will be generated for each well individually, nevertheless all the results (IVD parameters and population statistics) will be included. For instance, in the case of a sample run with AQUIOS STEM Panel, the report for the well#1 will include only the graphics from the well#1, but all the results from the 3 wells (Well#1, Well#2 and Control).

Refer to below examples of Reports for various specimens.

NOTE The report can be customized under System Setup to display the name, address, and facility logo.

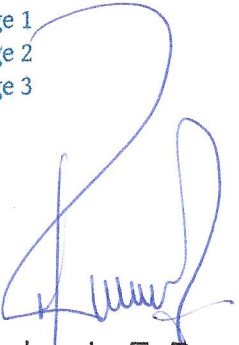
- Example report formats for STEM
 - [Figure A.1, Report: STEM Panel - Apheresis - Well #1 Page 1](#)
 - [Figure A.2, Report: STEM Panel - Apheresis - Well #1 Page 2](#)
 - [Figure A.3, Report: STEM Panel - Apheresis - Well #1 Page 3](#)
 - [Figure A.4, Report: STEM Panel - Apheresis - Summary Page 1](#)
 - [Figure A.5, Report: STEM Panel - Apheresis - Summary Page 2](#)
 - [Figure A.6, Report: STEM Panel - Apheresis - Summary Page 3](#)

NOTE The parameters with ** are population statistics.

Also refer to [Report Description](#) and [QC Report Description](#).



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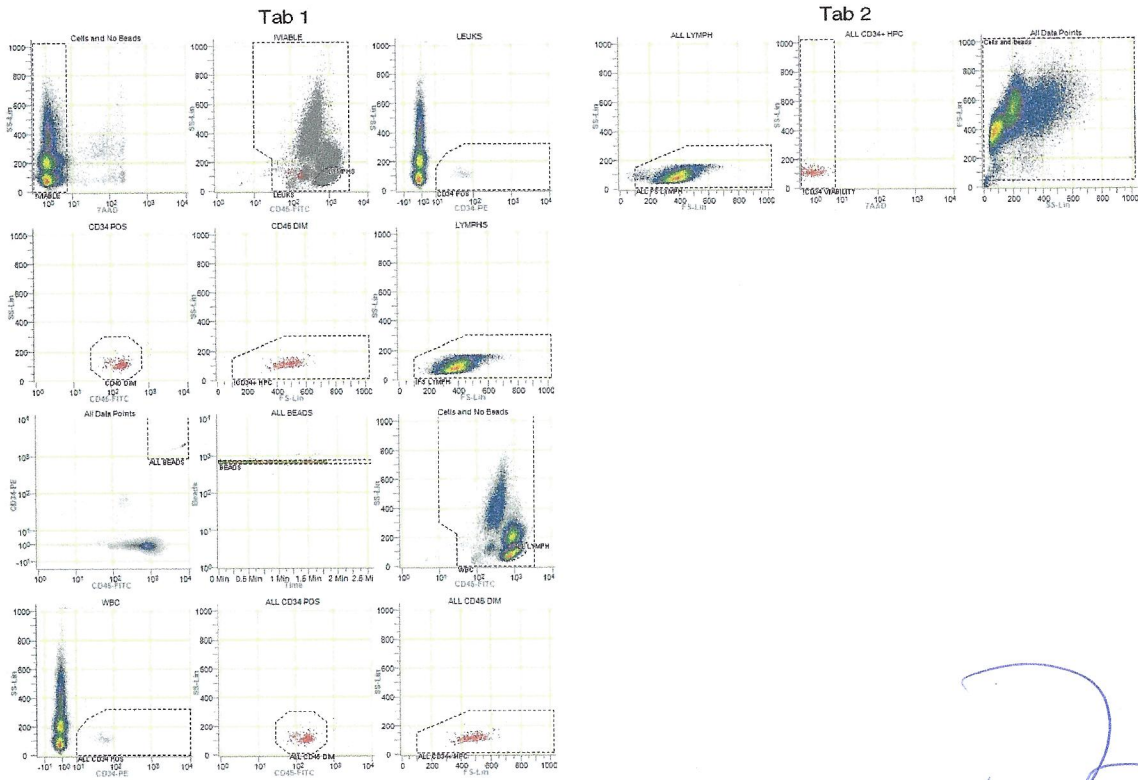


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Figure A.1 Report: STEM Panel - Apheresis - Well #1 Page 1

Sample ID: 89352211984
Run Date: 15 Mar 2022 15:56:15
User: Admin
Specimen Type: Apheresis
Patient ID:
Status:
Gender: F
Physician:
Instrument Serial #: AZ23062
Report: Well 1
Run Flags:
Run Notifications:
Comments:

Test: Stem Panel v1.0
Analysis Date: 15 Mar 2022 16:14:49
Collect Date: 14 Mar 2022
Patient Name:
Gov. ID:
Location:
Date Of Birth: 12 Oct 1977
Physician Code:
Harvest Volume (mL): 50
Weight (kg): 75 Dilution: 20



** Population Statistics

Page #1 of 3

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Figure A.2 Report: STEM Panel - Apheresis - Well #1 Page 2

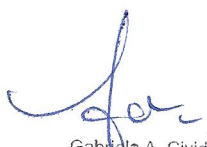
Sample ID: 89352211984

Test: Stem Panel v1.0

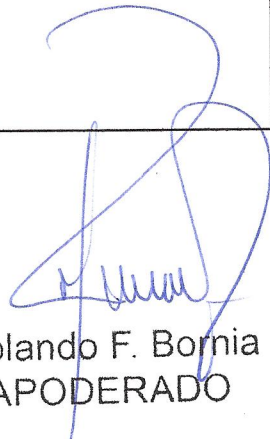
Run Date: 15 Mar 2022 15:56:15

Analysis Date: 15 Mar 2022 16:14:49

Result	Value	Flag	Normal Range	Action Range
Viable CD34+ HPC Count Well 1 (cells/uL)	31.61			
Viable CD34+ HPC Count Well 2 (cells/uL)	29.72			
AVG Viable CD34+ HPC Count (cells/uL)	30.66			
Viable CD34+ HPC % Diff (Well 1 vs Well 2)	3.08%			
Viable Leukocytes Count Well 1 (cells/uL)	9,308.80			
Viable Leukocytes Count Well 2 (cells/uL)	9,146.02			
AVG Viable Leukocytes Count (cells/uL)	9,227.41			
Viable CD34+ HPC Well 1 % (of Viable Leukocytes)	0.34%			
Viable CD34+ HPC Well 2 % (of Viable Leukocytes)	0.32%			
AVG Viable CD34+ HPC % (of Viable Leukocytes)	0.33%			
DF: Dilution Factor	20.00			
AVG Viable CD34+ HPC Count (cells/uL) (x DF)	613.25			
AVG Viable Leukocyte Count (cells/uL) (x DF)	184,548.21			
HV: Harvest Volume (mL)	50.00			
AVG Viable CD34+ HPC Count (x DF x HV)	30,662,346.20			
BW: Body Weight (kg)	75.00			
AVG Viable CD34+ HPC Count per kg (x DF x HV / BW)	408,831.28			
CAL	962			
Viable CD34+ HPC Count Negative Ctrl (cells/uL)	0.61			



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Figure A.3 Report: STEM Panel - Apheresis - Well #1 Page 3

Sample ID: 89352211984 Test: Stem Panel v1.0
Run Date: 15 Mar 2022 15:56:15 Analysis Date: 15 Mar 2022 16:14:49

Statistic	Value	Flag	Normal Range	Action Range
**CD34+ Viability Well 1 % (of total CD34+)	98.41%			
**CD34+ Viability Well 2 % (of total CD34+)	96.31%			
**AVG CD34+ Viability % (of total CD34+)	97.36%			
**Total CD34+ HPC Count Well 1 (cells/uL)	32.12			
**Total CD34+ HPC Count Well 2 (cells/uL)	30.86			
**AVG Total CD34+ HPC Count (cells/uL)	31.49			
**WBC Count Well 1 (cells/uL)	9,601.19			
**WBC Count Well 2 (cells/uL)	9,493.66			
**AVG WBC Count (cells/uL)	9,547.43			
**Sample Viability Well 1 % (of WBC)	96.96%			
**Sample Viability Well 2 % (of WBC)	96.34%			
**AVG Sample Viability % (of WBC)	96.65%			
**Total CD34+ HPC Count Negative Ctrl (cells/uL)	0.70			
**DF: Dilution Factor	20.00			
**AVG Total CD34+ HPC Count (cells/uL) (x DF)	629.75			
**AVG WBC Count (cells/uL) (x DF)	190,948.54			
**Viable Events Well 1	72,803			
**Viable Events Well 2	72,364			
**Viable Leukocytes Events Well 1	72,748			
**Viable Leukocytes Events Well 2	72,322			
**Viable CD34+ HPC Events Well 1	247			
**Viable CD34+ HPC Events Well 2	235			
**Viable CD34+ HPC Events Negative Ctrl	13			
**Single Beads Events Well 1	7,518			
**Single Beads Events Well 2	7,607			
**Single Beads Events Negative Ctrl	20,535			

Signature:


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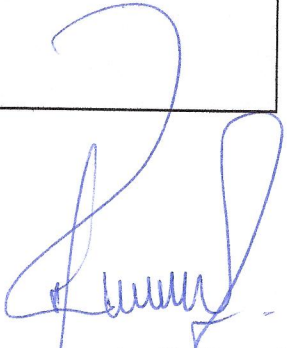
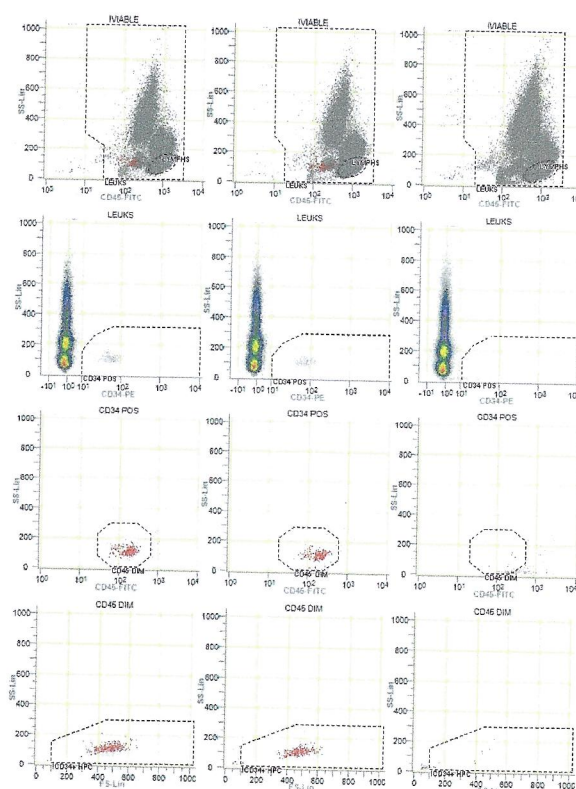

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Figure A.4 Report: STEM Panel - Apheresis - Summary Page 1

Sample ID:	89352211984	Test:	Stem Panel v1.0
Run Date:	15 Mar 2022 15:56:15	Analysis Date:	15 Mar 2022 16:14:49
User:	Admin	Collect Date:	14 Mar 2022
Specimen Type:	Apheresis	Patient Name:	
Patient ID:		Gov. ID:	
Status:		Location:	
Gender:	F	Date Of Birth:	12 Oct 1977
Physician:		Physician Code:	
Instrument Serial #:	AZ23062	Harvest Volume (mL):	50
Report:	Summary	Weight (kg):	75
Run Flags:		Dilution:	20
Run Notifications:			
Comments:			



** Population Statistics

Page #1 of 3

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Figure A.5 Report: STEM Panel - Apheresis - Summary Page 2

Sample ID: 89352211984 Test: Stem Panel v1.0
Run Date: 15 Mar 2022 15:56:15 Analysis Date: 15 Mar 2022 16:14:49

Result	Value	Flag	Normal Range	Action Range
Viable CD34+ HPC Count Well 1 (cells/uL)	31.61			
Viable CD34+ HPC Count Well 2 (cells/uL)	29.72			
AVG Viable CD34+ HPC Count (cells/uL)	30.66			
Viable CD34+ HPC % Diff (Well 1 vs Well 2)	3.08%			
Viable Leukocytes Count Well 1 (cells/uL)	9,308.80			
Viable Leukocytes Count Well 2 (cells/uL)	9,146.02			
AVG Viable Leukocytes Count (cells/uL)	9,227.41			
Viable CD34+ HPC Well 1 % (of Viable Leukocytes)	0.34%			
Viable CD34+ HPC Well 2 % (of Viable Leukocytes)	0.32%			
AVG Viable CD34+ HPC % (of Viable Leukocytes)	0.33%			
DF: Dilution Factor	20.00			
AVG Viable CD34+ HPC Count (cells/uL) (x DF)	613.25			
AVG Viable Leukocyte Count (cells/uL) (x DF)	184,548.21			
HV: Harvest Volume (mL)	50.00			
AVG Viable CD34+ HPC Count (x DF x HV)	30,662,346.20			
BW: Body Weight (kg)	75.00			
AVG Viable CD34+ HPC Count per kg (x DF x HV / BW)	408,831.28			
CAL	962			
Viable CD34+ HPC Count Negative Ctrl (cells/uL)	0.61			


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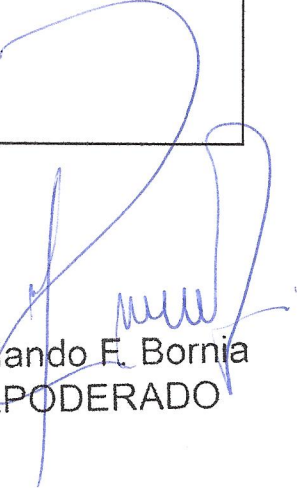

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Figure A.6 Report: STEM Panel - Apheresis - Summary Page 3

Sample ID: 89352211984

Test:

Stem Panel v1.0

Run Date: 15 Mar 2022 15:56:15

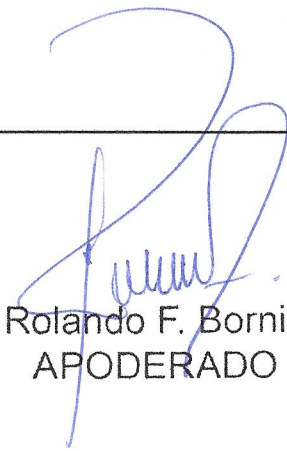
Analysis Date: 15 Mar 2022 16:14:49

Statistic	Value	Flag	Normal Range	Action Range
**CD34+ Viability Well 1 % (of total CD34+)	98.41%			
**CD34+ Viability Well 2 % (of total CD34+)	96.31%			
**AVG CD34+ Viability % (of total CD34+)	97.36%			
**Total CD34+ HPC Count Well 1 (cells/uL)	32.12			
**Total CD34+ HPC Count Well 2 (cells/uL)	30.86			
**AVG Total CD34+ HPC Count (cells/uL)	31.49			
**WBC Count Well 1 (cells/uL)	9,601.19			
**WBC Count Well 2 (cells/uL)	9,493.66			
**AVG WBC Count (cells/uL)	9,547.43			
**Sample Viability Well 1 % (of WBC)	96.96%			
**Sample Viability Well 2 % (of WBC)	96.34%			
**AVG Sample Viability % (of WBC)	96.65%			
**Total CD34+ HPC Count Negative Ctrl (cells/uL)	0.70			
**DF: Dilution Factor	20.00			
**AVG Total CD34+ HPC Count (cells/uL) (x DF)	629.75			
**AVG WBC Count (cells/uL) (x DF)	190,948.54			
**Viable Events Well 1	72,803			
**Viable Events Well 2	72,364			
**Viable Leukocytes Events Well 1	72,748			
**Viable Leukocytes Events Well 2	72,322			
**Viable CD34+ HPC Events Well 1	247			
**Viable CD34+ HPC Events Well 2	235			
**Viable CD34+ HPC Events Negative Ctrl	13			
**Single Beads Events Well 1	7,518			
**Single Beads Events Well 2	7,607			
**Single Beads Events Negative Ctrl	20,535			

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Report Description

Report Heading

For a description of how to set up report headings, refer to Appendix A, Software Screens in the AQUIOS CL Flow Cytometer Instructions for Use manual.

