Software Validation Pack

PA 800 *plus*
Pharmaceutical Analysis
System

BECKMAN
COULTER

Software Validation Pack
PA 800 *plus* Pharmaceutical Analysis System
PN A79486AB (February 2011)

Trademarks:
Following is a list of Beckman Coulter trademarks:

- Beckman Coulter®

- 32 Karat™

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Find us on the World Wide Web at:
www.beckmancoulter.com and www.CELeader.com

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Revision History

First Revision, A79486AB, February 2011

32 Karat Software version 9.1 patch

PA 800 *plus* Software version 1.1 patch

PA 800 *plus* Firmware version 9.2

Revised corporate address

Numerous syntax and grammatical edits

Initial Issue, A79486AA, April 2009

32 Karat Software version 9.1

PA 800 *plus* Software version 1.1

PA 800 *plus* Firmware version 9.0

A79486AB

Symbols and Labels

Introduction

The following is a description of symbols and labels used on the Beckman Coulter PA 800 *plus* Pharmaceutical Analysis System or shown in this manual.

> ⚠ **WARNING**
>
> **If the equipment is used in a manner not specified by Beckman Coulter, Inc., the protection provided by the instrument may be impaired.**

General Biohazard Symbol

This caution symbol indicates a possible biohazard risk from patient specimen contamination.

A011460L.PNG

Caution, Biohazard Label

This caution symbol indicates a caution to operate only with all covers in position to decrease risk of personal injury or biohazard.

CAUTION
TO REDUCE RISK OF PERSONAL INJURY,
OPERATE ONLY WITH ALL COVERS IN PLACE.

456161-B

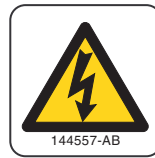A011459L.EPS
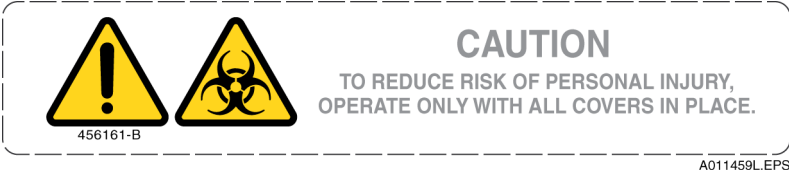
Caution, Moving Parts Label

This caution symbol warns the user of moving parts that can pinch or crush.

A015081L.EPS

High Voltage Electric Shock Risk Symbol

This symbol indicates that there is high voltage and there is a risk of electric shock when the user works in this area.

A016352L.EPS

Class 1 Laser Caution Label

A label reading "THIS PRODUCT CONFORMS TO APPLICABLE REQUIREMENTS OF 21 CFR 1040 AT THE DATE OF MANUFACTURE" is found near the Name Rating tag. The laser light beam is not visible.

A016350L.EPS

Sharp Object Label

A label reading "CAUTION SHARP OBJECTS" is found on the PA 800 *plus*.


A016351L.EPS

Recycling Label

This symbol is required in accordance with the Waste Electrical and Electronic Equipment (WEEE) Directive of the European Union. The presence of this marking on the product indicates:

1. The device was put on the European Market after August 13, 2005.

2. The device is not to be disposed of via the municipal waste collection system of any member state of the European Union.
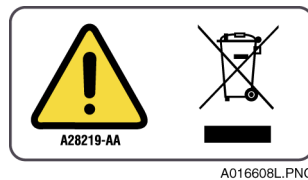
It is very important that customers understand and follow all laws regarding the proper decontamination and safe disposal of electrical equipment. For Beckman Coulter products bearing this label, please contact your dealer or local Beckman Coulter office for details on the take back program that facilitates the proper collection, treatment, recovery, recycling, and safe disposal of this device.

