piccolo *xpress*™
chemistry analyzer

Intelligent Quality Control (iQC) on the Piccolo xpress™ Point-of-Care Chemistry Analyzer

The Piccolo xpress™ Point-of-Care Chemistry Analyzer is a lightweight portable instrument that processes whole blood, serum, or plasma samples in self-contained, single-use reagent discs. Along with fully automated processing and onboard data handling, the Piccolo xpress™ incorporates a unique process called iQC ("intelligent Quality Control"). Transparent to the operator, iQC checks the analyzer, the reagent disc, and the sample during each run to verify correct electronic and chemistry performance. iQC automatically suppresses a single chemistry or the entire panel if it detects uncharacteristic performance, and immediately alerts the operator to any problems. From the self-test at power-up to the recording and printing of patient results, the Piccolo xpress™ conducts hundreds of QC checks automatically and simultaneously with each run. iQC ensures that the operator reports only accurate and reliable results.

Demands for improved patient care and greater cost control are driving profound changes in the structure of health care delivery. Within and outside of traditional hospital environments, evolving technology is permitting some types of diagnostic testing and patient monitoring to move from the clinical laboratory to the near-patient environment. Many health care professionals whose roles have traditionally involved hands-on patient care are now being asked to take a role in clinical chemistry testing as well. Laboratorians, with their training and experience, know that rigorous quality control (QC) is

an absolute necessity for accurate test results on which treatment decisions can confidently be based.

The Piccolo xpress™ Point-of-Care Chemistry Analyzer incorporates a process called iQC ("intelligent Quality Control") that meets established QC standards independently of the operator's skill level. iQC is a series of sophisticated automatic checks that verify the chemistry, optics, and electronics functions of the analyzer during each run, and ensures that operators in a wide range of environments report only accurate and reliable results.

ABAXIS

HOW iQC WORKS

In the Piccolo xpress™, a tiny volume of patient sample is introduced directly into the single-use, self-contained reagent disc, where sample preparation is handled automatically. All reactions, including analyte, reagent, and instrument QC testing, occur in solution within tiny cuvettes on the periphery of the disc. In contrast to most laboratory photometers, which use light of only a single wavelength per measurement, the Piccolo xpress™ generates powerful flashes of full-spectrum white light and measures absorption for each reaction at multiple wavelengths, from ultraviolet to near-infrared. To ensure accurate results, iQC verifies the composition and delivery within the disc of all substances participating in the reactions (chemistry); validates the performance of the light generating and detection components (optics); and audits the conversion of the light absorbance into digital values for use in mathematical algorithms (electronics).

CHEMISTRY AND iQC

Bar code
Time-consuming and error-prone reagent calibrations are not required with the Piccolo xpress™ nor is there any chance of using expired reagents. The barcode on the top surface of each disc encodes the type of test panel, the expiration date, and the reagent calibration factors. At the beginning of the run, iQC verifies the integrity of the information in the bar code by the use of a cyclic redundancy check (CRC). It then checks the expiration date of the disc against the analyzer's clock to verify that the expiration date has not been exceeded. The calibration information is transferred into the analyzer's memory to be used in the calculation of results. Disc-specific information is maintained with the system QC data in the analyzer's memory.

Fluidics
The metering and movement of fluids (sample, diluent, and diluted sample) are controlled at all stages of the run by the analyzer's motor and design features of the disc. In several precisely timed cycles, the disc is alternately spun to create centrifugal force, then held still to permit capillary action. These forces synchronize the movement of fluids into and out of the chambers, channels, and cuvettes within the disc as necessary for the correct timing of all reactions. They also control the rate of fluid movement, so that turbulence can be minimized or utilized, as appropriate for a particular function.