Displays: Generating Reports

Reports can be generated using the available pre-defined formats for data display. Use the Graph Format drop-down menu under the Review or Result screens to select the display desired for the report.

Result Table Heading

- **Result** - use to view the assay statistics
- **Value** - use to view the patient's result obtained with the AQUIOS system
- **Flag** - Results are flagged as H or L if they are outside the normal ranges, and HH or LL if outside of the action ranges
- **Normal Range** - Reference values defined by the user in the Setup window, Test Settings tab
- **Action Range** - Reference values defined by the user in the Setup window, Test Settings tab

Statistics: AQUIOS STEM Report

- Viable CD34+ HPC Count (cells/ μ L)
- Viable Leukocytes Count (cells/ μ L)
- Viable CD34+ HPC % (of Viable Leukocytes)

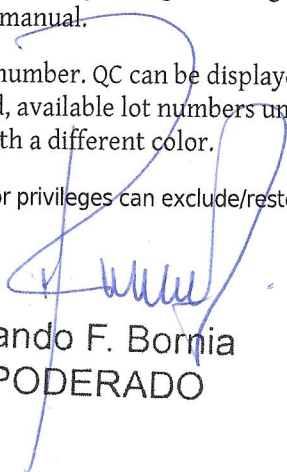
QC Report

The QC reports can be printed, saved (PDF) or created as a spreadsheet (CSV) file from any of the three QC screens. All three screens generate the same all-inclusive report containing the QC data in the following order: Results, Instrument, and Instrument Drift. Note that the QC report statistics depend on the assay selected under the Test drop-down menu. Also, the report can be customized under System Setup to display the name, address and facility logo. For generating a QC report, refer to the AQUIOS CL Flow Cytometer Instructions for Use manual.

The QC report can show all lot numbers or a single lot number. QC can be displayed for up to four months using the "Period" option. If lot (All) is selected, available lot numbers under this time frame will be displayed in the same graph identified with a different color.

NOTE Users with Administrator privileges or Reviewer/Editor privileges can exclude/restore data points.


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QC Report Description

QC Result Report Heading, QC Instrument Report Heading, QC Instrument Drift Report Heading

- **Facility Name** - location where test was performed.
- **Test** - assay used for the control.
- **Control** - AQUIOS control selected for the report.
- **Lot number** - single lot selected or (All) if plotting all available lots.
- **Date** - month, year, and period selected for the report.

NOTE QC can be displayed for up to four months using the "Period" option.

QC Result Displays & Statistics (Depend on Test Selected)

- Viable CD34+ HPC Count (cells/ μ L)
- Viable Leukocytes Count (cells/ μ L)
- Viable CD34+ HPC % (of Viable Leukocytes)

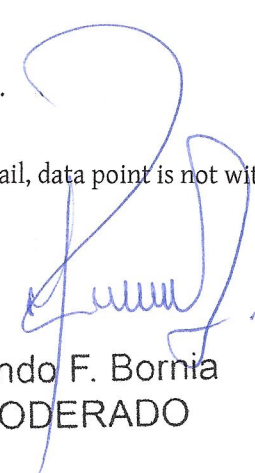
QC Result First Table Heading

- **Lot** - lot number used for the specified QC run.
- **Average** - average of all listed runs.
- **Min** - lowest value of all listed runs.
- **Max** - highest value of all listed runs.
- **CV** - coefficient of variation of all listed runs (Standard Deviation/Average) x 100
- **StDev** - standard deviation of all listed runs.

QC Result Second Table Heading, QC Instrument Second Table Heading, QC Instrument Drift Second Table Heading

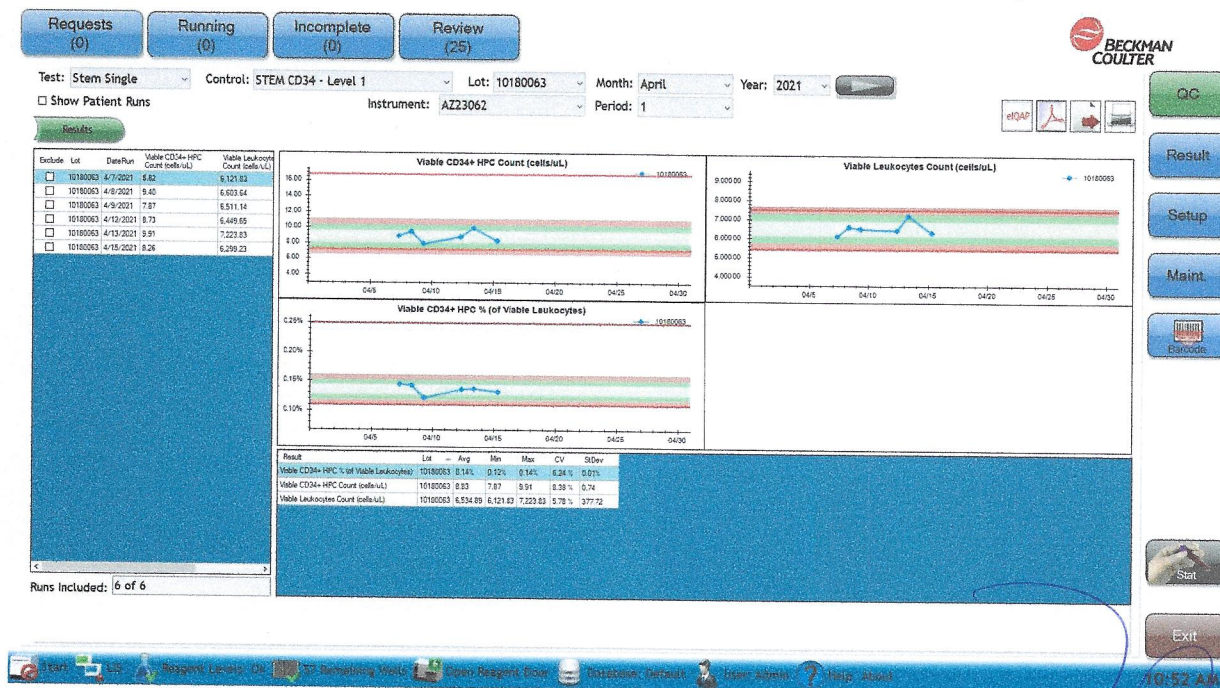
- **Exclude** - data points included or excluded in the report.
- **Lot** - single lot selected or (All) if plotting all available lots.
- **Date run** - date in which control was analyzed.
- **Pass/Fail** - If Pass, data point is within expected range. If Fail, data point is not within the expected range.
- **Assay statistics** - percent or count/ μ L of selected assay.


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QC Reports

Figure A.7 QC Results: Results View of AQUIOS STEM CD34 Control Cells Level 1, AQUIOS STEM Single



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Figure A.8 QC Results: AQUIOS STEM CD34 Control Cells Level 1, AQUIOS STEM Single (Page 1)

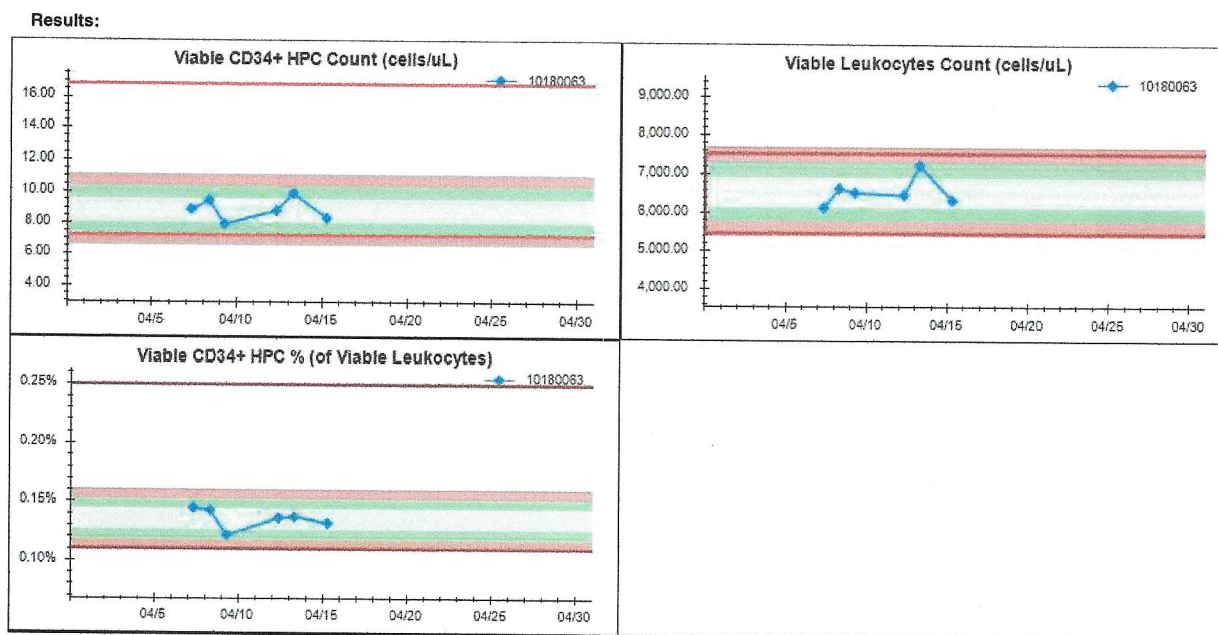


Figure A.9 QC Results: AQUIOS STEM CD34 Control Cells Level 1, AQUIOS STEM Single (Page 2)

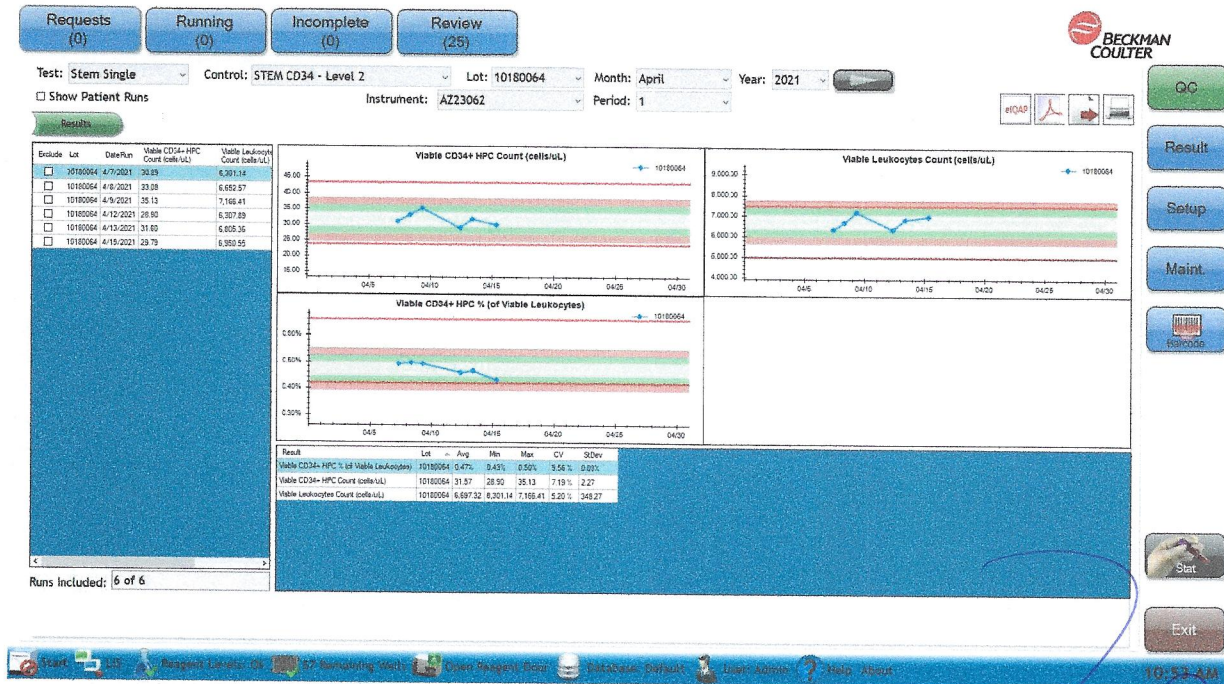
Result	Lot	Avg	Min	Max	CV	StDev
Viable CD34+ HPC Count (cells/uL)	10180063	8.83	7.87	9.91	8.38 %	0.74
Viable Leukocytes Count (cells/uL)	10180063	6,534.89	6,121.83	7,223.83	5.78 %	377.72
Viable CD34+ HPC % (of Viable Leukocytes)	10180063	0.14%	0.12%	0.14%	6.24 %	0.01%

Exclude (Yes/No)	Lot	DateRun	Instrument	Pass/Fail	Viable CD34+ HPC Count (cells/uL)	Viable Leukocytes Count (cells/uL)	Viable CD34+ HPC % (of Viable Leukocytes)
No	10180063	4/7/2021	5	Pass	8.82	6,121.83	0.14%
No	10180063	4/8/2021	5	Pass	9.40	6,603.64	0.14%
No	10180063	4/9/2021	5	Pass	7.87	6,511.14	0.12%
No	10180063	4/12/2021	5	Pass	8.73	6,449.65	0.14%
No	10180063	4/13/2021	5	Pass	9.91	7,223.83	0.14%
No	10180063	4/15/2021	5	Pass	8.26	6,299.23	0.13%

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Figure A.10 QC Results: Results View of AQUIOS STEM CD34 Control Cells Level 2, AQUIOS STEM Single



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Figure A.11 QC Results: AQUIOS STEM CD34 Control Cells Level 2, AQUIOS STEM Single (Page 1)

Results:

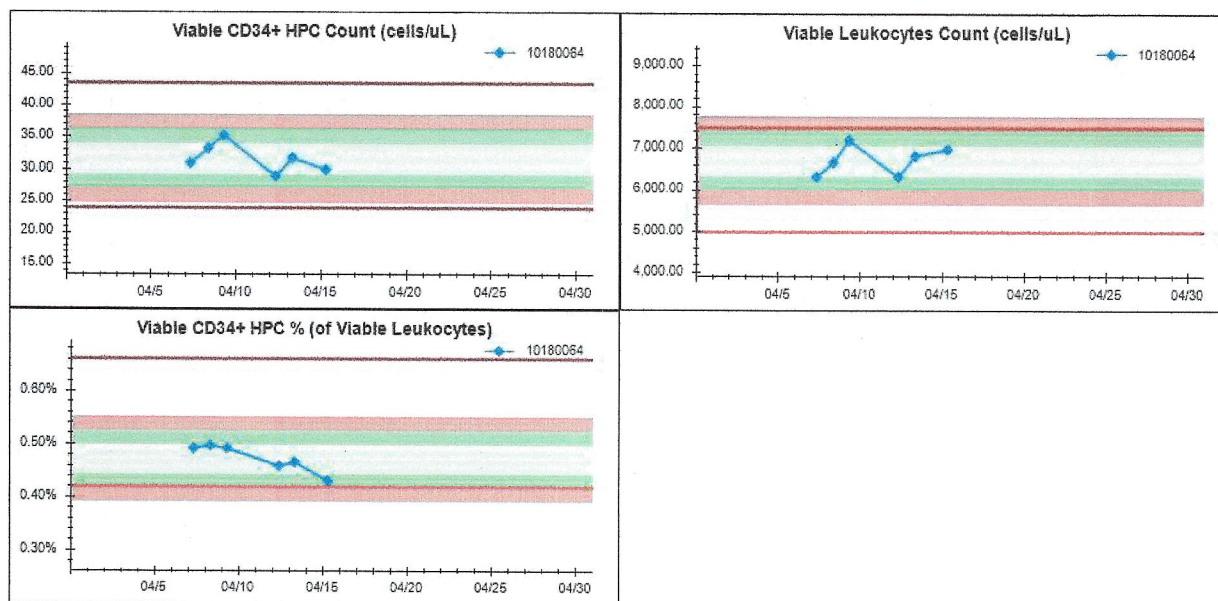


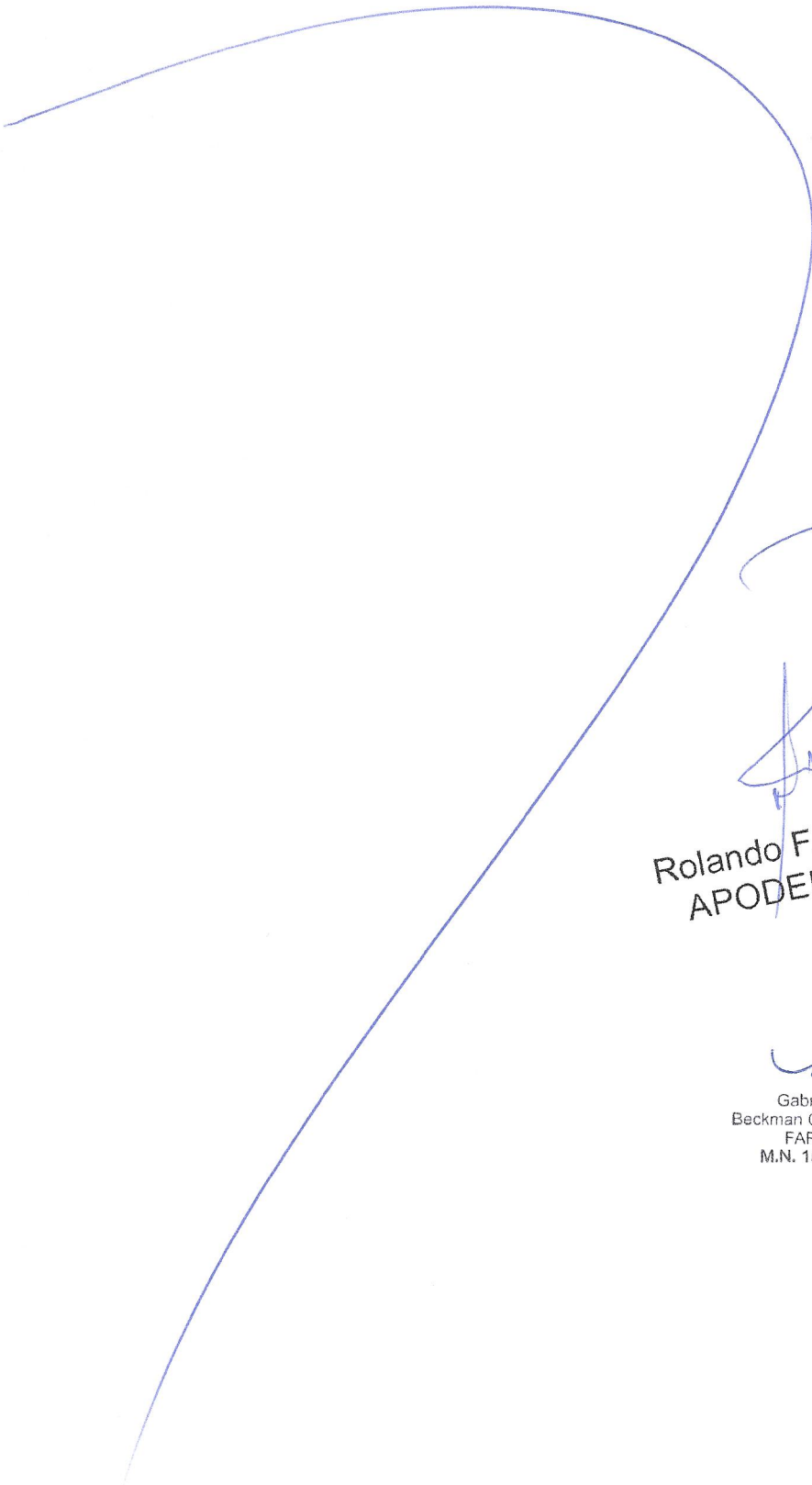
Figure A.12 QC Results: AQUIOS STEM CD34 Control Cells Level 2, AQUIOS STEM Single (page 2)

Result	Lot	Avg	Min	Max	CV	StDev
Viable CD34+ HPC Count (cells/uL)	10180064	31.57	28.90	35.13	7.19 %	2.27
Viable Leukocytes Count (cells/uL)	10180064	6,697.32	6,301.14	7,166.41	5.20 %	348.27
Viable CD34+ HPC % (of Viable Leukocytes)	10180064	0.47%	0.43%	0.50%	5.56 %	0.03%

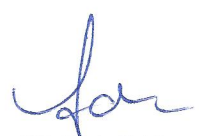
Exclude (Yes/No)	Lot	DateRun	Instrument	Pass/Fail	Viable CD34+ HPC Count (cells/uL)	Viable Leukocytes Count (cells/uL)	Viable CD34+ HPC % (of Viable Leukocytes)
No	10180064	4/7/2021	5	Pass	30.89	6,301.14	0.49%
No	10180064	4/8/2021	5	Pass	33.08	6,652.57	0.50%
No	10180064	4/9/2021	5	Pass	35.13	7,166.41	0.49%
No	10180064	4/12/2021	5	Pass	28.90	6,307.89	0.46%
No	10180064	4/13/2021	5	Pass	31.60	6,805.36	0.46%
No	10180064	4/15/2021	5	Pass	29.79	6,950.55	0.43%

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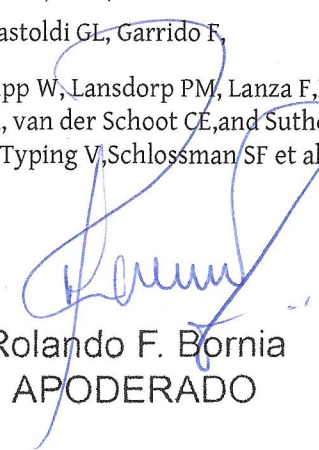
References

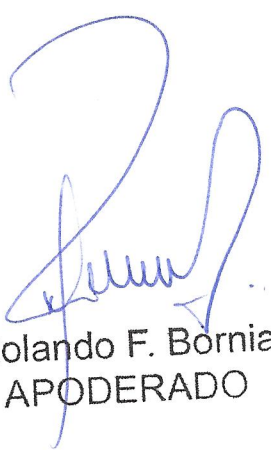
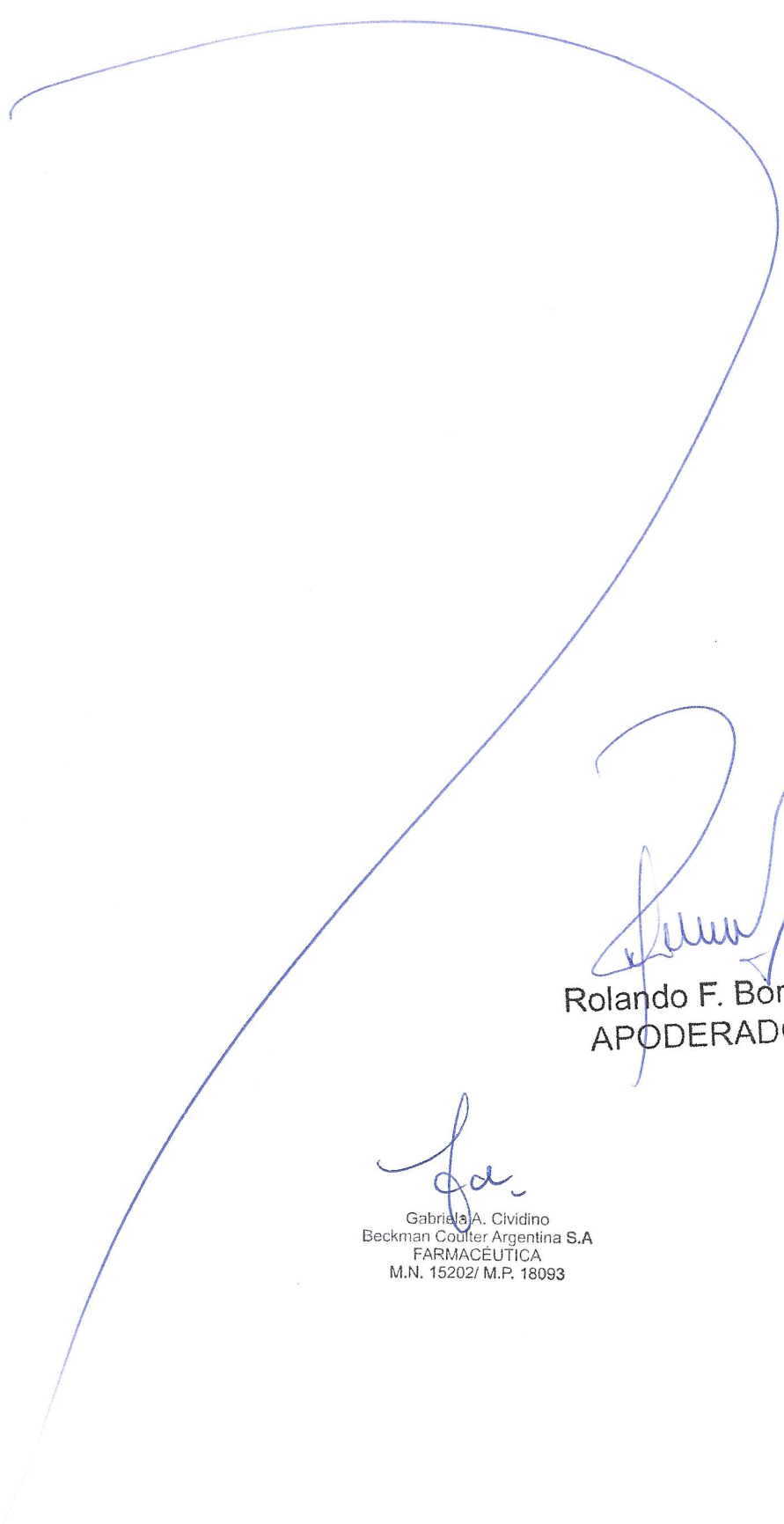
1. Centers for Disease Control and Prevention. 2003 Guidelines for performing single-platform absolute CD4+ T-cell determinations with CD45 gating for persons infected with Human Immunodeficiency Virus (HIV). MMWR 2003; 57 (No. RR. 2): 1-13.
2. Nicholson JKA, Hubbard M and Jones BM. Use of CD45 fluorescence and side scatter characteristics for gating lymphocytes when using the whole blood lysis procedure and flow cytometry. Cytometry (Communications in Clinical Cytometry), 1996; 26: 16-21.
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A

- Action Toolbox
 - Review screen, 5-9
- adjust compensation
 - manually, 5-11
- Analysis Algorithm
 - 3-dimensional lymphocyte gating, 2-4
 - overview, 2-4
- Analysis reagent
 - Sheath Fluid, 1-5
- AQUIOS Manuals
 - Use, xv
- AQUIOS STEM Panel monoclonal antibody
 - reagents, 1-4
- AQUIOS Tetra System software
 - used with, 1-3

B

- bar codes
 - smart-track monitoring, 1-3
- Beckman Coulter Customer Support Center,
 - contacting, ii
- blood volume
 - minimum required per specimen tube, 4-3

C

- call center, contact information, ii
- compensation
 - to manually adjust, 5-11
- contact information, Beckman Coulter
 - Customer Support Center, ii
- control lot number, registering. *See* Starting a New Lot of Beckman Coulter Control in Chapter 9 of AQUIOS CL Flow Cytometer Instructions for Use

D

- Daily Startup. *See* Startup in Chapter 3 of AQUIOS CL Flow Cytometer Instructions for Use


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- data sheets, material safety
 - how to order, 1-6
- disclaimer
 - graphics, xviii

F

- Flags and Notifications, 5-16

G

- graphic
 - options, 5-6
- graphics disclaimer, xviii

H

- help, Beckman Coulter Customer Support Center, ii

I

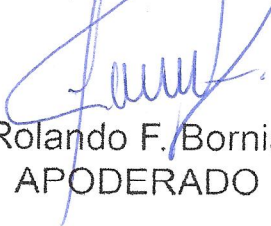
- intended use, 1-1

L

- limitations, 1-6
- linearity, 6-1
- Lymphocyte Immunophenotyping Panels
 - Tetra-1 Panel, 2-3

M

- manual overview, xv
- manual, updates (primary entry), -iii
- manually adjust
 - compensation, 5-11
- material safety data sheets (MSDS/SDS)
 - how to order, 1-6
- method comparison, 6-4
- MSDS (material safety data sheets)
 - how to order, 1-6


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O

- options
 - graphic, 5-6
 - running specimens, 4-10
- overview
 - 3-dimensional lymphocyte gating, 2-4
 - Analysis Algorithm, 2-4

P

- Parameter results of STEM Single, Duplicate, and Panel
 - parameter results, 2-3
- population statistics, 5-11
 - recommended use, 3-1, 3-7, 5-11
- precision
 - Precision Performance of Quantitative Measurement Methods, 6-7
- preparation
 - monoclonal antibodies, 1-4
 - Tetra-1 sample, 7-1
- Principles of Tetra Tests, 2-1

Q

- Q C workflow, 3-1
- QC
 - report, A-8
 - report description, A-9
 - Results screen, 3-16
- QC materials
 - required, 3-2
- QC overview, 3-2
- QC process, 3-3
- Quality Control, 6-8
- Quality Control reagents
 - AQUIOS STEM CD34 Control Cells, 1-5

R

- reagent
 - specificity, 6-8
- reference ranges, 6-6
- registering control lot number. *See* Starting a New Lot of Beckman Coulter Control in Chapter 9 of AQUIOS CL Flow Cytometer Instructions for Use, 3-3
- replacing reagents and consumables. *See* AQUIOS CL Flow Cytometer Instructions for Use

- report
 - QC, A-8
- report description
 - displays
 - generating reports, A-8
 - QC, A-9
 - report heading, A-8
 - result table heading, A-8
 - statistics, Tetra-1 Report, A-8
- reports, A-1
- Results screen
 - search menu, 5-15
 - selecting data for review, 5-15
- Review screen
 - Action Toolbox, 5-9
 - display areas, 5-2
 - samples pending transmission, 5-1
- Running screen, 4-12
- running specimens
 - options, 4-10