Disposal of Devices Containing Mercury Components
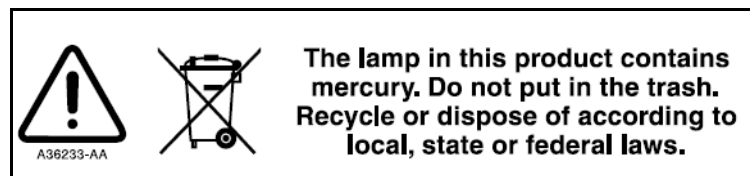
This product contains a mercury-added part. Recycle or dispose of according to local, state, or federal laws. It is very important that you understand and comply with the safe and proper disposal of devices containing mercury components (switch, lamp, battery, relay, or electrode). The mercury component indicator label can vary depending on the type of device.

Restriction of Hazardous Substances (RoHS) Labels

These labels and materials declaration table (the Table of Hazardous Substance's Name and Concentration) are to meet People's Republic of China Electronic Industry Standard SJ/T11364-2006 "Marking for Control of Pollution Caused by Electronic Information Products" requirements.

RoHS Caution Label

This logo indicates that this electronic information product contains certain toxic or hazardous elements, and can be used safely during its environmental protection use period. The number in the middle of the logo indicates the environmental protection use period for the product. The outer circle indicates that the product can be recycled. The logo also signifies that the product should be recycled immediately after its environmental protection use period has expired. The date on the label indicates the date of manufacture.

RoHS Environmental Label

This logo indicates that the product does not contain any toxic or hazardous substances or elements. The "e" stands for electrical, electronic, and environmental electronic information products. This logo indicates that this electronic information product does not contain any toxic or hazardous substances or elements, and is green and is environmental. The outer circle indicates that the product can be recycled. The logo also signifies that the product can be recycled after being discarded, and should not be casually discarded.

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Alerts for Warning, Caution, Important, and Note

⚠ **WARNING**

WARNING indicates a potentially hazardous situation which, if not avoided, could result in death or serious injury. The warning can be used to indicate the possibility of erroneous data that could result in an incorrect diagnosis (does not apply to all products).

⚠ **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. The caution can be used to indicate the possibility of erroneous data that could result in an incorrect diagnosis (does not apply to all products).

IMPORTANT IMPORTANT is used for comments that add value to the step or procedure being performed. Following the advice in the IMPORTANT notice 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 installation, use, or servicing of this equipment.

Contents

Contents

System Overview

Identification

32 Karat Workstation Software, Version 9.1 software patch was released April 2009. The software version can be confirmed by selecting **Help > About 32 Karat** on the File Menu of the 32 Karat Software. The 32 Karat Workstation Software, Version 9.1 software patch was released February 2011. To check for the patch version of the software, navigate the following path: **Programs > 32 Karat > Software Qualification**.

Intended Use

32 Karat Software is intended to be used as a single-point controller for Beckman Coulter PA 800 *Enhanced* and PA 800 *plus* systems and as a general chromatography data system for CE instruments supplying analog data outputs. The history is included above.

General Description

The 32 Karat Software, Version 9.1 software package runs on the Windows XP operating system. It incorporates instrument control for Beckman Coulter PA 800 *Enhanced* and PA 800 *plus* systems with complete data acquisition, analysis, reporting and archiving capabilities.

The following general functions are provided:

Control - Bi-directional communication with Beckman Coulter's hardware modules is accomplished through a GPIB communications adapter. Software features include automatic system configuration, automatic systems shutdown, configurable instrument status and control, system suitability.

Acquisition - Data acquisition from Beckman Coulter's hardware is accomplished digitally via the GPIB communication bus. There is no analog to digital or digital to analog conversion; the hardware communicates with the PC hosting 32 Karat Software via an RS422 protocol. Data acquisition from other manufacturers' equipment is accomplished through an analog to digital converter 35900E device. Software features include real time system status and electropherogram display, audit trails for method and data files and acquisition of three dimensional diode array data.

Analysis - Software features include reliable integration algorithms with graphical or automatic setup, peak identification with reference peaks, up to 10 level linear or nonlinear calibrations, statistical analysis of batch runs and system suitability calculations.

Reporting - Software features include a completely user customizable report or pre-formatted report types, the ability to incorporate objects such as company logos into report templates, and results sign-off.