At the start of the run, the sample and the diluent are moved along separate but parallel pathways within the disc. The sample (~100 µL of serum, plasma, or whole blood)

is drawn by capillary action from the sample port into the application chamber, then through a small channel into the plasma metering chamber. During the first spin cycle, the red cells are separated from whole blood samples and sequestered in a cell trap chamber. The analyzer verifies the presence of adequate sample volume by sensing overflow into the "sufficient-sample" cuvette. iQC will abort the run if the presence of sufficient sample cannot be verified.

Centrifugal force transfers the diluent from a reservoir within the disc into the diluent metering chamber and four system cuvettes where reagent and system iQC reactions take place. (Refer to iQC reactions, below.) iQC will abort the run if insufficient volume of diluent is detected, or if the QC reactions indicate reagent degradation.

When spinning stops, capillary forces pull precise quantities of sample and diluent into a mixing chamber. A spin cycle that alternately accelerates and decelerates the disc ensures complete mixing. At the end of this cycle, the aliquot (diluted sample) flows through the exit siphon and along the distribution channel to the reaction cuvettes. The design of the cuvettes permits air to outflow and aliquot to inflow, preventing the formation of air bubbles inside the cuvette and ensuring the correct concentration of the reaction solution. If iQC detects no aliquot in a reservoir beyond the last reaction cuvette, the presence of sufficient aliquot in all reaction cuvettes cannot be verified, and the run will abort. Otherwise, the disc spins alternately clockwise and counterclockwise to dissolve the reagent beads in the diluted sample and start the reactions.

iQC reactions
Four system cuvettes are used for reagent and system testing. Chemistry QC reagent beads reveal and quantify any degradation of the analyte-specific reagents in the

disc due to suboptimal storage conditions (moisture and temperature). If degradation exceeds a defined level, the run is aborted and an error message is displayed on the analyzer screen. System cuvettes containing a dye are used to verify the accuracy and precision of the instrument. An individual chemistry or the entire panel will be suppressed if any abnormality is detected. System and reagent QC data from each run are stored in the analyzer's memory with the sample results. Standard information storage and retrieval techniques are employed to ensure the integrity of the data. All QC data stored in memory can be called up for review at any time.

Sample evaluation

iQC eliminates the need for visual evaluation of the sample for physical interferents (hemolysis, lipemia, and icterus), a task that may be impossible when dealing with whole blood or a very small sample. The Piccolo xpress™ evaluates the quality of the sample, and reports the measured values for each interferent. Different chemistries within one type of disc may have different sensitivities to physical interferents. If a limit is reached for one or more analytes, results are suppressed for those analytes only; the level of interference is indicated on the Result card. Results for analytes less sensitive to that interferent are reported normally.

Reaction monitoring

iQC monitors the analyte-specific reactions. For rate chemistries, it confirms that the reactions are linear; that the absorbencies from which the rates are calculated, as well as the rates themselves, are within defined ranges; and whether the substrate has been depleted. In endpoint chemistries, the analyzer verifies that all measurements are within the dynamic range of the photometer and that the reaction has reached completion.

Optics and iQC

Controlling and measuring the light

The optical system consists of a xenon arc stroboscopic lamp that generates the incident beam; a family of beam splitters and filters that select defined wavelengths; and photodetectors that convert the light intensity at each wavelength into electric current. The current is routed to one of two multiplexers, which select the signals of interest and send them through variable-gain amplifiers. The amplified signal goes on to the analog-to-digital converter where the light intensity is converted to a digital number that can be used in the calculations.

Because the Piccolo xpress™ measures absorbance at multiple wavelengths, the full spectrum of the reactions can be utilized in the determination of the analyte concentration. For analytes known to be present in a wide range of concentrations in clinical samples, e.g., glucose, chemistries optimized at several different wavelengths can be included on a single disc and results measured simultaneously in the same sample. The ability to measure absorption at several wavelengths gives the Piccolo xpress™ an extremely wide dynamic range.