S

- safety symbols, xviii
 - potentially infectious, xviii
- sample populations
 - to automatically identify and enumerate, 2-4
- SDS (safety data sheets)
 - how to order, 1-6
- service, contact information, ii
- specificity
 - reagent, 6-8
- STEM
 - throughput, 7-1
- STEM Application
 - Workflow, 4-2
- STEM Single, Duplicate, Panel Results, 2-3
- storage conditions and stability
 - reagents, 4-4
 - Whole Blood Specimen, 4-4
- support, Beckman Coulter customer, ii
- System Components
 - "closed" system, 1-3
 - autoloader, 1-2
 - fully automatic operation, 1-2
 - load & go feature, 1-3
 - Single-tube Loader, 1-2
- System Guide
 - about, xvi

system limitations, 1-6

T

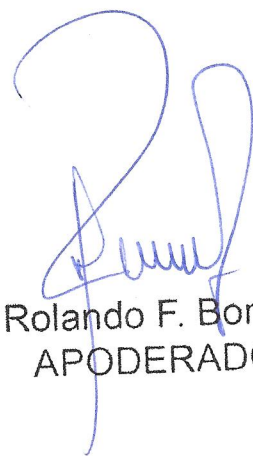
throughput
STEM, 7-1

W

Workflow
STEM Application, 4-2



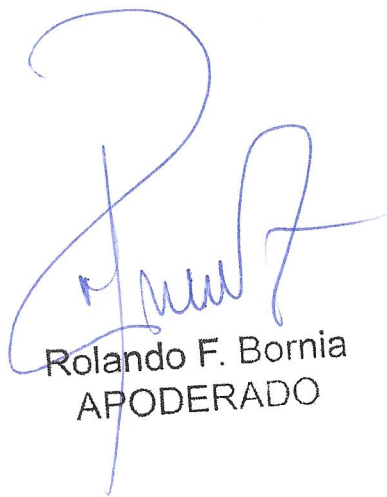
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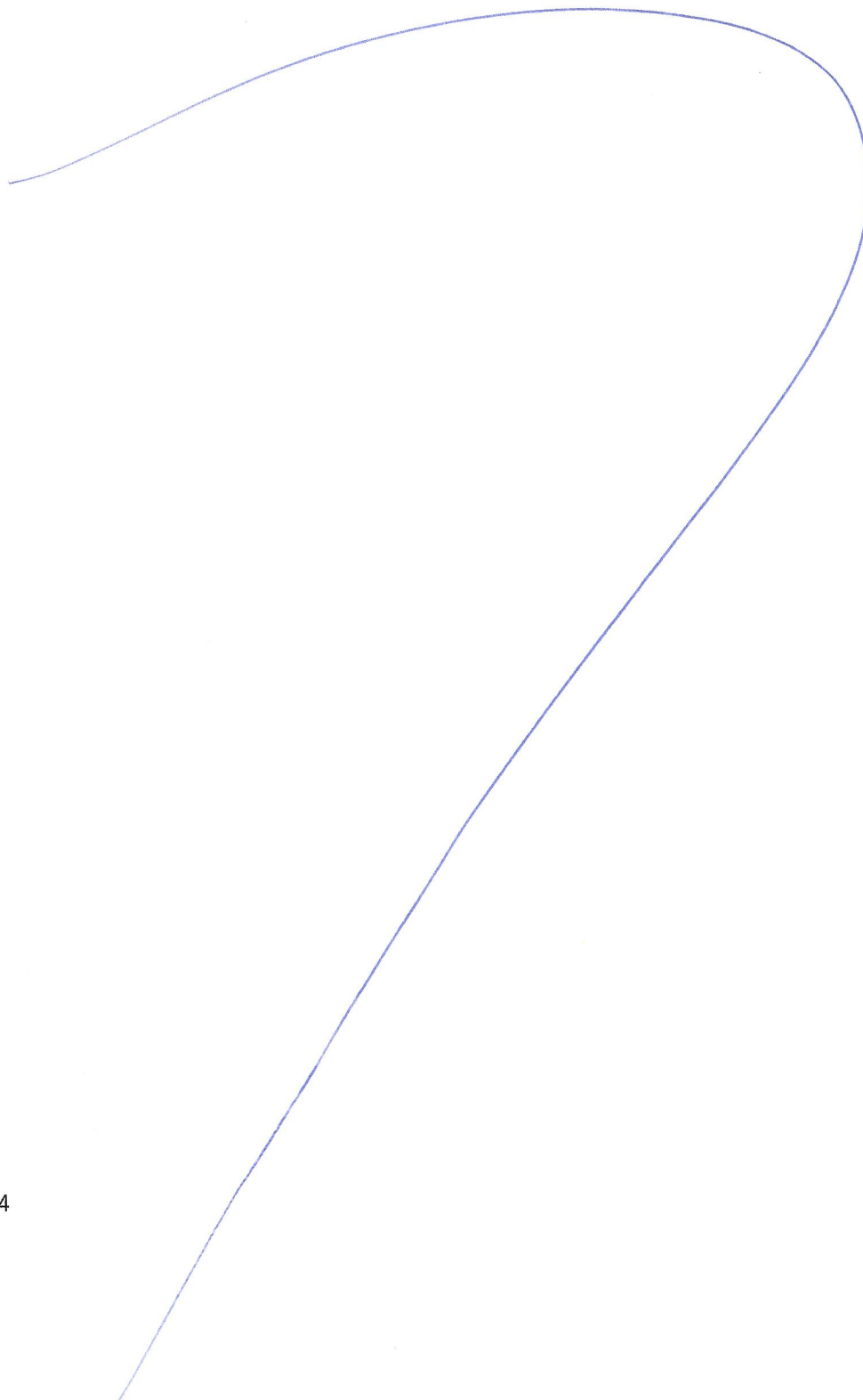
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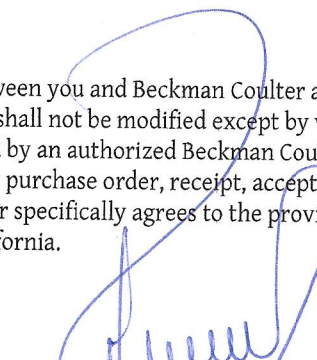
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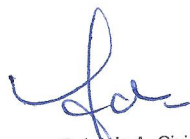
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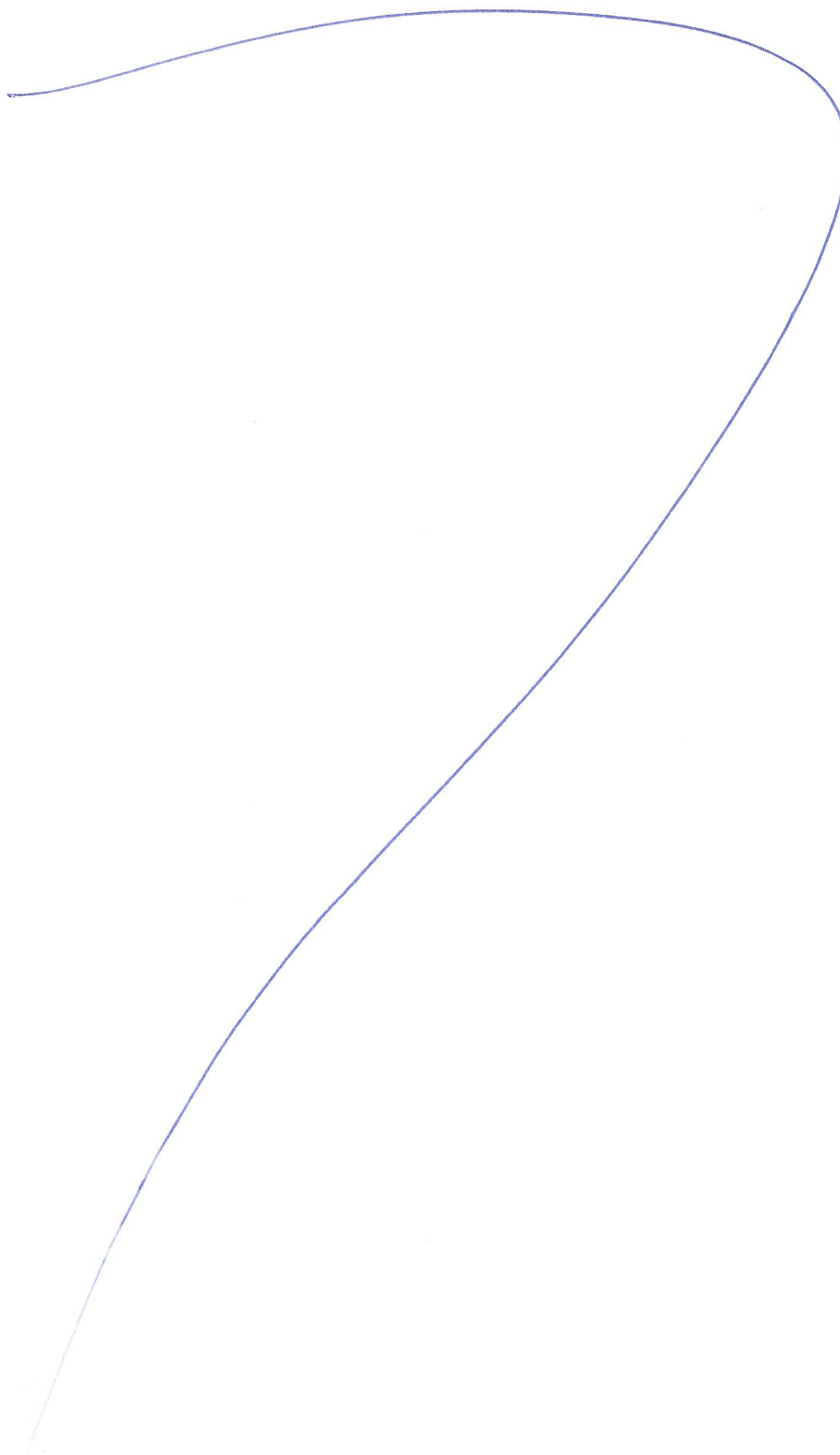
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Related Documents

Your AQUIOS documentation can be found on our Web site at www.beckman.com

AQUIOS STEM System Guide

PN B75978

AQUIOS CL Flow Cytometer Instructions for Use

PN B21896

AQUIOS STEM LIS Host Transmission

PN C62645

Cytometry Interlaboratory Quality Assurance Program Procedure Manual

PN 4206384



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PROYECTOS DE RÓTULO EXTERNO

Nota: por art. 1° de la **Disposición n° 4043/2005** ANMAT, se acepta el uso de los 24 símbolos descritos y definidos en el Anexo I de la citada norma en reemplazo del texto de la información requerida en la presente Disposición en los rótulos de los productos para diagnóstico de uso in vitro.

RÓTULO ORIGINAL DEL PRODUCTO

2) B77691 AQUIOS STEM Kit Reagents

REF B77691 AQUIOS STEM Kit **IVD** **CE**

CONTENTS 2 x 0.64 mL **CONJ REAG** 2 x 10 mL **FLUOROSPHERES**
 1 x 0.64 mL **CONJ REAG**
 3 x 0.64 mL **T-AAD**
 3 x 26.5 mL **BOLN LYBING**

INFORMATION FOR USA ONLY
 Reagent for the identification and enumeration of human hematopoietic progenitor cells.
 Reactive ingredients: Formaldehyde <1%, Pyrrolidine <5%, EDTA <1%, Disodium Salt <1%, Potassium Bicarbonate <1%,
 7-Aminoclonomycin D 0.005%, Carbonic Anhydrase <1%, Bovine Serum Albumine <1%, Polystyrene Latex Beads <5%,
 Monoclonal Antibodies (Murine Source) <1%.

May be covered by one or more pat. - see www.beckmancoulter.com/patents.

BECKMAN COULTER **IMMUNOTECH SAS**
 a Beckman Coulter Company
 13276 Marseille Cedex 9 France, + (33) 4 91 17 27 27

DANGER
 H315 H317 H319 H341 H350
 Formaldehyde <3%, Dimethyl
 Sulfoxide 1 - 2%, Pyrrolidina
 1.0 - 1.5%.

SDS
 beckman.com/techdocs
 HXXXXX AA
 C26037 AA

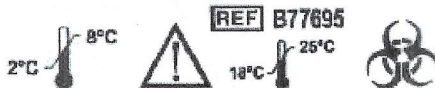
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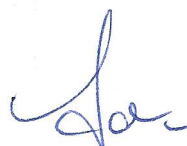
1. Nombre del Producto	AQUIOS STEM Kit
2.	Rótulo Local
a) Nombre y dirección del Importador	Rótulo Local
b) Nombre del Director Técnico	Rótulo Local
c) Nombre y dirección del Elaborador	Rótulo Local
d) Nombre y dirección del Fabricante Legal	Immunotech S.A.S., A Beckman Coulter Company, 130 Avenue de Lattre de Tassigny-BP177- 13276 Marseille, Cedex 9-France.
3. Leyenda "Autorizado por la ANMAT"	Rótulo Local
4. Número de lote o partida	LOT

5. Fecha de Vencimiento	
6. Constitución del equipo (relación de los componentes)	Conj Reag 2 x 0.64 mL Conj Reag 1 x 0.64 mL 7-AAD 3 x 0.64 mL SOLN LYSING 3 x 26.5 mL FLUOROSPHERES 2 x 10 mL
7. Leyenda "Uso In Vitro"	
8. Descripción de la finalidad de uso del producto	
9. Descripción de las precauciones	
10. Indicación de las condiciones adecuadas de almacenamiento y transporte del producto	2-8°C

RÓTULO LOCAL (APUESTO POR EL IMPORTADOR/DISTRIBUIDOR EN ARGENTINA)

Beckman Coulter Argentina, Gral. Martin M. Güemes. 4168 B1603EN Villa Martelli, Bs. As
 Directora Técnica: Farmacéutica Gabriela A. Cividino
 Fabricante: Immunotech S.A.S., A Beckman Coulter Company, 130 Avenue de Lattre de Tassigny-BP177- 13276 Marseille, Cedex 9-France.
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PROYECTO DE RÓTULO INTERNO

Nota: por art. 1° de la Disposición n° 4043/2005 ANMAT, se acepta el uso de los 24 símbolos descritos y definidos en el Anexo I de la citada norma en reemplazo del texto de la información requerida en la presente Disposición en los rótulos de los productos para diagnóstico de uso in vitro.