Compliance Features

Features designed to assist the regulated laboratory in recording and providing documentation for compliance include the following:

- Key information, such as date/time, operator name, method used for collection, instrument configuration, original results, and audit trail is saved in a single inseparable raw data file.
- All methods include both data acquisition and analysis parameters as well as instrument conditions when used with Beckman Coulter PA 800 *Enhanced* and PA 800 *plus* instruments.
- The software provides controls to prevent overwriting of data files, method and data file audit trails, and results sign-off.
- Each method has an embedded audit trail stream where every change to the method is logged to identify the parameter that was changed and the old and new values along with the operator name, time and date.
- The software provides data files, methods, and audit trails in human readable and electronic forms suitable for inspection review and copying.
- The 32 Karat software system authenticates users based on both user name and password security. Rights to each function are assigned per individual by the system administrator.
- The 32 Karat software system provides an electronic signature feature which records the printed name of the signer, the date and time the signature was executed, and the meaning of the signing. The identification of the signer is confirmed using a combination of user identification and password. The authority of signature is granted by the system administrator.
- The software system does not allow two users to have the same user name and password.
- In 32 Karat software, records are in checksum and cannot be changed without revoking the signature, all of which is recorded in the audit trail. This checksum prevents the signature from being copied to another file.
- System Suitability parameters are calculated and stored as evidence of the proper system performance.
- System activity and error conditions are reported in a printable log.

Customer Base

32 Karat software is installed in commercial, academic and governmental research, analytical services, and quality control laboratories worldwide.

Product History

PA 800 *plus* Development/Release History

The PA 800 instrument was introduced in June 2003. The PA 800 *Enhanced* Protein Characterization System was introduced in December 2008, and the PA 800 *plus* Pharmaceutical Analysis System was introduced in April 2009.

32 Karat Software, Version 7.0 April 2003

This is the original software release for the PA 800 system. Major features include:

- The system runs with full functionality on Windows 2000.
- Supports PA 800 instruments and its applications. Applications include: peptide mapping, carbohydrate analysis, isoelectric focusing, and SDS-Gel MW analysis.
- Any combination of PA 800, MDQ and HPLC components up to four are allowed, with the single limitation that the total number of HPLC PDA detectors on a workstation may not exceed two (four PA 800 PDA detectors may be used.)

Version 8.0 June 2006

The following features were added:

- A USB flash drive license is now used. The software licenses for previous versions were installed from a diskette and have been replaced by a USB hardware license. This license is portable and does not require uninstalling.
- Range annotations for Groups have been enhanced. In addition, there was no range bar that displayed the range of the group. This new feature will display the group name only once, at the right side of the range bar of the group. The start, stop, and position of the range bar can be graphically updated. The changes are reflected in the Group Table.
- Graphical adjustments of retention time window (annotated as RT Window) has been enhanced. The user can graphically change the RT Window's start, stop and position, using the graphical toolbar icons at the bottom of the instrument screen. The changes are then reflected in the Peak Table.
- Post-export user program has been enhanced. Users can now launch custom programs at the very end of the post-run acquisition. This allows users to export data, and then have the custom program look at the exported information.
- Mandatory Audit Trails have been enhanced to allow turn on audit trailing on a project-by-project basis, through the System Administration Wizard, for methods and sequences. This enhancement allows the user to also activate the audit trails on a project by project basis.
- Default project lockout has been added. This enhancement makes it possible to create new projects even if the Default project is missing. This feature also allows creation of new projects even when the Default/Template directory has been deleted.
- Peak centroid calculation has been added. This feature calculates the "mean" time for the area of a peak.
- Single user login has been added. This feature allows the user's login (domain or local) to be associated with instruments and projects. A login can also be specified so that a user can login once to an instrument, then not be required to log into any other instruments.

This feature allows users to:

— Login to the first instrument, then not have to login to any others; they would just open.

— Use their computer login in place of the instrument/project login.

- In PA 800, the Qualitative Analysis Report has been enhanced in the following three areas; 1) the Y axis is on scale; 2) the type of curve fit now matches the line drawn; and 3) mobility values have sufficient decimal units to show a significant mobility value.

