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| Abbott Laboratories |
| Prognostic Health Notification for ALINITY i Optics Dark Counts |
| ALINITY i Immunoassay Analyzer |
|  |
| **R&D Quality Engineering, Version 1.0** |
| **4/11/2017** |

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# Purpose

To implement a Prognostic Health Notification (PHN) for ALINITY i Analyzers that will detect degrading Background Read performance before the customer begins experiencing an increase in Error: 1401 Unable to process test, background read failure.

**Note:** The previous design document for ICQ dark counts (D000021403/A) was a preliminary predictive algorithm that was based on very limited data from prototype instruments that were still under development. Until that predictive algorithm can be re-optimized, this Alinity i threshold-based PHN alert will take its place.

# 2. Introduction

## 2.1 Scope

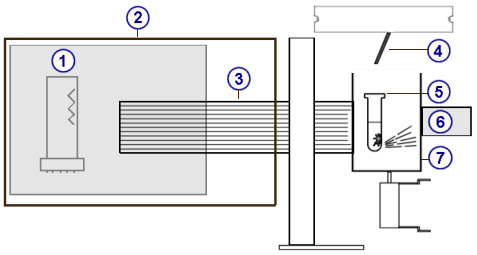
This document describes the recommended specifications for the IA Dark count PHN alert for the ALINITY i Analyzers.

## 2.2 Notification Profiles

|  |  |
| --- | --- |
| PHN Alert | Optics Dark Counts Alert |
| Platform | ALINITY i Immunoassay Analyzer |
| Data Source | IDAQOWNER |
| Notification | Daily Report / Instrument Serial Number |
| Analysis Frequency | Daily |
| Recommended Action | Troubleshoot 1401 Unable to process test, background read failure |
| IDA Table(s) Required | ICQ\_RESULTS |
| ODR Table Fields Required | MODULESN, TESTID, LOGDATE\_LOCAL, INTEGRATEDDARKCOUNT |
| Minimum number of tests required in a day to apply algorithm | 10 |
| Definition of Day | Calendar Day |
| Calculations Required | By MODULESN   * Daily N Unique TESTIDs Where INTEGRATEDDARKCOUNT is not missing * Daily INTEGRATEDDARKCOUNT Max * Daily INTEGRATEDDARKCOUNT Std Deviation |
| Flag Criteria | If INTEGRATEDDARKCOUNT Daily Max >= 543, and INTEGRATEDDARKCOUNT Daily Std Dev >= 110, then Flag, else no Flag. |

## 2.3 Overview

The ALINITY i CMIA optics module collects data during a background read prior to every sample read performed. The optics reader takes 30 sub reads over a 3 second period, the light collected by the optics module is converted into RLUs (Relative Light Units). The counts are generated before the Trigger solution is added and the sample signal read occurs (activated read). Optical system



Legend:

1. Photomultiplier tube (PMT)

2. CMIA reader

3. Light pipe

4. Trigger Solution delivery nozzle

5. Reaction vessel

6. Magnet

7. CMIA shutter assembly

Optical measurement is the process an ALINITY i system uses to obtain RLU(relative light unit) readings, and then convert them to assay-specific analyte concentration units or qualitative interpretations for index (cutoff) assays. A background read is performed prior to any activated read to ensure proper CMIA optics operation.

## 2.4 Abbreviations

|  |  |
| --- | --- |
| AUC | Area Under Curve |
| IDAQOWNER | Instrument Data Analytics Database |
| CMIA | Chemiluminescent Microparticle Immunoassay |
| EDA | Exploratory Data Analysis |
| IA | Immunoassay |
| IDA | Instrument Data Analytics Database |
| IHN | Instrument Health Notification |
| ODR | On-board Data Recorder |
| PHM | Prognostic Health Monitoring |
| ROC | Receiver-Operating Characteristic |
| RUL | Remaining Useful Life |
| RVC | Read Validity Check |

# Data

## 3.1 Source

The ALINITY i background read data is collected for every replicate that makes it to the trigger and read stage of assay processing. The data is sent to the ODR. The data goes from the ODR to the IDA via the AbbottLink connection and is stored in the table: IDAQOWNER.ICQ\_RESULTS.

**Note: Table names and field names may change when data transitions to the Production IDA**.

## 3.2 Fields Needed

The background read is taken as a measure of ambient light noise and is subtracted from the signal (triggered) read. Typically, ALINITY i background reads are between 10 to 500 RLUs.