AQUIOS STEM Kit REF B77692 CD45-FITC CD34-PE 0.64mL IMMUNOTECH SAS a Beckman Coulter Company 13278 Marseille Cedex 9 France BECKMAN COULTER CE IVD 2022-04-21 LOT 123456 C20039 AA	AQUIOS STEM Kit REF B77693 CD45-FITC IsoClonic Control-PE 0.64mL IMMUNOTECH SAS a Beckman Coulter Company 13278 Marseille Cedex 9 France BECKMAN COULTER CE IVD 2022-04-21 LOT 123456 C20040 AA
AQUIOS STEM Kit REF B77694 7-AAD Viability Dye 0.64mL IMMUNOTECH SAS a Beckman Coulter Company 13278 Marseille Cedex 9 France +33(0) 4 91 17 27 27 BECKMAN COULTER CE IVD 2022-04-21 LOT 123456 C20041 AA	AQUIOS STEM Kit Lysing Solution REF B77695 20.5 mL BECKMAN COULTER CE IVD 2023-12-31 LOT 123457 C: 01779 WARNING H315 H319 IMMUNOTECH SAS, a Beckman Coulter Company 13278 Marseille Cedex 9 France +33(0) 4 91 17 27 27
AQUIOS STEM Kit STEM-Count Fluorospheres REF B77696 Stem-Count Value 947/μL 10 mL IMMUNOTECH SAS a Beckman Coulter Company 13278 Marseille Cedex 9 France +33(0) 4 91 17 27 27 BECKMAN COULTER CE IVD 2022-05-24 LOT 0200013 C29336-AA	

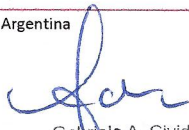
1. Nombre del Producto	AQUIOS STEM Kit CD45-FITC/ CD34-PE
2. Número de lote o partida	LOT
3. Fecha de Vencimiento	

4. Indicación de las unidades métricas, tales como volumen, peso, actividad u otra unidad característica de cada componente del producto	0.64 mL
5. Indicación de las condiciones adecuadas de almacenamiento y transporte del producto	2-8°C

1. Nombre del Producto	AQUIOS STEM Kit CD45-FITC IsoClonic Control PE
2. Número de lote o partida	LOT
3. Fecha de Vencimiento	
4. Indicación de las unidades métricas, tales como volumen, peso, actividad u otra unidad característica de cada componente del producto	0.64 mL
5. Indicación de las condiciones adecuadas de almacenamiento y transporte del producto	2-8°C

1. Nombre del Producto	AQUIOS STEM Kit 7-AAD Visibility Dye
2. Número de lote o partida	LOT
3. Fecha de Vencimiento	
4. Indicación de las unidades métricas, tales como volumen, peso, actividad u otra unidad característica de cada componente del producto	0.64 mL
5. Indicación de las condiciones adecuadas de almacenamiento y transporte del producto	2-8°C

1. Nombre del Producto	AQUIOS STEM Kit Lysing Solution
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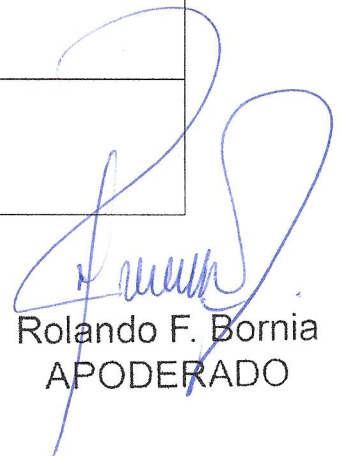

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2. Número de lote o partida	LOT
3. Fecha de Vencimiento	
4. Indicación de las unidades métricas, tales como volumen, peso, actividad u otra unidad característica de cada componente del producto	26.5 mL
5. Indicación de las condiciones adecuadas de almacenamiento y transporte del producto	18-25°C

1. Nombre del Producto	AQUIOS STEM Kit Stem Count Fluorospheres
2. Número de lote o partida	LOT
3. Fecha de Vencimiento	
4. Indicación de las unidades métricas, tales como volumen, peso, actividad u otra unidad característica de cada componente del producto	10.0 mL
5. Indicación de las condiciones adecuadas de almacenamiento y transporte del producto	2-8°C



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PROYECTOS DE RÓTULO EXTERNO

Nota: por art. 1° de la **Disposición n° 4043/2005** ANMAT, se acepta el uso de los 24 símbolos descritos y definidos en el Anexo I de la citada norma en reemplazo del texto de la información requerida en la presente Disposición en los rótulos de los productos para diagnóstico de uso in vitro.

RÓTULO ORIGINAL DEL PRODUCTO

3) C43667 AQUIOS STEM CD34 Control Cells Kit

AQUIOS STEM CD34 Control Cells IVD Info. for USA Only Rx Only Intended as an assayed, lysable whole blood quality control product for immunophenotyping analysis using monoclonal antibody reagents for flow cytometry. Reactive Ingredients: Stabilized Human Erythrocyte and Leukocyte Preparation 2 x 3 mL May be covered by one or more pat. – see www.beckman.com/patents. Manufactured for IMMUNOTECH S.A.S. a Beckman Coulter Company  beckman.com/techdocs  IMMUNOTECH S.A.S. a Beckman Coulter Company 130, avenue de Lattre de Tassigny, BP 177 13276 Marseille cedex 9, France Tél. (33) 491 172 727 C43555-AA Made in U.S.A.	AQUIOS STEM CD34 Control Cells REF C43667 CONTENTS 1x 3 mL Level 1 CONTENTS 1x 3 mL Level 2 Package Insert 2°C 8°C  BECKMAN COULTER C43550-AA
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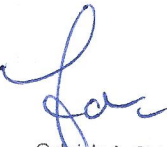
1. Nombre del Producto	AQUIOS STEM CD34 Control Cells
2.	Rótulo Local
a) Nombre y dirección del Importador	Rótulo Local
b) Nombre del Director Técnico	Rótulo Local
c) Nombre y dirección del Elaborador	Rótulo Local

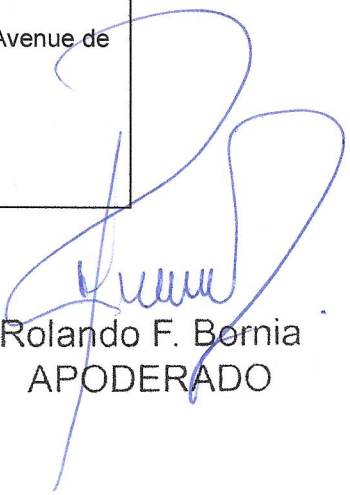
d) Nombre y dirección del Fabricante Legal	Immunotech S.A.S., A Beckman Coulter Company, 130 Avenue de Lattre de Tassigny-BP177- 13276 Marseille, Cedex 9-France.
3. Leyenda "Autorizado por la ANMAT"	Rótulo Local
4. Número de lote o partida	
5. Fecha de Vencimiento	
6. Constitución del equipo (relación de los componentes)	Level 1: 1 x 3.0 mL Level 2: 1 x 3.0 mL
7. Leyenda "Uso In Vitro"	
8. Descripción de la finalidad de uso del producto	
9. Descripción de las precauciones	
10. Indicación de las condiciones adecuadas de almacenamiento y transporte del producto	2-8°C

RÓTULO LOCAL (APUESTO POR EL IMPORTADOR/DISTRIBUIDOR EN ARGENTINA)

Beckman Coulter Argentina, Gral. Martin M. Güemes. 4168 B1603EN Villa Martelli, Bs. As
Directora Técnica: Farmacéutica Gabriela A. Cividino
Fabricante: Immunotech S.A.S., A Beckman Coulter Company, 130 Avenue de Lattre de Tassigny-BP177- 13276 Marseille, Cedex 9-France.
"USO PROFESIONAL EXCLUSIVO - VENTA EXCLUSIVA A LABORATORIOS DE ANÁLISIS CLÍNICOS"

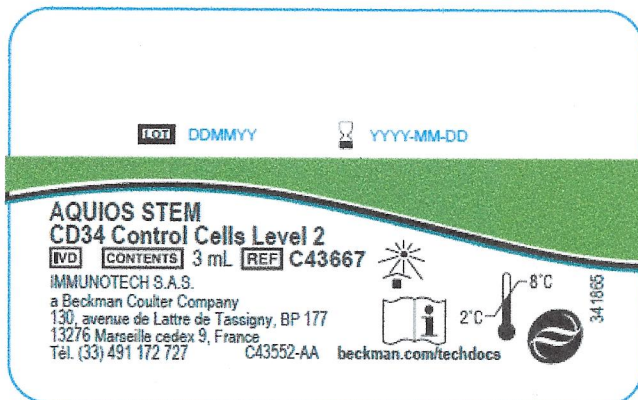
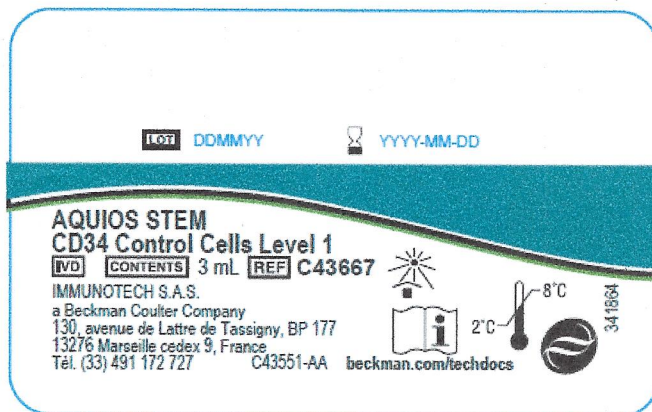
Autorizado por ANMAT- PM 1109-495


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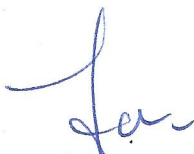
PROYECTO DE RÓTULO INTERNO

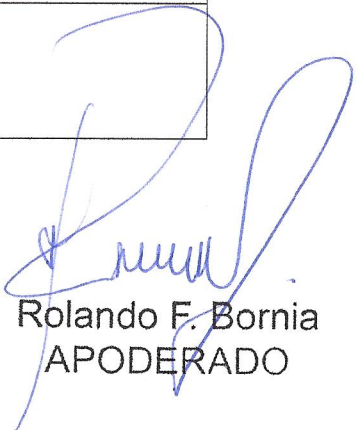
Nota: por art. 1° de la Disposición n° 4043/2005 ANMAT, se acepta el uso de los 24 símbolos descritos y definidos en el Anexo I de la citada norma en reemplazo del texto de la información requerida en la presente Disposición en los rótulos de los productos para diagnóstico de uso in vitro.



1. Nombre del Producto	AQUIOS STEM CD34 Control Cells Level 1
2. Número de lote o partida	LOT
3. Fecha de Vencimiento	
4. Indicación de las unidades métricas, tales como volumen, peso, actividad u otra unidad característica de cada componente del producto	3.0 mL
5. Indicación de las condiciones adecuadas de almacenamiento y transporte del producto	2-8°C

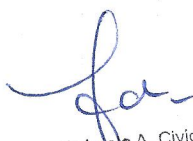
1. Nombre del Producto	AQUIOS STEM CD34 Control Cells Level 2
2. Número de lote o partida	LOT
3. Fecha de Vencimiento	
4. Indicación de las unidades métricas, tales como volumen, peso, actividad u otra unidad característica de cada componente del producto	3.0 mL
5. Indicación de las condiciones adecuadas de almacenamiento y transporte del producto	2-8°C


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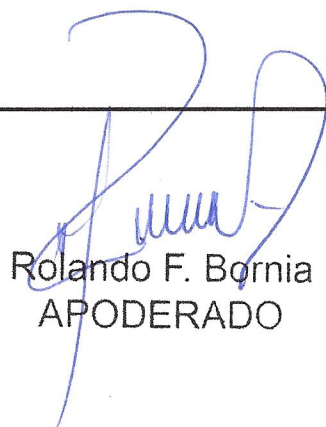

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PROYECTO DE MANUAL DE INSTRUCCIONES

Ver adjunto Instrucciones de Uso del Producto.



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AQUIOS STEM Kit

REF B77691 50 análisis

Para uso diagnóstico *in vitro*

USO PREVISTO

El kit AQUIOS STEM es un producto sanitario de diagnóstico *in vitro* indicado para su uso por profesionales de laboratorio para la detección de los parámetros en los tipos de muestras mostrados en la Tabla 1, Parámetros del sistema, en el sistema automatizado de citometría de flujo AQUIOS CL.

Este es un ensayo cuantitativo utilizado para la identificación y el recuento de las poblaciones celulares especificadas en la Tabla 1, Parámetros del sistema, en pacientes que se están preparando para un trasplante de células progenitoras hematopoyéticas autólogo o alogénico y en donantes que se someten a programas de movilización o recogida para trasplantes de células progenitoras hematopoyéticas autólogos o alogénicos.

Tabla 1: Parámetros del sistema

Tipo de espécimen	Anticoagulante						Kits/Parámetros
	K ₂ EDTA	K ₃ EDTA	Heparina	Mezcla de heparina y ACD-A	ACD-A	CPD	Kit AQUIOS STEM
Sangre total	X	X	X				Porcentaje de CD34
Sangre total movilizada	X	X	X				
Médula ósea recién extraída o descongelada	X	X	X	X			Recuento absoluto de CD34
Producto de aféresis recién extraído o descongelado				X	X		Recuento absoluto de CD45
Sangre del cordón umbilical recién extraída o descongelada					X	X	

IMPORTANCIA CLÍNICA

El kit AQUIOS STEM permite la detección cualitativa, cuantitativa y automatizada, así como el recuento, de la población de células progenitoras hematopoyéticas viables que expresan CD45+ y CD45+/CD34+ (doble positivas) mediante citometría de flujo en muestras biológicas humanas.

Cuando se usa según lo previsto, el kit AQUIOS STEM puede utilizarse para una o más de las siguientes funciones:

- Para el cribado o monitorización de muestras de donantes que se someten a esquemas de movilización o recolección para trasplantes autólogos o alogénicos de células progenitoras hematopoyéticas.
- Para la monitorización de muestras de pacientes que se preparan para trasplante autólogo o alogénico de células progenitoras hematopoyéticas.

RESUMEN

Células progenitoras hematopoyéticas (HPC)

El kit AQUIOS STEM está diseñado para identificar células madre hematopoyéticas humanas y células progenitoras hematopoyéticas (CPH) humanas utilizando los siguientes criterios: «Las células CD34+ verdaderas: (a) expresan el antígeno CD34, (b) expresan el antígeno CD45 con una intensidad de tinción característica de los blastocitos (es decir, se pueden detectar fácilmente, pero a niveles menores que los linfocitos y monocitos) y (c) presentan la dispersión de la luz de ángulo lateral baja y la dispersión de la luz de ángulo frontal baja o intermedia características de los blastocitos» (1). La exclusión de las CPH CD34+ muertas del recuento de CPH CD34+ viables se consigue utilizando el Viability Dye 7-AAD (2).

CD34

El antígeno CD34 es una familia de glucoproteínas transmembranarias monocatenarias de tipo I glucosiladas de manera diferencial (3,4,5). Se expresa en prácticamente todas las células progenitoras hematopoyéticas, incluso en las células madre multipotentes. Los epítomos del antígeno CD34 se han dividido en tres clases en función de su sensibilidad a la neuraminidasa y a la glucoproteasa de *Pasteurella haemolytica* (6). El anticuerpo monoclonal (AcM) anti-CD34 utilizado en el kit AQUIOS STEM se denomina 581. Reconoce específicamente un epítipo de clase III de la molécula de CD34 (7), tal y

como definen los patrones de escisión enzimática (6,8). El anticuerpo monoclonal 581 se asignó al antígeno CD34 durante el «5th HLDA Workshop on Human Leukocyte Differentiation Antigens» (5.º seminario sobre los antígenos de diferenciación de los leucocitos humanos [HLDA]), que tuvo lugar en Boston (Massachusetts, EE. UU.) en 1993 (7).

CD45

El anticuerpo anti-CD45 reconoce a los miembros de la familia CD45 de antígenos panleucocitarios con un peso molecular de 180, 190, 210 y 220 kD (9,10,11). También se conoce como el antígeno común leucocitario (LCA). El antígeno CD45 se expresa en todos los tipos de células hematopoyéticas, a excepción de los eritrocitos maduros y sus progenitores inmediatos (11,12). No se ha detectado en el tejido no hematopoyético diferenciado (12,13,14,15). El AcM anti-CD45 utilizado en el kit AQUIOS STEM se denomina J33. Se asignó al antígeno CD45 durante el «3rd HLDA Workshop on Human Leukocyte Differentiation Antigens» (3er seminario sobre los antígenos de diferenciación de los leucocitos humanos [HLDA]), que tuvo lugar en Oxford (Inglaterra) en 1986 (16).

7-AAD

El marcador de viabilidad 7-aminoactinomicina D (7-AAD) es un producto análogo de la actinomicina D que contiene un grupo amino sustituido en la posición 7 del cromóforo. El marcador de viabilidad 7-AAD se intercala entre las bases citosina y guanina del ADN (15). Las actinomicinas son compuestos biológicamente activos que contienen un cromóforo 2-amino-4, 6 dimetilfenoxazona-3 y dos pentapéptidos cíclicos (17). Las actinomicinas forman complejos estables con el ácido desoxirribonucleico (ADN) de doble cadena, pero nunca con el ácido ribonucleico (ARN) de doble cadena ni con híbridos de ADN y ARN ni ADN o ARN de cadena simple (15, 18).