- In PA 800, the units for drift in the Suitability set up table and in the report are now Drift/Min.

- In PA 800, the sequence wizard has been enhanced so when the Advance box is unchecked, the outlet vial does not advance for the calibration vial. When the Advance box is checked, the outlet vial does advance for the calibration vial.

- In PA 800, mobility values calculated with the LIF detector are now in the same units as the mobility values for the UV and PDA detector.

Version 9.0 December 2008
The following features were added:

32 Karat version 9.0 Improvements

- The 32 Karat version 9.0 Software supports only PA 800 *Enhanced* series instruments.

- You can open and process method, sequence, data, and template files from previous versions. However, once you create or open a file using version 9.0, you cannot reopen it using a version prior to 9.0.

- The design takes advantage of Windows XP environment and uses the Window XP look and feel. This includes Windows XP styling for toolbars, dialog boxes, and icons, with an Outlook 2003 navigation pane to access software functionality.

- The user interface layout allows greater graphical consistency. This release includes:

— New default color scheme

— More consistent menu behavior

— Improved user interface for graphical integration

- The on-screen help for certain functions has been reformatted and expanded. For example, several functions have additional messages in small text in the data window or in the status bar at the bottom of the screen, while other functions have new pop-up windows with instructions.

- The export feature now includes a customized graphical depiction of the electropherogram in a scalable (wmf) graphics format.

- You can add the following new annotations to an electropherogram: Group #, Area, Area Percent, Start Time, End Time, ESTD Concentration, ISTD Concentration, and NORM Concentration.

- A new system administration report utility can display the configuration for project settings, users and permission, instrument configurations, and enterprise-wide settings.

- A new sequence table report can print sequence table information in a more condensed fashion, including a format that limits the printout to the width of a single page. You can also select specified columns, change column widths, and print columns separately or as a group.

- This version adds support for multi-level bracketed calibrations.

- You can now stop a run independent of the sequence.

- Baseline File has been added as a new sequence run type. This feature is not currently supported.

- You can specify either peak or system-wide custom parameters on a run-by-run basis. These parameters are not used in any intrinsic calculations, but are available as graph annotations, for export, in custom parameters and in advanced reports.

- To improve the speed of connection to large domains, you can now enter a name to quickly select a user.

- With PDA detection, you can specify a reference channel for subtraction from selected multielectropherogram data.

- System administrators can now predefine reasons for audit trails that users can select while setting up audit trails. You can also provide customized reasons.

- The PA 800 *Enhanced* system can perform longer capillary rinses at up to 100 psi. Select **For Capillary Fill** on the 32 Karat Inject screen to access this feature. You can enter a pressure up to 100 psi and a duration up to 999 seconds. This feature is ideal for applications such as capillary isoelectric focusing in which you fill the entire capillary volume. This release also identifies injections as sample events when performing an injection instead of a rinse, thereby simplifying reports and sample incrementing the sequence.

- This release has enhanced error messages that include suggestion for addressing the errors.

PA 800 *plus* version 1.0 Initial Release

This release of 32 Karat includes the addition of a new software interface called PA 800 *plus* software. The PA 800 *plus* software interfaces to the 32 Karat software and simplifies routine operation of the PA 800 *Enhanced* system.

Version 9.1 April 2009
The product continues to support the PA 800 *Enhanced* Protein Characterization System and now the PA 800 *plus* Pharmaceutical Analysis System. Both instruments require firmware version 9.0

32 Karat version 9.1 Improvements

- The 32 karat Help System was updated, broken links fixed, and missing content filled in.

- Instrument error messages were reviewed and updated to present more information.

- The LIF Calibration Wizard was improved to be more reliable.

- Training videos were added and can be accessed from shortcuts on the desktop.

PA 800 *plus* version 1.1 Improvements.

- The PA 800 *plus* Help System was updated with more content.

- Increased the Run task graph to display more trace colors.

- Training videos were added and a video viewer was built in.

- Cosmetic changes were made to improve the appearance.

- Corrections were made to fix software errors that most users would not typically run across, but have been fixed to prevent possibility of occurrence.