Signal adjustments

The uniquely designed variable-gain front-end amplifiers define the noise performance of the system and its dynamic range. The dynamic range and the noise performance of the analyzer are optimized through a complex set of measurements that involve both the disc and the electronics.

The brightness of the lamp flash changes very gradually with time and use (declining to 50% intensity after a minimum 40 million flashes, or 20 years of normal use). These changes are normal and expected, and generally affect all wavelengths more or less equally. However, to retain maximum sensitivity, the analyzer adjusts for those changes. iQC includes a series of flashes through the "minimum-absorbance" cuvette at the beginning of each run that prompts the variable gain amplifiers to adjust for maximum dynamic range (1 to ~64,000). Simultaneously with the adjustment of the gain, the analyzer verifies that the noise associated with the light intensity at any wavelength is within acceptable limits. When changes in the lamp intensity exceed the range of the variable-gain amplifiers for any wavelength, iQC will abort the run and display an error message.

Background noise is ever-present in every system. iQC includes a series of flashes through the "maximum absorbance" cuvette at the beginning of each run to

The Piccolo® reagent disc in iQC

The Piccolo reagent disc contains components that are integrated with the optical, electronic, and mechanical functions of the analyzer, and takes part in all phases of the analysis of the sample.

A bar code ring on the top of the disc contains the ID code, lot number, expiration date, and calibration data. The transfer of this data to the analyzer software is verified by a cyclic redundancy check (CRC).

The disc works with the analyzer's optical and electronic components in the calibration of the signals and rigorous checks of system functioning.

Sophisticated fluidics are employed to measure and mix the sample and diluent, and deliver them at precisely the right time to cuvettes located around the disc periphery. The cuvettes have specialized functions:

- A minimum-absorbance cuvette is used in signal adjustments that optimize sensitivity
- A maximum-absorbance cuvette is used in quantifying the noise performance of the electronic components to ensure the accuracy of all readings
- 1 cuvette contains reagent beads for chemistry QC
- 2 cuvettes contain dye beads for instrument QC

- 1 "empty" cuvette fills with diluent only, as a control on the system cuvettes
- 21 cuvettes contain test-specific lyophilized reagent beads
- 2 cuvettes verify the presence of sufficient sample and diluent, respectively
- 1 cuvette verifies that diluted sample was delivered to all the reaction cuvettes
- The disc contains miscellaneous reservoirs to isolate excess fluids.

measure the amount of background noise registered by the photometer at each wavelength. Higher than expected background noise at the different wavelengths usually indicates problems associated with the electronics in the analyzer or variable light leaks into the photometer from sources other than the primary light path. These problems can degrade the accuracy and precision of the readings, especially at higher absorbencies. When the level or the noise in the background signal is outside acceptable limits, iQC will abort the run and display an error message. The effect of the inherent flash-to-flash variation in light intensity is eliminated by the use of a reference wavelength. This reference wavelength also minimizes the inherent variability in the disc due to the manufacturing process or introduced by handling (scratches, fingerprints).

Electronics and iQC

Microprocessors and memory

The architecture of the instrument consists of two microprocessors: a real-time controller that monitors and controls all the measurements; and an I/O (input/output) controller for memory management, calculations, and data storage. The two processors interact continuously, which allows a very high level of confidence in the workings of the instrument, and consequently in the integrity of the data and in the results. The analyzer stores 150 patient results, 75 control results, and system QC data.

Software

The analyzer software comprises two matched programs. One program processes the information and controls the measurement engine itself, i.e., it synchronizes the flashing of the lamp with the position of specific cuvettes, and collects the light intensity data for different cuvettes at different times during the run; and it collects all the information generated in the analytical part of the instrument. The second program reports analyte concentrations. It also stores data related to each run (time, date, user ID, patient results, and control data).