Las propiedades espectrales del Viability Dye 7-AAD permiten que esta molécula sea especialmente adecuada para el análisis mediante citometría de flujo (17). La absorción máxima del complejo 7-AAD/ADN se sitúa en la región espectral verde y, por tanto, es adecuada para un láser con una longitud de onda de excitación de 488 nm (15). La emisión de fluorescencia roja intensa del Viability Dye 7-AAD (de 635 a 675 nm) facilita la utilización de esta sonda en combinación con los anticuerpos conjugados a isotiocianato de fluoresceína (FITC) y ficoeritrina (PE). Esto se debe a que, a diferencia del yoduro de propidio (PI), el complejo 7-AAD/ADN presenta una superposición espectral mínima con el FITC y la PE (17).

Las células necróticas, apoptóticas o dañadas son fuentes de interferencia en el análisis de las células viables mediante citometría de flujo. Las células no viables se deben evaluar y distinguir a partir de la tinción de 7-AAD positivo; las células no viables quedarán sin teñir (negativas) (19).

Sistemas de citómetro de flujo

Los sistemas de citometría de flujo utilizan los principios de la citometría de flujo para analizar las muestras biológicas con el fin de identificar diversas poblaciones celulares determinadas por los anticuerpos monoclonales y los fluorocromos específicos utilizados. Esta prueba utiliza el sistema de citometría de flujo AQUIOS CL para procesar y analizar las muestras.

PRINCIPIO

Esta prueba depende de la capacidad de un anticuerpo monoclonal de unirse a la superficie de células que expresan determinantes antigénicos distintos. El reactivo CD45-FITC/CD34-PE del kit AQUIOS STEM es una combinación de dos anticuerpos monoclonales murinos, cada uno de ellos conjugado a un fluorocromo concreto y específico para un antígeno de la superficie celular diferente. La tinción específica de la superficie celular se logra incubando muestras de una muestra biológica con el reactivo bicolor CD45-FITC/CD34-PE.

En una prueba adicional, la misma muestra se tiñe con el reactivo CD45-FITC/IsoClonic Control-PE del kit AQUIOS STEM para comprobar la unión inespecífica del anticuerpo monoclonal anti-CD34-PE. El Viability Dye 7-AAD, un tinte de ácido nucleico que se une a los pares de bases accesibles (ADN celular), se utiliza para diferenciar las células viables de las no viables. Los eritrocitos presentes en cada muestra se lisan con la solución de lisis del kit AQUIOS STEM, un agente de lisis muy específico y muy suave, listo para usar, que se utiliza a temperatura ambiente. Se añaden las fluoroesferas STEM-Count del kit AQUIOS STEM y las células restantes se analizan mediante citometría de flujo.

Los siguientes reactivos de control del proceso y control de calidad son necesarios, pero no se suministran: fluoroesferas FLOW-CHECK y células de control CD34 AQUIOS STEM de nivel 1 y nivel 2.

El sistema AQUIOS STEM, que consiste en el kit AQUIOS STEM, el sistema de citometría de flujo AQUIOS CL y el software AQUIOS STEM, está equipado con las funciones de carga automatizada, preparación de la muestra, manipulación de reactivos y escaneo de códigos de barras, así como con la función de análisis de datos y conectividad LIS bidireccional en una sola plataforma.

Documento relacionado

Para obtener más información, consulte el documento «AQUIOS STEM System Guide» (Guía del sistema AQUIOS STEM) que podrá encontrar en nuestro sitio web: www.beckman.com.

Contenido del material

El kit AQUIOS STEM contiene 6 tapones con membrana de goma para los reactivos de anticuerpos y el Viability Dye 7-AAD y 2 tapones de rosca con orificio para las fluoroesferas STEM-Count del kit AQUIOS STEM, todos ellos en una bolsa de plástico.

CONTENIDO DEL REACTIVO

El kit AQUIOS STEM contiene los siguientes reactivos:

- CD45-FITC/CD34-PE del kit AQUIOS STEM: 2 viales
- CD45-FITC/IsoClonic Control-PE del kit AQUIOS STEM: 1 vial
- Viability Dye 7-AAD del kit AQUIOS STEM: 3 viales
- Solución de lisis del kit AQUIOS STEM: 3 viales
- Fluoroesferas STEM-Count del kit AQUIOS STEM: 2 viales

IMPORTANTE: Estos reactivos deben utilizarse de manera conjunta, tal y como se suministran en el kit.

1. El reactivo CD45-FITC/CD34-PE del kit AQUIOS STEM es un reactivo bicolor listo para usar que se suministra en una solución salina tamponada con fosfato (PBS) que contiene 2 mg/mL de albúmina sérica bovina (BSA) y un 0,1 % de azida sódica como conservante.
2. El reactivo CD45-FITC/IsoClonic Control-PE del kit AQUIOS STEM es un reactivo bicolor listo para usar que se suministra en una solución salina tamponada con fosfato (PBS) que contiene 2 mg/mL de albúmina sérica bovina (BSA) y un 0,1 % de azida sódica como conservante. El reactivo CD45-FITC/IsoClonic Control-PE del kit AQUIOS STEM es una mezcla de anticuerpo monoclonal no conjugado y conjugado a PE (idéntico al anti-CD34) (clon 581). Esta mezcla actúa como un control isomorfológico apropiado para verificar la unión inespecífica del AcM anti-CD34-PE.

IMPORTANTE: Los reactivos CD45-FITC/CD34-PE del kit AQUIOS STEM y CD45-FITC/IsoClonic Control-PE del kit AQUIOS STEM no deben utilizarse por separado. Al llevar a cabo las pruebas y los análisis de los controles, debe prestarse especial atención a que ambos reactivos tengan el mismo número de lote en la etiqueta del vial.

Resumen de características de anticuerpos

Especificidad	CD45	CD34
Clon	J33	581
Hibridoma	NS1 x balb/c	NSO x Balb/c
Inmunógeno	Human LAZ 221 ALL cell line	Human KG-1a cell line
Cadena Ig	Cadenas ligeras de IgG1, κ	Cadenas ligeras de IgG1, κ
Especie	Ratón	Ratón
conjugaci	Isotiocianato de fluoresceína (FITC)	R ficoeritrina (PE)
Proporción molar	5,5-7,5 moles de FITC/mol de Ig	0,5-1,5 mol PE/mol Ig
Longitud de onda de excitación	488 nM (azul-verde)	488 nM (azul-verde)
Emisión de fluorescencia	de 504 a 541 nm (principalmente naranja)	de 568 a 590 nm (principalmente naranja)

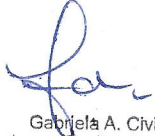
3. Las fluoroesferas STEM-Count del kit AQUIOS STEM consisten en fluoroesferas de poliestireno de 10 μ m (diámetro nominal) en un medio de suspensión acuoso que contiene un tensioactivo y un 1 % de formaldehído. Cada fluoroesfera contiene un tinte que tiene un rango de emisión de fluorescencia de 525 nm a 700 nm cuando se excita a 488 nm. El valor de la concentración de microesferas específica del lote se indica en la etiqueta del vial.
4. El Viability Dye 7-AAD del kit AQUIOS STEM es un reactivo listo para usar suministrado en una solución salina tamponada con fosfato (PBS) que contiene un 1 % de dimetilsulfóxido (DMSO).
5. La solución de lisis del kit AQUIOS STEM es un reactivo que se suministra listo para usar. Una etiqueta adicional situada en el lateral del frasco permite asociar la solución de lisis del kit AQUIOS STEM al número de lote del kit.

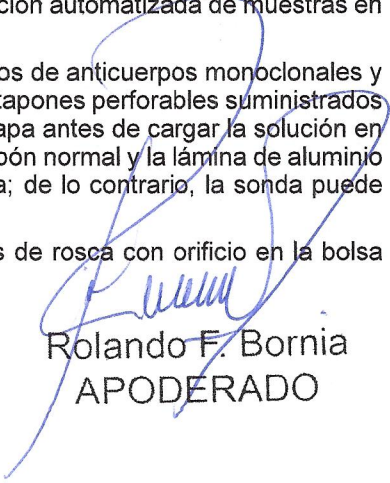
ADVERTENCIAS Y PRECAUCIONES

1. Tras su recepción, retire la solución de lisis del kit AQUIOS STEM y almacénela a temperatura ambiente (de 18 a 25 °C). Almacene los componentes restantes del kit de 2 a 8 °C.
2. Los reactivos del kit AQUIOS STEM están diseñados exclusivamente para la preparación automatizada de muestras en el sistema de citometría de flujo AQUIOS CL.
3. PRECAUCIÓN: existe riesgo de que los instrumentos sufran daños. Para los reactivos de anticuerpos monoclonales y Viability Dye 7-AAD, asegúrese de sustituir los tapones con los que se envían por los tapones perforables suministrados con el envase del reactivo. Para la solución de lisis del kit AQUIOS STEM, retire la tapa antes de cargar la solución en el sistema. Para las fluoroesferas STEM-Count del kit AQUIOS STEM, sustituya el tapón normal y la lámina de aluminio de termosellado por un tapón de rosca con orificio antes de cargarlas en el sistema; de lo contrario, la sonda puede dañarse.
4. Mantenga los tapones perforables (tapones con membrana de goma) y los tapones de rosca con orificio en la bolsa suministrada hasta su uso.

C26036-AB

35 of 231


Gabriela A. Cividino
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5. Los reactivos CD45-FITC/CD34-PE del kit AQUIOS STEM y CD45-FITC/IsoClonic Control-PE del kit AQUIOS STEM contienen un 0,1 % de azida sódica. En condiciones ácidas, la azida sódica produce ácido hidrazoico, un compuesto extremadamente tóxico. Su eliminación a los sistemas de alcantarillado se debe acompañar de grandes cantidades de agua corriente para evitar su acumulación en las tuberías metálicas y posibles explosiones.
6. Las muestras, así como todo el material que entre en contacto con ellas, deben manipularse con cuidado (en particular, utilizando batas, gafas y guantes de protección), ya que pueden transmitir infecciones, y deben desecharse tomando las precauciones adecuadas.
7. Nunca pipetee con la boca y evite el contacto de las muestras o reactivos con la piel y las mucosas.
8. No utilice los reactivos del kit AQUIOS STEM después de la fecha de caducidad indicada en la etiqueta del kit.
9. No exponga los reactivos del kit AQUIOS STEM directamente a la luz o al calor durante su almacenamiento o su utilización.
10. Los reactivos del kit AQUIOS STEM se utilizan directamente del vial. No los divida en alícuotas ni los congele; de lo contrario, pueden generarse resultados erróneos.
11. Evite la contaminación microbiana de los reactivos del kit AQUIOS STEM, ya que puede generar resultados erróneos.
12. El uso de tiempos de incubación o de mezcla, o de temperaturas diferentes a los especificados puede dar lugar a resultados erróneos.
13. Las fluoroesferas STEM-Count del kit AQUIOS STEM contienen un 1 % de formaldehído. Evite el contacto con la piel y los ojos, ya que el formaldehído puede provocar efectos irreversibles en estos tejidos. Evite respirar los vapores emanados. Lleve puesto el equipo de seguridad apropiado, por ejemplo, guantes y gafas protectoras.
14. Debe retirarse toda la lámina de aluminio de termosellado situada en la parte superior del frasco de las fluoroesferas STEM-Count del kit AQUIOS STEM. El aluminio residual reacciona con el formaldehído y puede alterar el aspecto de las fluoroesferas STEM-Count del kit AQUIOS STEM.
15. Las fluoroesferas STEM-Count del kit AQUIOS STEM sedimentarán si transcurren periodos de tiempo prolongados. Asegúrese de que las fluoroesferas estén resuspendidas por completo antes de utilizarlas. Mezcle en vórtice las fluoroesferas STEM-Count del kit AQUIOS STEM durante 10-12 segundos. Evite mezclar en exceso a fin de minimizar la formación de burbujas de aire.
16. Durante el día, cuando se le solicite que vuelva a mezclar las fluoroesferas STEM-Count del kit AQUIOS STEM, retire el tapón de rosca con orificio del frasco y sustitúyalo por el tapón estándar antes de mezclar en vórtice. Después de mezclar, sustituya el tapón estándar por el tapón de rosca con orificio antes de volver a colocarlas en el instrumento.
17. Evite la evaporación y pérdida de las fluoroesferas STEM-Count del kit AQUIOS STEM; de lo contrario, pueden generarse resultados erróneos. Al final del día, retire el frasco del sistema y sustituya el tapón de rosca con orificio por el tapón estándar. Seque la superficie interna del tapón de rosca con orificio con papel de seda, que apenas forma pelusas, antes de guardarlo en la caja del kit. Almacene la caja del kit de 2 a 8 °C hasta el siguiente uso.
18. No refrigere la solución de lisis del kit AQUIOS STEM. La temperatura de almacenamiento es de 18 a 25 °C.
19. Vuelva a tapar el vial de fluoroesferas STEM-Count del kit AQUIOS STEM con el tapón estándar y la solución de lisis del kit AQUIOS STEM cuando no se utilicen para realizar pruebas en el sistema.
20. El marcador de viabilidad 7-AAD contiene un 0,005 % de 7-AAD. El 7-AAD puro puede causar cáncer. Aunque este compuesto se diluye en gran medida, recomendamos que se evite el contacto con la piel y los ojos, y el uso de ropa y guantes de protección adecuados, así como protección facial/ocular.
21. Confirme la finalización del CC superado antes de analizar las muestras clínicas.
22. Revise todos los gráficos de datos y todos los histogramas antes de notificar los resultados. Es posible que los profesionales del laboratorio necesiten realizar una optimización manual para alguna muestra clínica en particular. Consulte el documento «AQUIOS STEM System Guide» (Guía del sistema AQUIOS STEM) para obtener más detalles sobre la estrategia de selección para la citometría de flujo y para consultar los ejemplos de gráficos de datos.
23. Siga las prácticas de laboratorio recomendadas al manipular los reactivos.
24. No haga funcionar el sistema con un vial destapado de reactivo de anticuerpo.
25. Una vez que se ha perforado el tapón con membrana de goma, los viales pueden presentar fugas si no se almacenan en posición vertical.
26. Las muestras, así como todo el material que entre en contacto con el reactivo, deben manipularse como si pudieran de transmitir infecciones y deben desecharse tomando las precauciones adecuadas.

CLASIFICACIÓN DE MATERIAL PELIGROSO SEGÚN EL SGA

AQUIOS STEM Kit 7-AAD ATENCIÓN
Viability Dye

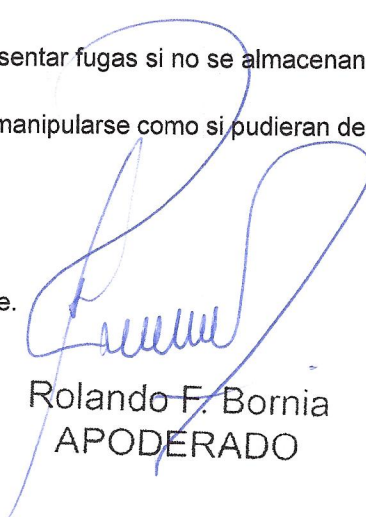
H316

Provoca irritación cutánea leve.