Version 9.1 Software Patch February 2011
The product continues to support the PA 800 *Enhanced* Protein Characterization System and PA 800 *plus* Pharmaceutical Analysis System. Both instruments require firmware version 9.0 or later.

32 Karat version 9.1 Software Patch Fixes

- The 32 Karat abnormal termination issue caused by mismatching of the Caesar option instrument configuration has been corrected. This issue would occur when a data file was acquired or analyzed in an instrument with the Caesar configuration option disabled, and then opened in an instrument with the Caesar configuration option enabled. Abnormal termination might also occur when reprocessing a sequence with mismatching Caesar configuration data files.

- The 32 Karat will now display a warning dialog box during the opening of a data file if the instrument has been configured with more than one detector. This issue would occur with analyzed data acquired on an instrument previously configured with an SS420x A/D converter accessory, or on an HPLC system. When such a data file was opened, the data integration settings would not be properly applied. An analysis might then be performed where the correct parameters would not be applied to the data, and this might yield a passing result on a defective product or a failing result on a good product.

- The 9.1 software patch adds two additional error messages to the error message definition file to support the next firmware release. The two error messages added are: "Error 8 – The system control board was not detected" and "Error 136 – The processor board for the photo-diode array detector was not detected. No action is necessary if running UV or LIF detection."

- The 9.1 software patch updates the Software Qualification program within the 32 karat software. This update is for the Operational Qualification (OQ) procedure.

- The 9.1 software patch will install the latest manual updates.

Technical Description

Computer Hardware Requirements

Beckman Coulter validated 32 Karat version 9.1 software and PA 800 *plus* software for use with the Microsoft Windows XP operating system. In addition, the PA 800 *plus* software design incorporates wide-screen monitor capability for increased workspace. The recommended monitor size is 22 inches with a 1680 x 1050 aspect ratio.

NOTE To operate the system properly, use a validated controller.

Beckman Coulter validates the controllers we provide to meet all system requirements. The specifications for the controller used in validation at the time of product release follow.

Item	Description
CPU	IBM PC (currently validated on IBM M52, M58 and M57 models)
Memory	1024 Mb (minimum)
Hard Drive	40 Gb or larger
CD/DVD RW	Required
USB Ports	Required for license key
Monitor/Resolution/Colors	1680 x 1050/True Color
Keyboard	101 key
Mouse	Microsoft compatible
Interface	GPIB Data Communications Interface PCIe board or USB cable (National Instruments)
Printer	Any Microsoft Windows XP-compatible printer
Operating System	Any Microsoft Windows XP Pro with Service Pack 2 or 3
Software	32 Karat version 9.1 and PA 800 *plus* version 1.1

IMPORTANT Users must have Administrator or Power user permission on the local workstation.

IMPORTANT Install 32 Karat software in the C:\32Karat folder.

Operating Software Requirements

Operating System: Windows XP with Service Pack 2 or 3

Beckman Coulter, Inc., Directly Supported

32 Karat 9.1 Software is designed to communicate directly with PA 800 *Enhanced* and PA 800 *plus* systems with firmware version 9.0 or later.

Underlying Database

ODBC data export supported.

Additional Information

Additional Literature

The 32 Karat Online Help is integrated with the software.

Upgrade Manual (PN A66590)

See www.ceLeader.com for more information

Options

Hardware

Instruments featuring analog outputs are supported through the 35900E analog-to-digital device.

Software

A Reprocessing Key is available for data manipulation without instrument control, PN A65879.

Support Policies

Warranty

The subject software product is warranted on an "as is" basis without fitness for any specific purpose with the exception of the media that is warranted against defects in materials or workmanship for a period of one year.

Installation

Installation of the 32 Karat Software on an appropriate personal computer is available through the Service organization at the time of installation of the 32 Karat Workstation. Installation is performed by trained engineers.

Customer Training

Up to four hours of in-lab training (for a maximum of two operators) is included with the purchase of the 32 Karat Workstation and software. Training is performed by trained field engineers or product specialists.

Product Support

Software support via telephone is provided through field offices worldwide for all purchasers of the 32 Karat Workstation.