Calculations from absorbance data

In normal functioning, each reported absorbance is calculated from a series of 10 flashes through the cuvette. Before being reported, the calculations are verified by a series of rigorous mathematical algorithms programmed into the analyzer software. These algorithms can detect errors in the absorbance data resulting from excess noise in the intensity of the flashes or from abnormalities in the reaction itself, as well as the integrity of the calculations. When such errors are detected, results for a particular analyte, or, in certain cases, for the entire panel, are suppressed. Point-of-care testing is a rapidly evolving area of laboratory diagnostics. iQC on the Piccolo system provides the health care facility with innovative solutions that ensure quality testing while meeting regulatory requirements.

How to read the QC Report

Run-specific information is found at the top of the QC Report.

Instrument QC data are arranged in two columns below the run-specific information. Level 1 iQC 1 through 8 refers to the eight different system checks that the analyzer carries out at the beginning of each run. The allowable values for all components are normalized, with 90% equaling the minimum allowed value and 110% equaling the maximum allowed value. For the run to pass iQC, the values obtained by flashing through the minimum- and maximum-absorbance cuvettes at the beginning of the run must be within these limits for all components.

Level 2 QC data concerns precision. Two system cuvettes contain 1 dye bead and 2 dye beads, respectively. At the beginning of the run, the analyzer calculates the ratio of the absorbances in the 1-bead and the 2-bead cuvettes at all wavelengths. It then averages the ratios and determines the precision of the measurements. The precision is reported to the right of "LEVEL 2." The values to the right of each specified wavelength indicate the mathematical relationship between the normalized ratio obtained at that wavelength and the average for all wavelengths. For the run to pass iQC, the precision must be between 95 and 105% overall and for each specific wavelength.

The results obtained in the chemistry iQC testing are given at the bottom of the card, along with the minimum acceptable value for this test. Any value above the minimum indicates that the disc was stored correctly and all chemistries in the disc were viable at the time of testing.

How to recall and print the QC Report

System QC data are compiled for each run and stored in the analyzer memory with the run results. For any run that remains in memory, these data can be recalled and a copy of the QC Report can be printed. Refer to the Piccolo Operator's Manual for instructions on recalling and printing system QC data.

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        Piccolo xpress
     Comprehensive Metabolic
12 Jun 2006              03:50 PM
Sample Type:             Patient
Sample ID:                   789
Alternate ID:                845
Gender:                     Male
Age:                    24 Years
Operator ID:                 423
Disc Lot Number:           5200D
Serial Number:        0000P02618
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Instrument QC:               100
iQC 1:      100    340 nm:    100
iQC 2:      100    405 nm:    100
iQC 3:      100    467 nm:    100
iQC 4:      100    500 nm:    100
iQC 5:      100    515 nm:    100
iQC 6:      100    550 nm:    100
iQC 7:      100    600 nm:    100
iQC 8:      100    630 nm:    100
Range: 90-110              95-105
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Summary of iQC checks

Bar code
- Verifies current dating.
- Cyclic redundancy check verifies accurate transfer of the reagent calibration data to the analyzer software.

Chemistry
- Confirms the viability of the analyte-specific reagents.
- Monitors all reactions in process.

Fluidics
- Verifies the presence of sufficient sample and diluent.
- Verifies the presence of diluted sample in all reagent cuvettes.

Sample
- Quantifies physical interferents (hemolysis, lipemia, icterus).
- Suppresses results for any reaction where the limits of sensitivity to an interferent have been exceeded.

Signal adjustment
- Monitors changes in flash intensity and adjusts for maximum dynamic range.
- Monitors the noise associated with the lamp intensity at all wavelengths.
- Measures the background noise to detect electrical and other problems.
- Uses a reference wavelength to minimize the effect of flash-to-flash intensity variation.

Software / memory
- The architecture of the two microprocessors optimizes real time performance.
- Synchronizes the flashing of the lamp with the position of specific cuvettes.
- Detects errors in absorbance data and errors in the calculations.

piccolo *xpress*™
c h e m i s t r y   a n a l y z e r

brought to you by:

ABAXIS