Multiple Read Validity Checks (RVC) are placed on the background, signal and corrected reads. If a background read is flagged by a RVC, the AIM error 1401 "Unable to process test, background read failure" occurs and the system will send the test to exception and not generate a result.

Data fields that are included in the ICQ\_RESULTS table that are needed for this PHN include the following:

|  |  |
| --- | --- |
| Table Field Name | Definition |
| MODULESN | Instrument Serial Number Identifier |
| LOGDATE\_LOCAL | Instrument Local Date and Time Stamp |
| TESTID | Number that identifies the test replicate (or RV) that data is being reported for. Also known as “Replicate ID” |
| INTEGRATEDDARKCOUNT | Sum of the 30 background sub-reads for each Test ID |

# Alert

## 4.1 Calculation for ALINITY I Optics Dark Counts PHN Flag

|  |  |  |
| --- | --- | --- |
| Model | Score | Threshold |
| Partition | Flag or No Flag | N/A |

**Note:** This algorithm is based on prototype data and should be evaluated periodically for field performance and re-optimized when necessary.

## 4.2 Root Cause

Salt build up or corrosion from fluidics leaking into the process path such as buffer from the Wash Zone manifolds or valves, leaks from the Pre-Trigger/Trigger manifold or valves, Pre-trigger/Trigger inversion, defective optics assemblies, prolonged exposure to ambient light (from loose covers, cracks in shutter), shutter movement problems, and wash buffer made incorrectly are amongst the common causes of raised Background/Dark counts

## 4.3 Recommended Action

Troubleshoot Error: 1401 unable to process test, background read failure (Refer to Knowledge Management Articles and ALINITY i Service & Support Manual). General cleaning of the Process Path, looking for signs of salt buildup due to leaks and drips, check optics.

# Methods and Supporting Evidence

## 5.1 Acquisition of ALINITY i Background Read Data

Data was queried from the BSQD1I IDA database table ODR\_RESULTSICQ from 11/1/2016 – 2/15/2017. Any day with <10 replicates with integrated dark counts was excluded due to insufficient data. This resulted in data from 67 distinct ALINITY i Verification Prototype (VP) and Manufacturing Prototype (MP) instruments. A total of 1,583 unique days of data comprised the data set used.

## 5.2 Data Pre-processing

For each instrument, the following summary statistics were calculated by Day:

* Maximum and Standard Deviation of
  + INTEGRATEDDARKCOUNT
* Sum of the number of background read failures (tests sent to exception with “Unable to process test, background read failure” message)
  + Any day with at least 3 background read failure was considered a failure.
* Data was split into 70% Training and 30% Validation

## 5.3 Model

Using JMP Pro version 12.1.0, the Partition Modeling Platform was used to create the model for this alert. Model performance statistics are as follows:

**Partition for Fail**



|  | **RSquare** | **N** | **Number of Splits** |
| --- | --- | --- | --- |
| Training | 0.765 | 1110 | 2 |
| Validation | 0.749 | 473 | 2 |



**Split History**



Validation Data in Red

**Fit Details**

| **Measure** | **Training** | **Validation** | **Definition** |
| --- | --- | --- | --- |
| Entropy RSquare | 0.7650 | 0.7489 | 1-Loglike(model)/Loglike(0) |
| Generalized RSquare | 0.7763 | 0.7598 | (1-(L(0)/L(model))^(2/n))/(1-L(0)^(2/n)) |
| Mean -Log p | 0.0150 | 0.0147 | ∑ -Log(ρ[j])/n |
| RMSE | 0.0733 | 0.0728 | √ ∑(y[j]-ρ[j])²/n |
| Mean Abs Dev | 0.0108 | 0.0106 | ∑ |y[j]-ρ[j]|/n |
| Misclassification Rate | 0.0099 | 0.0106 | ∑ (ρ[j]≠ρMax)/n |
| N | 1110 | 473 | n |

**Confusion Matrix**

Training Validation

| **Actual** | **Predicted** | |
| --- | --- | --- |
| **Fail** | **0** | **1** |
| 0 | 1086 | 11 |
| 1 | 0 | 13 |

| **Actual** | **Predicted** | |
| --- | --- | --- |
| **Fail** | **0** | **1** |
| 0 | 463 | 5 |
| 1 | 0 | 5 |

**Receiver Operating Characteristic**



|  | **Fail** | **Area** |
| --- | --- | --- |
|  | 0 | 0.9950 |
|  | 1 | 0.9950 |

**Receiver Operating Characteristic on Validation Data**



|  | **Fail** | **Area** |
| --- | --- | --- |
|  | 0 | 0.9947 |
|  | 1 | 0.9947 |