Updates

From time to time, Beckman Coulter, Inc. updates the subject product to incorporate new features, support new devices, or to implement corrective actions. To the greatest reasonable extent, but at the sole discretion of Beckman Coulter, Inc., updated versions are compatible with data and method files, instrument and PC hardware used, and/or created by the immediately preceding version. Such new versions are available to both existing and potential customers. Contact your local sales representative for current 32 Karat update information.
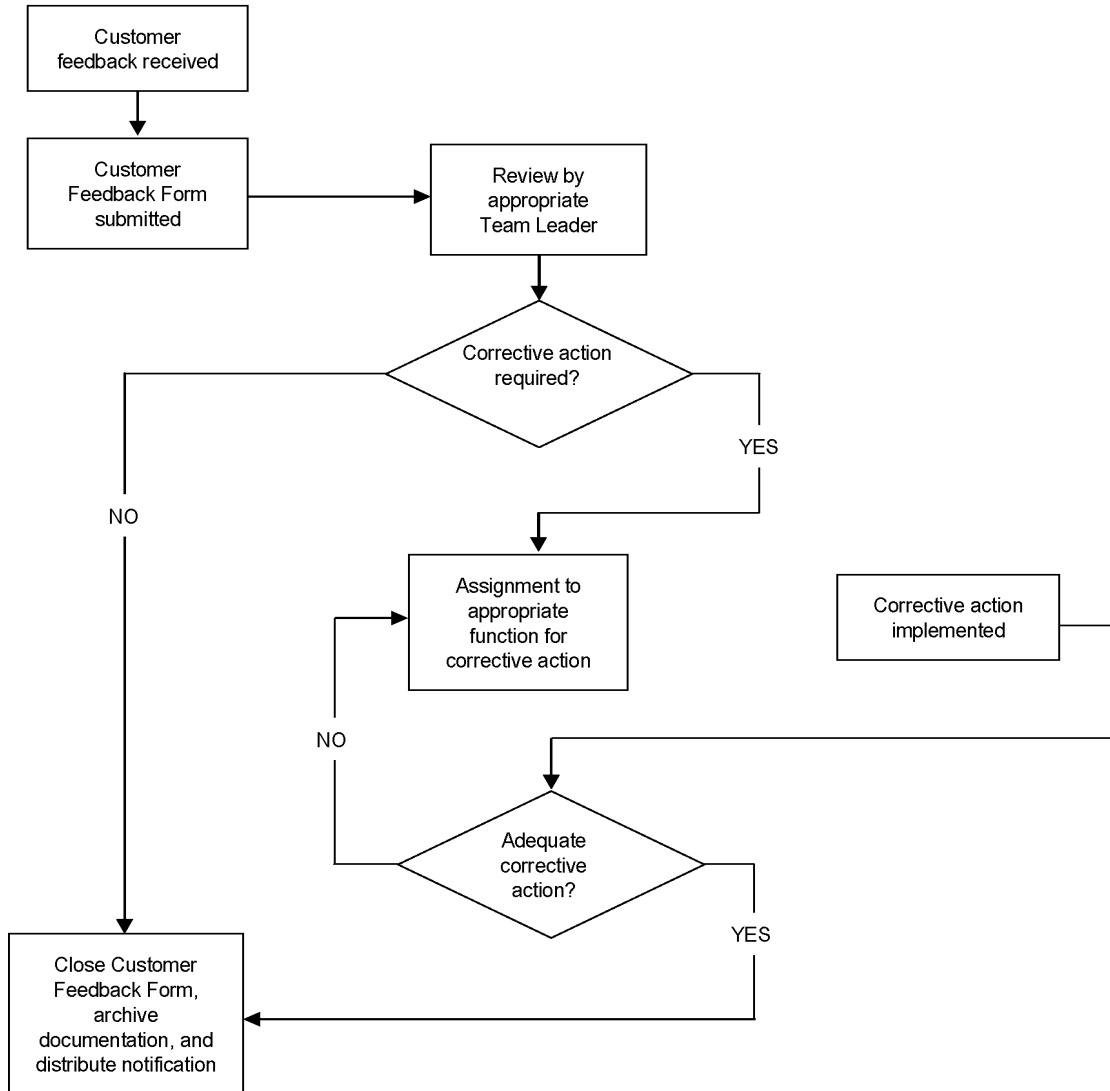
Customer Feedback Reporting

All Customer Feedback reported for released versions of software are handled according to the Beckman Coulter, Inc. Customer Feedback Procedure Document, BCP001.