C26036-AB

36 of 231


Gabriela A. Cividino
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Rolando F. Bornia
APODERADO

AQUIOS STEM Kit Lysing Solution	P332+P313	En caso de irritación cutánea: consultar a un médico. Dimetilsulfóxido 1 - 2 %
	ATENCIÓN	
		
AQUIOS STEM Kit STEM-Count Fluorospheres	H315	Provoca irritación cutánea.
	H319	Provoca irritación ocular grave.
	P280	Use guantes, ropa y equipo de protección para los ojos y la cara.
	P337+P313	Si la irritación ocular persiste: consultar a un médico.
		Pirrolidina 1,0 - 1,5 %
	PELIGRO	
		
		
	H315	Provoca irritación cutánea.
	H317	Puede provocar una reacción cutánea alérgica.
	H319	Provoca irritación ocular grave.
	H341	Susceptible de provocar defectos genéticos.
	H350	Puede causar cáncer.
	P201	Procurarse las instrucciones antes del uso.
	P280	Use guantes, ropa y equipo de protección para los ojos y la cara.
	P308+P313	EN CASO DE exposición confirmada o supuesta: consultar a un médico.
	P333+P313	En caso de irritación cutánea o sarpullido: consulte a un médico.
	P337+P313	Si la irritación ocular persiste: consultar a un médico.
		Formaldehído <3 %

SDS La ficha de datos de seguridad está disponible en beckmancoulter.com/techdocs

CONDICIONES DE CONSERVACIÓN Y ESTABILIDAD

Importante: Tras su recepción, retire la solución de lisis del kit AQUIOS STEM y almacénela a temperatura ambiente (de 18 a 25 °C). Almacene los componentes restantes del kit de 2 a 8 °C.

Si ha refrigerado la solución de lisis del kit AQUIOS STEM, lleve la solución a temperatura ambiente (18-25 °C) antes de utilizarla en el citómetro de flujo AQUIOS CL.

Importante: Pueden generarse resultados erróneos si se producen fugas de fluoroesferas STEM-Count del kit AQUIOS STEM. Para su almacenamiento, coloque el tapón estándar sobre las fluoroesferas STEM-Count del kit AQUIOS STEM y almacénelas en posición vertical para impedir cualquier posible fuga.

Los reactivos sin abrir son estables hasta la fecha de caducidad indicada en el vial si se almacenan a la temperatura apropiada y en ausencia de luz. No los utilice después de la fecha de caducidad.

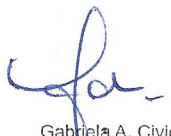
- De 18 a 25 °C para la solución de lisis del kit AQUIOS STEM.
- De 2 a 8 °C para todos los demás reactivos del kit AQUIOS STEM

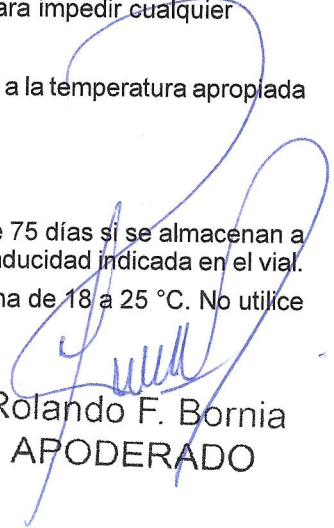
A excepción de la solución de lisis del kit AQUIOS STEM, los viales abiertos son estables durante 75 días si se almacenan a una temperatura de 2 a 8 °C en ausencia de luz. No utilice este reactivo después de la fecha de caducidad indicada en el vial.

El vial abierto de solución de lisis del kit AQUIOS STEM es estable durante 75 días si se almacena de 18 a 25 °C. No utilice el reactivo después de la fecha de caducidad indicada en el vial.

C26036-AB

37 of 231


Gabriela A. Cividino
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M.N. 15202/ M.P. 18093


Rolando F. Bornia
APODERADO

Los reactivos del kit AQUIOS STEM son estables durante un tiempo acumulado de 70 horas cuando se utilizan en el sistema AQUIOS.

Los viales de solución de lisis del kit AQUIOS STEM y los frascos de fluoroesferas STEM-Count del kit AQUIOS STEM deben volver a taparse con sus correspondiente tapones estándar inmediatamente después de utilizarlos y almacenarse a sus correspondientes temperaturas de almacenamiento (véanse las temperaturas indicadas anteriormente).

No congele los reactivos. Vuelva a llevar los reactivos a una temperatura de 2 a 8 °C inmediatamente después de usarlos, excepto el reactivo de lisis del kit AQUIOS STEM, que debe mantenerse de 18 a 25 °C.

SIGNOS DE DETERIORO

Las siguientes situaciones pueden dar lugar al deterioro:

Reactivos del kit AQUIOS STEM, excepto las fluoroesferas STEM-Count del kit AQUIOS STEM

Alteración del aspecto normal tal como se indica a continuación.

Reactivo	Aspecto normal
CD45-FITC/CD34-PE del kit AQUIOS STEM	Líquido transparente, ligeramente rosa
CD45-FITC/IsoClonic del kit AQUIOS STEM	Líquido de transparente a ligeramente rosa
Viability Dye 7-AAD del kit AQUIOS STEM	Líquido transparente, de ligeramente rosa a rojizo
Solución de lisis del kit AQUIOS STEM	Líquido transparente e incoloro

Fluoroesferas STEM-Count del kit AQUIOS STEM

Cualquier posible alteración de su aspecto normal, teniendo en cuenta que su aspecto normal es el de un líquido turbio e incoloro.

Preparación de los Reactivos

Los reactivos del kit AQUIOS STEM se utilizan directamente del frasco, sin necesidad de dilución. Acondicione los reactivos del kit AQUIOS STEM a una temperatura de 18 a 25 °C antes de utilizarlos.

Para las fluoroesferas STEM-Count del kit AQUIOS STEM, retire toda la lámina de aluminio de termosellado situada en la parte superior del frasco antes de utilizarlo por primera vez. Mezcle correctamente (mezcle en vórtice de 10 a 12 segundos) con el tapón estándar colocado y, a continuación, sustituya el tapón estándar por el tapón de rosca con orificio antes de cargar las fluoroesferas en el sistema AQUIOS.

Para el reactivo CD45-FITC/CD34-PE del kit AQUIOS STEM y el reactivo CD45-FITC/IsoClonic Control-PE del kit AQUIOS STEM, así como para el Viability Dye 7-AAD del kit AQUIOS STEM, asegúrese de retirar el tapón suministrado en su envío y sustituirlo por el tapón con membrana de goma suministrado en el envase antes de colocar el vial en el carrusel del sistema.

MANEJO DE MUESTRAS

Requisitos de muestras

1. Consulte el documento «AQUIOS STEM System Guide» (Guía del sistema AQUIOS STEM) para obtener más detalles sobre el volumen mínimo de muestra necesario para el análisis.
2. Recoja la muestra de manera aséptica en un tubo estéril para la recogida de sangre al vacío provisto del anticoagulante adecuado.
3. Las muestras biológicas pueden ser muestras de sangre total periférica recién extraída o movilizada (recogida en heparina, K3EDTA y K2EDTA), médula ósea recién extraída o descongelada (recogida en heparina, K2EDTA, K3EDTA y una mezcla de heparina/ACD-A), productos de aféresis recién extraídos o descongelados (recogidos en una mezcla de heparina/ACD-A y ACD-A) y muestras de sangre del cordón umbilical recién extraída o descongelada (recogida en ACD-A y CPD).
4. Las muestras de sangre total normales son estables durante hasta 20 horas si se almacenan de 18 a 25 °C.
5. Las muestras de sangre total movilizada son estables durante hasta 20 horas si se almacenan de 18 a 25 °C.
6. Las muestras de sangre del cordón umbilical son estables durante hasta 24 horas si se almacenan de 18 a 25 °C.
7. Las muestras de aféresis son estables durante hasta 24 horas si se almacenan de 2 a 8 °C.
8. Las muestras de médula ósea son estables durante hasta 24 horas si se almacenan de 2 a 8 °C.
9. La sangre total periférica recién extraída o movilizada y la sangre del cordón umbilical recién extraída se debe almacenar a temperatura ambiente (de 18 a 25 °C) hasta la tinción (que se debe realizar en un plazo máximo de 24 horas).
10. Los productos de aféresis recién extraídos y los productos de médula ósea recién extraídos se deben almacenar de 2 a 8 °C hasta la tinción (que se debe realizar en un plazo máximo de 24 horas).

11. Antes de la preparación de la muestra, asegúrese de que la concentración de leucocitos (LEU) no sea superior a 30×10^9 LEU/L. Si es necesario, diluya la muestra con un 6 % de albúmina sérica bovina (BSA)-1 x solución salina tamponada con fosfato (PBS). Anote el factor de dilución para el cálculo del recuento absoluto final.
12. Los productos de aféresis congelados, la sangre del cordón umbilical congelada y la médula ósea congelada deben procesarse en un plazo máximo de 15 minutos después de la descongelación y deben mantenerse en hielo. Se recomienda analizar las muestras descongeladas utilizando la función de cargador de tubo único del AQUIOS CL.
13. La dilución de las muestras debe realizarse con un tampón enriquecido con proteínas (por ejemplo, 6 % de albúmina sérica bovina [BSA]-1 x solución salina tamponada con fosfato [PBS]).

Procedimiento de Tratamiento de los Especímenes

La prueba AQUIOS STEM se realiza de conformidad con el documento «The ISHAGE guidelines for CD34+ cell determination by flow cytometry» (Directrices de la ISHAGE para la determinación de células CD34+ mediante citometría de flujo) (1).

Consulte el documento «AQUIOS STEM System Guide» (Guía del sistema AQUIOS STEM) para obtener más detalles.

CONTENIDO

El conservante de azida sódica puede formar compuestos explosivos en las tuberías metálicas del desagüe. Véase el NIOSH Bulletin: Explosive Azide Hazard (Boletín de NIOSH: Peligro de explosión con la azida) (16/8/76).

Para evitar la posible acumulación de compuestos de azida, limpie con agua los tubos de desagüe tras la eliminación del reactivo sin diluir. Para desechar la azida sódica deben seguirse las normativas locales adecuadas.

MATERIALES NECESARIOS PERO NO SUMINISTRADOS CON EL KIT:

1. Células de control CD34 AQUIOS STEM de nivel 1 y nivel 2 (Ref. C43667)
2. Flow-Check Fluorospheres (Ref. 6605359)
3. Solución envolvente AQUIOS (Ref. B25697)
4. Placas de 96 pocillos profundos AQUIOS (Ref. B23502)
5. Agente de limpieza AQUIOS (Ref. B25698)
6. Hipoclorito de sodio AQUIOS (Ref. B23536)
7. Tubos para la recogida de sangre provistos de anticoagulante
8. Tampón enriquecido con proteínas (por ejemplo, 6 % de albúmina sérica bovina (BSA)-1 x solución salina tamponada con fosfato [PBS])
9. PBS (Ref. 6603369)
10. Mezclador de tipo vortex
11. Sistema AQUIOS CL con la aplicación STEM

CÁLCULO DE LAS CPH CD34+ Y CD45+ VIABLES Y DEL PORCENTAJE DE CD34

Consulte el documento «AQUIOS STEM System Guide» (Guía del sistema AQUIOS STEM) para obtener más detalles sobre la determinación de las células madre CD34+ viables (células/ μ L y porcentaje) y CD45+ viables (células/ μ L).

CONTROL DE CALIDAD

El control de calidad diario es un componente crítico para garantizar el rendimiento del sistema para la aplicación STEM. Consulte el documento «AQUIOS STEM System Guide» (Guía del sistema AQUIOS STEM) y las IFU de las células de control para obtener más detalles.

RENDIMIENTO

Consulte el documento «AQUIOS STEM System Guide» (Guía del sistema AQUIOS STEM) para obtener más detalles sobre los intervalos de referencia, la linealidad, la comparación de procedimientos de medición, la precisión y los intervalos de medición analítica.

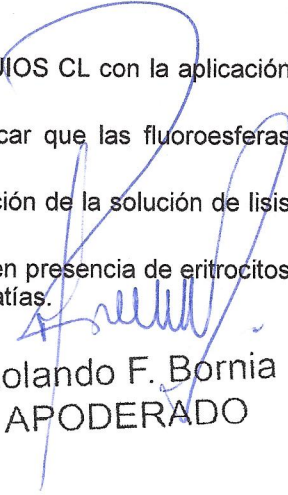
LIMITACIONES

1. Los reactivos del kit AQUIOS STEM son para uso exclusivo en los citómetros de flujo AQUIOS CL con la aplicación STEM.
2. La adición de disolventes orgánicos o de soluciones de fuerza iónica alta puede provocar que las fluoroesferas STEM-Count del kit AQUIOS STEM se hinchen o se agreguen irreversiblemente.
3. La acetazolamida, un inhibidor de la anhidrasa carbónica, puede inhibir por completo la acción de la solución de lisis del kit AQUIOS STEM (20).
4. Es posible que no se lisen por completo todos los eritrocitos en las siguientes situaciones: en presencia de eritrocitos nucleados, una concentración anómala de proteínas, coágulos sanguíneos o hemoglobinopatías.

C26036-AB

39 of 231


Gabriela A. Cividino
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FARMACÉUTICA
M.N. 15202/ M.P. 18093


Rolando F. Bornia
APODERADO

5. No diluya, divida en alícuotas o congele los reactivos del kit AQUIOS STEM. Utilice los reactivos tal y como se suministran en sus correspondientes envases.
6. Si es necesario realizar un segundo análisis de una muestra descongelada, prepare siempre la muestra a partir de un vial congelado nuevo para realizar las pruebas adicionales, ya que la estabilidad de las muestras congeladas es limitada.
7. Las muestras descongeladas deben analizarse solas, cuando no se estén analizando otras muestras en AQUIOS.
8. Algunos pacientes pueden presentar problemas especiales debido a los recuentos alterados o muy bajos de determinadas poblaciones celulares.
9. Si el láser en el citómetro de flujo está desalineado o las puertas (gates) están ajustadas incorrectamente, los resultados obtenidos con la citometría de flujo pueden ser erróneos.
10. Una muestra hemolizada o una muestra lipémica no serían apropiadas para la prueba.

MARCAS COMERCIALES

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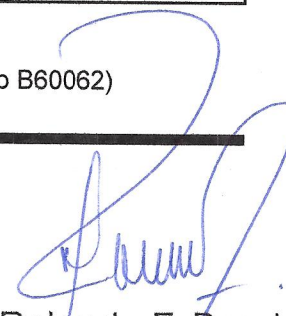
HISTORIAL DE REVISIONES

REVISIÓN AA:	
Creación	

Lista de símbolos

El glosario de símbolos está disponible en beckman.com/techdocs (número de documento B60062)


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AQUIOS STEM CD34

Células de control

REF C43667: Nivel 1 (15 pruebas)
y Nivel 2 (15 pruebas)

Ref. C43554-AA



IVD

USO PREVISTO

Las células de control AQUIOS STEM CD34 Nivel 1 y Nivel 2 son dispositivos médicos de diagnóstico in vitro destinados a ser utilizados por los profesionales de laboratorio como controles de proceso para la verificación de los parámetros CD34 y CD45 como parte del sistema AQUIOS STEM en el sistema automatizado de citometría de flujo AQUIOS CL.

Las células de control AQUIOS STEM CD34 son preparaciones líquidas de leucocitos humanos estabilizados (linfocitos, monocitos y granulocitos) y eritrocitos que tienen propiedades de lisado, dispersión de luz, expresión de antígenos y tinción de anticuerpos representativas de las que se encuentran en las muestras de sangre humana completa.¹

El kit contiene 2 niveles de controles de células positivas CD34 con aproximadamente 10 células CD34+/µl (nivel 1) y aproximadamente 30 células CD34+/µl (nivel 2) que se procesan de la misma manera que la sangre completa. Esto permite verificar el rendimiento de la aplicación. Las células de control AQUIOS STEM CD34 Nivel 1 y Nivel 2 son controles cuantitativos que se utilizan en combinación con el kit AQUIOS STEM como parte del sistema AQUIOS STEM, para realizar el seguimiento de pacientes que se preparan para un trasplante de células progenitoras hematopoyéticas autólogas o alogénicas, y de donantes que se someten a esquemas de movilización o recolección para trasplantes de células progenitoras hematopoyéticas autólogas o alogénicas.

USUARIO PREVISTO

Este producto está previsto para el uso profesional en laboratorio.