The process model is depicted in the following figure:

Figure 1 Customer Feedback Reporting

Customer Feedback Reporting

Supplier Information

Company Description

Beckman Coulter, Inc. designs, manufactures, markets, and services a broad range of laboratory systems, reagents, and related products that address the needs of diagnostic laboratories as well as bioanalytical laboratories in the life science market, including those in universities, research institutes, pharmaceutical companies, and biotechnology companies. Generally, the products of the Company simplify and automate laboratory processes, saving time and money.

Products for clinical diagnostic laboratories include general and special chemistry systems together with reagents, accessories, and software that are used to detect and quantify various substances of clinical interest in human blood and other body fluids. Products for life science laboratories include centrifuges, high-performance liquid chromatography, spectrophotometers, laboratory robotic workstations, capillary electrophoresis systems, nuclear counters, protein sequencers, DNA synthesizers, and the reagents and supplies for their operation. Beckman Coulter, Inc. supports its products with a worldwide sales and service network.

Beckman Coulter, Inc. is a publicly-owned company incorporated in Delaware. Common shares are traded on the New York Stock Exchange. The company maintains offices or authorized sales and service representation in numerous countries throughout the world.

For additional information or a current annual report to the shareholders, contact:

Beckman Coulter, Inc.
Director, Shareholder Services
250 S. Kraemer Boulevard
Brea, California 92821

Product Specific Experience

Beckman Coulter, Inc. has been a manufacturer of analytical instrumentation since being founded in 1936. Beckman Coulter, Inc. has been developing and manufacturing high-performance separation instrumentation for over 40 years.

Development Environment

Project Identification

Project Name: 32 Karat 9.1

Development Center: Instrument Systems Development Center (ISDC), Brea, CA, USA

Software Product Development Environment

Configuration Management System: Source Safe 6.0

Source Language: C++ for 32 Karat, C# for PA 800 *plus*

Compilers: MSVC C++ 2003 for 32 Karat, Microsoft VS 2008 C# for PA 800 *plus*

Operating System: Windows XP

Prototype and Simulator: Build-in

Software Metric and Evaluation Tools: QA Partner for 32 Karat

Quality Management System

32 Karat Software, Version 9.1 was designed, evaluated, validated, inspected, and tested to approved specified Quality requirements of Beckman Coulter, Inc., in accordance with the following:

- ISO 13485: 2003 Certified Quality Management System registration number MD 19.0062 issued by the National Standards Authority of Ireland (NSAI).
  It is further certified that:
- The software was developed, verified, and controlled by qualified professionals.
- Source code is annotated and contains unique version control identification.
- All source code, development tools, and production documentation are archived for reasonable periods with all necessary version control information retained and with archive tapes secured in an off-site vault.
- Documentation for error reports and error report management are retained at the Brea, CA and Indianapolis, IN facilities
- Operational software has been monitored to verify continuing compliance with system and software requirements, to provide proper tracking, review, disposition, and testing of system errors in post-release software, and to provide for prompt notification of affected customers.

Product Development Life Cycle

32 Karat Software was developed following the Beckman Coulter, Inc. Product Development Cycle described in Procedure Document BMRDP-200. A model of this process is depicted in the figure below. The processes used to manage and control the development phase activities and interfaces are included in the Product Development Cycle Description. The Problem Report Process, BMRDP-430 is used to document, manage and control all changes resulting from errors encountered during the development phases.

Figure 2 Beckman Coulter Product Development Life Cycle
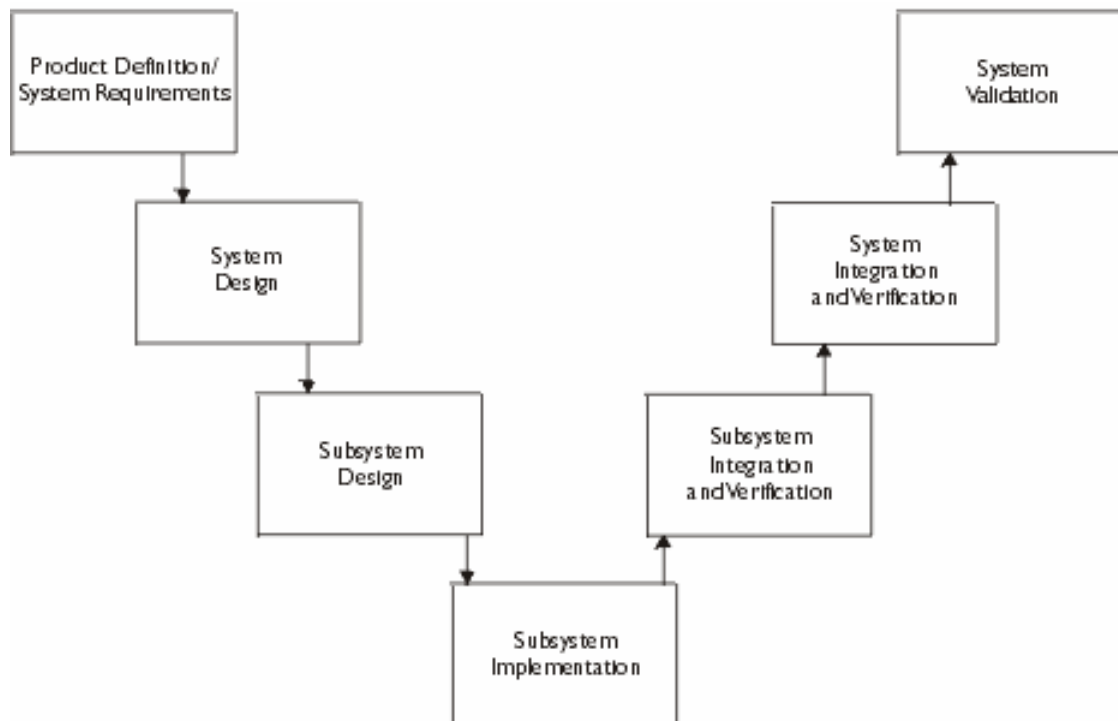
Audits and Reviews

Customer reviews and audits of Beckman Coulter, Inc. software development procedures, documentation, and source code for the purpose of complying with regulatory requirements related to software validation or verifying the quality management system are available by contacting the Quality Manager for the Brea site.

Beckman Coulter, Inc. will maintain possession of all documents and their reproductions and may require a non-disclosure agreement to be provided by those requiring access to these documents.
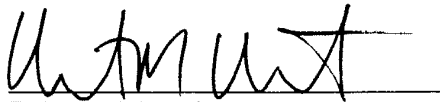
Supporting Documents

Notices

This information presented here, although believed to be correct at the time of approval, is not warranted for accuracy or completeness. Some of the information presented here is subject to change without notice.

Unless explicitly noted herein, direct questions for additional detail, current status or corrections and classifications to:
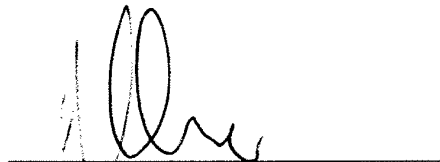
Beckman Coulter, Inc.
Quality Manager
250 S. Kraemer Boulevard
Brea, CA 92821

Approved:

Robert Weinstein
Quality Director
Discovery Product Business Center

4/29/09
Date

Jeff Chapman
Director
Discovery Product Business Center

4/28/09
Date

Supporting Beckman Coulter Procedures and Documents

Beckman Coulter, Inc. will maintain possession of all documents and their reproductions, and may require a non-disclosure agreement to be provided by those requiring access to these documents.