RESUMEN Y EXPLICACIÓN

El análisis de inmunofenotipado mediante citometría de flujo proporciona una evaluación exacta de células diana en muestras de sangre completa y otros tipos de muestra. Las muestras de sangre completa se tiñen con anticuerpos monoclonales y los eritrocitos se lisan antes del análisis con citometría de flujo. Se requiere un control celular positivo para verificar el rendimiento del reactivo, métodos de preparación de muestras, así como procedimientos de tinción, y debe imitar una muestra de sangre completa representativa en términos de rendimiento de anticuerpo monoclonal, lisis de eritrocitos y análisis con citometría de flujo.

Las células de control AQUIOS STEM CD34 están diseñadas para distinguir las células progenitoras CD34+ en función de las propiedades de dispersión y la expresión del antígeno CD34 siguiendo el protocolo ISHAGE.^{2,3,4} Las células de control Nivel 1 y Nivel 2 proporcionan valores de referencia que abarcan los

niveles de decisión clínica para la movilización de células progenitoras dentro de los intervalos de la hoja de ensayo.

FUNDAMENTOS DE LA DETERMINACIÓN

Las células de control AQUIOS STEM CD34 constan de dos componentes principales: leucocitos y eritrocitos. Los leucocitos actúan como el componente celular positivo de las células de control AQUIOS STEM CD34 y tienen antígenos de superficie presentes en las células diana que se unen al componente de anticuerpo de los reactivos de los reactivos del kit AQUIOS STEM. Los eritrocitos actúan como el componente lisable de las células de control AQUIOS STEM CD34. El análisis con citometría de flujo de las muestras teñidas y lisadas determina el porcentaje y el recuento absoluto de las células diana. Los resultados previstos se determinan en sistemas validados AQUIOS CL.

REACTIVOS

Las células de control AQUIOS STEM CD34 Nivel 1 y Nivel 2 contienen leucocitos y eritrocitos humanos estabilizados en un medio de conservación.

ADVERTENCIAS

SDS Puede descargar la hoja de datos de seguridad en beckman.com/techdocs.

1. MATERIALES CON PELIGRO BIOLÓGICO

Cada unidad de donante utilizada en la preparación de este material se comprobó mediante un método aprobado por la FDA para verificar la presencia de anticuerpos del virus de inmunodeficiencia humana (VIH 1, VIH 2), del RN del VZK y del virus de la hepatitis C (VHC), así como del antígeno de superficie del virus de la hepatitis B (HBsAg) y de la enfermedad de Chagas, y resultó negativa (no fueron reactivos repetidamente). Puesto que ningún método de ensayo puede ofrecer una garantía completa de la ausencia de VIH, VHC, virus de la hepatitis B (VHB), enfermedad de Chagas u otros agentes infecciosos, este reactivo debe manipularse con el nivel de bioseguridad 2, tal como se recomienda para cualquier muestra de sangre o suero humano potencialmente infeccioso en el manual de los Centros para el Control y la Prevención de Enfermedades y el Instituto Nacional de la Salud de EE. UU. "Biosafety in Microbiological and Biomedical Laboratories" (Bioseguridad en laboratorios microbiológicos y biomédicos).⁵

2. Nunca pipetee con la boca y evite el contacto de muestras con la piel y las membranas mucosas.
3. No congele los reactivos.
4. Evite la contaminación microbiana del reactivo, ya que podrían producirse resultados erróneos.
5. Utilice las prácticas de laboratorio recomendadas (GLP) al manipular este reactivo.
6. Siga los procedimientos recomendados para alcanzar resultados óptimos.
7. Reduzca al mínimo la exposición a la luz durante los procesos de manipulación, lisado, tinción y adquisición.
8. Asegúrese de que se han seleccionado los protocolos correctos y de que se aplique la configuración correcta al respectivo proceso.
9. El producto no debe desecharse como un residuo general, sino con los residuos médicos infecciosos.
10. El producto se ha diseñado para su uso tal como se suministra. La adulteración mediante dilución o adición de cualquier material al vial del producto invalida todo uso diagnóstico que se realice del producto.

ALMACENAMIENTO Y ESTABILIDAD

No utilice el reactivo después de la fecha de caducidad que se indica en la etiqueta del vial. Los reactivos sin abrir son estables hasta la fecha de caducidad indicada en la etiqueta del frasco cuando se almacena a 2-8 °C. El reactivo abierto es estable durante un máximo de 30 días si se conserva a una temperatura de 2-8 °C. No lo congele.

SIGNOS DE DETERIORO

Si los valores de las células de control AQUIOS STEM CD34 no están dentro de la escala anticipada en la hoja de ensayo:

1. Revise el prospecto del producto de control, la hoja de análisis y los procedimientos de funcionamiento del instrumento.
2. Compruebe la fecha de caducidad del frasco del producto. Deseche los productos caducados.
3. El agrupamiento de la suspensión celular indica inestabilidad o deterioro, en cuyo caso no se debe usar el reactivo.
4. Analice un vial sin abrir de células de control AQUIOS STEM CD34. Si los resultados aún están fuera de la escala anticipada, póngase en contacto con un representante local de Beckman Coulter.

PROCEDIMIENTO

1. Para cada nuevo lote de controles, seleccione el botón de código de barras en la pantalla principal del software AQUIOS y escanee el código de barras de la hoja de ensayo para cargar los valores del ensayo.

NOTA: En caso de un fallo del código de barras, consulte la sección **INTRODUCCIÓN MANUAL DE LOS VALORES DEL ENSAYO** a continuación. Asegúrese de que la alineación diaria del sistema con fluoroesferas Flow-Check es correcta antes de ejecutar las células de control. Consulte la AQUIOS STEM System Guide (Guía del sistema AQUIOS STEM) para obtener información detallada sobre los procedimientos de alineación y CC.

2. Cuando utilice la prueba AQUIOS STEM, lleve el reactivo de control y el anticuerpo a 18-25 °C.
3. Gire o invierta con suavidad el reactivo de control para mezclar el producto de un modo similar a la manipulación de una muestra de sangre completa (no se recomienda mezclar con un vórtex o con rotador).
4. Para crear una solicitud de CC, utilice el menú desplegable Test (Prueba) para seleccionar la prueba deseada. Seleccione «Stem Single» (Stem individual), de lo contrario se activará el aviso «Missing QC» (CC ausente). Escanee el código de barras del tubo de control y toda la información se rellenará automáticamente.
5. CARGUE los controles, sin quitar los tapones, en el sistema AQUIOS CL.
 - En el cargador automático, inserte los tubos de control en el casete del instrumento (casete Tipo 1, Ref. B25218) y coloque el casete en el sistema.
 - En el cargador de un solo tubo, mezcle el control inmediatamente antes de colocar el tubo en el área de muestreo del tubo. Escanee el tubo y colóquelo en el sistema.
6. GO se inicia automáticamente cuando los controles se sitúan en el sistema.
 - En el cargador automático, el sistema procesa los controles cuando se carga el casete.
 - En el cargador de un tubo, el sistema procesa el control cuando se cierra la puerta.
7. Deje que el sistema prepare los controles y realice el análisis.
8. Cuando el sistema haya procesado el tubo, guarde los controles en posición vertical en el refrigerador.

INTRODUCCIÓN MANUAL DE LOS VALORES DEL ENSAYO:

1. Seleccione Setup (Configuración).
2. Seleccione Reagent Info (Información de reactivo).
3. Seleccione Stem Single Test (Prueba de Stem individual).
4. Seleccione AQUIOS STEM CD34 Control Cells (Células de control AQUIOS STEM CD34) de la lista desplegable Reagent/Sample (Reactivo/Muestra).
5. Seleccione Edit (Editar).

Rolando F. Bornia
APODERADO

6. Seleccione el Lot Number (Número de lote) en la lista desplegable Lot Number (Número de lote) o haga clic en + para agregar un nuevo Lot Number (Número de lote).
7. Introduzca la fecha de caducidad.
8. Introduzca los valores de la hoja de ensayo en las columnas Min (Min.) y Max (Máx.) de la tabla.

NOTA: Para las entradas manuales, los porcentajes deben introducirse como decimales, tal como se indica en la hoja de ensayo.

9. Seleccione Save (Guardar).

Consulte las AQUIOS CL Flow Cytometer Instructions for Use (IFU) (Instrucciones de uso [IFU] del citómetro de flujo AQUIOS CL), para obtener información detallada sobre el registro de valores de control.

MATERIALES NECESARIOS, PERO NO SUMINISTRADOS

Sistema de citometría de flujo AQUIOS CL

Software AQUIOS STEM

Kit AQUIOS STEM

Fluoróscopos Flow-Check

RESULTADOS PREVISTOS

Los valores del ensayo se determinan utilizando el sistema de citometría de flujo AQUIOS CL con los reactivos del kit AQUIOS STEM y el software AQUIOS STEM. En estas condiciones, los valores recuperados deben estar dentro de la escala anticipada indicada. Cada laboratorio debe establecer sus propios valores de ensayo e intervalos esperados para cada antígeno analizado que reflejen las condiciones y protocolos específicos del laboratorio. Estos valores del ensayo de control establecidos deben estar dentro de los rangos esperados publicados en las hojas de ensayo específicas del lote.

La participación en el Interlaboratory Quality Assurance Program (IQAP o Programa de Sistemas de Calidad entre Laboratorios) de Beckman Coulter ofrece una comparación para laboratorios externos y permite mejorar el programa de garantía de calidad de un laboratorio. Consulte Interlaboratory Quality Assurance Program, Cytometry (Programa de garantía de calidad interlaboratorios, citometría) Ref. 4206384 para obtener información detallada.

IMPORTANTE: NO mueva las regiones.

Los datos presentados representan el rendimiento previsto para el sistema AQUIOS STEM.

El Nivel 1 y el Nivel 2 de las células de control AQUIOS STEM CD34 siguen la misma estrategia de creación de ventanas de selección secuencial. Los siguientes gráficos muestran la estrategia de creación de ventanas de selección secuencial para el Nivel 2 de las células de control AQUIOS STEM CD34.

Figura 1. Este histograma está seleccionado en «Cells and No Beads» (Células y sin esferas). El gráfico 7-AAD frente a SS identifica las células viables basadas en la tinción negativa con 7-AAD. Sin embargo, en el caso de las células de control AQUIOS STEM CD34, al tratarse de células estabilizadas, la región rectangular «!VIABLE» (Viable) de este gráfico se amplía para crear la ventana de selección al total de eventos teñidos por 7-AAD.

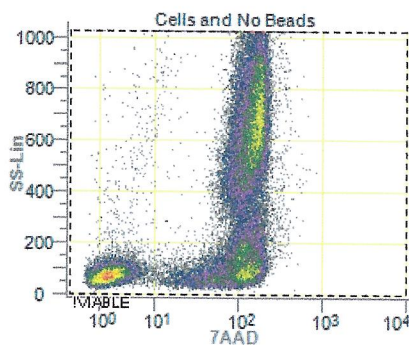


Figura 2. Este histograma está seleccionado en «Cells and No Beads» (Células y sin esferas) y la región «!VIABLE» (Viable). El primer gráfico 45/SS aísla los leucocitos («Leuks») y proporciona un segundo nivel de creación de ventanas de selección. Se dibuja una región de ventana de selección automática («Lymphs») alrededor de la población de linfocitos. Esta ventana de selección se utiliza para eliminar los residuos. Las células CD34+ se resaltan en rojo. El cálculo del recuento de leucocitos viables (células/uL) se realiza a partir de la región «LEUKS».

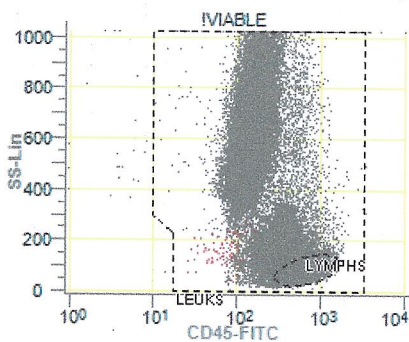


Figura 3. Este histograma está seleccionado en «Cells and No Beads» (Células y sin esferas) y las regiones «!VIABLE» (Viable) y «LEUKS». Un gráfico en SS/CD34 permite aislar los leucocitos que son positivos para CD34 («CD34Pos»).

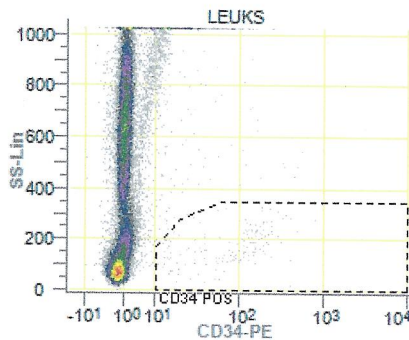


Figura 4. Este histograma está seleccionado en «Cells and No Beads» (Células y sin esferas) y las regiones «!VIABLE» (Viable), «LEUKS» y «CD34 POS». Se produce un nivel adicional de ventana de selección en un segundo gráfico SS/CD45. La región «CD45 DIM» se ajusta alrededor de los eventos CD45 DIM.

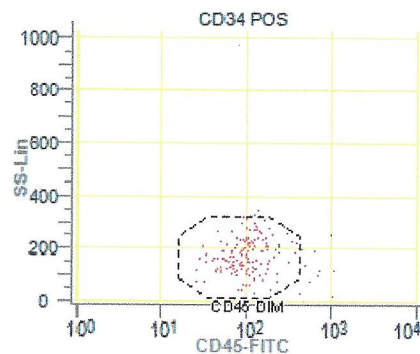
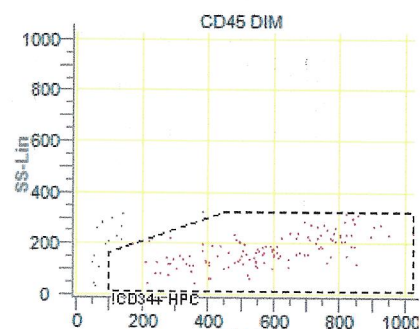


Figura 5. Este histograma está seleccionado en «Cells and No Beads» (Células y sin esferas) y las regiones «!VIABLE» (Viable), «LEUKS», «CD34 POS» y «CD45 DIM».

La región «!CD34+HPC» identifica un grupo de eventos que cumplen todos los criterios de fluorescencia y dispersión de luz de las directrices ISHAGE para CD34+ HPC viables. El cálculo de las células madre (recuento de CD34+ HPC viables [células/uL]) se realiza a partir de esta última región.



LIMITACIONES

1. Pueden producirse resultados erróneos si el citómetro de flujo no está correctamente alineado o estandarizado para fluorescencia o si las poblaciones celulares se han seleccionado incorrectamente.
2. Es posible que los resultados determinados con citómetros de flujo, sistemas de lisis o anticuerpos que sean diferentes de los utilizados para determinar los resultados previstos, no se encuentren dentro de la escala anticipada.
3. No se recomienda el uso de células de control AQUIOS STEM CD34 con anticuerpos dirigidos a los epítopos de clase I y clase II de CD34.

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DISPONIBILIDAD DEL PRODUCTO

Células de control AQUIOS STEM CD34

 C43667: Nivel 1 (15 pruebas) y Nivel 2 (15 pruebas)

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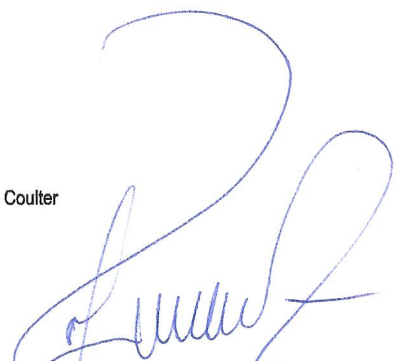
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