Diasensor 2000

Patient Data Analysis Software Validation Plan

1. Introduction

This document describes the test procedures for each requirement listed in the Diasensor 2000 Patient Data Analysis Software Requirement Specifications (SRS). The results of the test are documented in Software Verification and Validation Report (SVVR).

1.1 References

31000-RQ	Design Requirements Document, Diasensor 2000 Non-Invasive Blood Glucose Monitor
31259-SS	Diasensor 2000 Patient Data Analysis Software Requirement Specifications (SRS)
31259-SD	Diasensor 2000 Patient Data Analysis Software Design Description (SDD)

1.2 Acronyms

D1000 – Diasensor 1000 Non-Invasive Glucose Monitor, the predecessor of the D2000

D2000 - Diasensor 2000 Non-Invasive Glucose Monitor

DRD - Design Requirements Document

PCMCIA - Personal Computer Memory Card International Association

PDA – Patient Data Analysis

QM – Quality Monitoring

SRS – Software Requirements Specification

SDD – Software Design Description

2. Purpose

The purpose of the Validation Test Plan is to verify specific functional requirements listed in the SRS in a controlled manner.

3. Apparatus and Setup

3.1 Equipment

This software was developed and tested on the Sun ES-4000 UNIX computer (host name mule). The applications are invoked from the S-Plus or Unix environment.

3.2 Existing Conditions

Programs were tested during normal working hours on the ES-4000 or PC hardware.

3.3 Diagram of Apparatus

N/A. No special apparatus or equipment was used to conduct these tests.

4. Verification Procedure

The following sections describe the tests used to verify the requirements provided in SRS.

4.1 Requirements for All Incoming Data

4.1.1 The software must be able to split the incoming Diasensor data into up to four files, one file for each of four possible patients that can use a Diasensor. It must also create an

Alert file, indicating when enough data has been collected, when necessary.

Software Requirement: 3.1.1

Use D2000 data that has more than one patient on the device. If one does not already exist, place an alert record in the file or create a file containing an alert record. Also use D2000 data that includes both spectral data and measurement data for at least one patient. Make sure that there is at least one other problem with the data, such as the collection date and time stamp being out of sequence.

1. Confirm that an entry is created for the error and that it is included in the error log.
2. Confirm that the software correctly splits the data into one file for each patient.
3. Confirm that at least one file contains both reading and spectral data.
4. Confirm that the data files are in the correct directory.
5. Confirm that the software creates an Alert file that contains the following information:

Table 1: Alert File

Column	Field Name	Description	Range
1	distributorId	first 4 digits of the Bico_user_id	4 digits
2	userId	last 6 digits of the Bico_user_id	numeric, 6 digits max.
3	date	Date in the format: yyyymmdd	
4	time	Time in the format: hhmmss	
5	mode	instrument operating mode	1 = calibration 2 = evaluation 3 = measurement 4 = recalibration
6	status	alert status code	2 digits

4.1.2 The software must be able to translate binary Diasensor data to S-PLUS format file(s) (objects).

Software Requirement: 3.1.2

Use the files that are output in section 4.1.1 as input.

1. Confirm that reading data is placed in a file with the extension: .rdg, and is in the correct format.
2. Confirm that spectral data is placed in a file with the extension: .ska, and is in the correct format.
3. Confirm that the output file name parameter can be used.
4. Confirm that the output file names use the convention of adding a letter to the file name parameter to indicate the mode the data was collected in, e.g. "C"alibration, "E"valuation, etc.
5. Confirm that the software warns the user of problems, such as the date and time stamp being out of sequence.
6. Confirm that normally, only "good" data (data with status codes 0, 18, 19) is translated, but that a parameter can be used to override this and get all the data. The data formats are as follows:

Table 2: SKA Structure Format

Column	Field Name	Description	Range
1	spectrumType	Type of spectrum in data buffer. Type 3 = index is not really a spectrum type. It is used by protomgr for indexing.	0 = spectrum_status 1 = control 2 = dark 3 = index 4 = reference 5 = skin 6 =control_absorbance 7 = dark_absorbance 8 = ref._absorbance 9 = skin_absorbance
2	distributorId	first 4 digits of the Bico_user_id	4 digits, 0-4294
3	userId	last 6 digits of the Bico_user_id	numeric, 6 digits max. 0-967295
4	date	Date in the format: yyyymmdd	numeric
5	time	Time in the format: hhmmss	numeric warning: no leading zeros
6	invasive	Corresponding invasive meter reading	0 to 65,535
7	mode	instrument operating mode	1 = calibration 2 = evaluation 3 = measurement 4 = recalibration
8	sittCount	Sitting count. (the number of good spectrum status records for all the data (e.g. a whole Calibration)) or if all data is wanted, the number of spectrum status records.	1 – 65,535 The sitting number while using this mode of operation. (normally, cal. sittings would be 1-120).
9	sessCount	Session count	1 – 6 for Cal. or Re-cal., 1-1 for Evaluation or Measurement mode. The session number within the above sitting.
10	todCode	Time-Of-Day class code.	1 = before breakfast 2 = after breakfast 3 = before lunch 4 = after lunch 5 = before dinner 6 = after dinner 7 = bedtime 8 = night 9 = other
11	spectrum[1]	Spectral data of spectrum_type	up to 15 digits
12	spectrum[2]	Spectral data of spectrum_type	up to 15 digits
13-73	spectrum[3 to 63]	Spectral data of spectrum_type	up to 15 digits
74	spectrum[64]	Spectral data of spectrum_type	up to 15 digits
75	sensor[1]	sensor data	up to 15 digits
76	sensor[2]	sensor data	up to 15 digits
77-84	sensor[3 to 10]	sensor data	up to 15 digits
85	statusCode	error code from spectrum status	2 digits

Table 3: RDG Structure

Column	Field Name	Description	Range
1	distributorId	first 4 digits of the Bico_user_id	4 digits
2	userId	last 6 digits of the Bico_user_id	numeric, 6 digits max
3	mode	Instrument operating mode	1 = calibration 2 = evaluation 3 = measurement 4 = recalibration
4	date	Date in the format: yyyymmdd	numeric
5	time	Time in the format: hhmmss	numeric warning: no leading zeros
6	glucose	measured blood glucose (mg/dL)	-32,768 to 32,767
7	control	control sample (absorbance * 100,000)	-32,768 to 32,767
8	invasive	invasive meter measurement (mg/dL)	-32,768 to 32,767
9	todCode	Time-Of-Day class code	1 = before breakfast 2 = after breakfast 3 = before lunch 4 = after lunch 5 = before dinner 6 = after dinner 7 = bedtime 8 = night 9 = other
10	qmFlag	quality monitoring indicator; if nonzero, then this reading was used for QM purposes	0 or 1
11	status	measurement algorithm completion status code	Usage specific
12	correction	bias correction value used to get this measurement. in units of mg/dL	-32,768 to 32,767

4.2 Requirements for Calibration and Re-calibration Data

4.2.1 The software will create an S-PLUS object that contains one HemoCue reading per sitting of spectral data (.hc object).

Software Requirement: 3.1.3

Use the .ska object that is the output from section 4.1.2 as input.

1. Confirm that the output file name parameter can be used.
2. Confirm that a vector of HemoCue data is placed in an S-PLUS format file, and that there is one HemoCue record for each sitting of spectral data.

4.2.2 There will be software to create several preliminary plots.

Software Requirement: 3.1.4

Copy some Diasensor 1000 S-Plus spectral data (in the old .ska format) and associated HemoCue readings, and re-format the data for the Diasensor 2000, including creating a .hc file of HemoCue readings. Run the Diasensor 1000 PDA software, then run the D2000 format of the same data through the Diasensor 2000 PDA software. Use channels 16-58 for both D1000 and D2000 data. The plots should be very similar, but may not be identical, because we no longer make every session look like a sitting, and the HemoCue readings are now one per sitting. With the D1000, we matched the data to the HemoCue that was closest in time, which was not always the same as one HemoCue per sitting. However, we are using D1000 format data converted to D2000 format data (the channels have already been reversed).

Compare the output of the D1000 PDA software and the D2000 PDA software for the following plots:

1) A histogram of the HemoCue

2) HemoCue readings vs. data collection time
3) Raw Diasensor skin data vs. channel
4) Mean Diasensor skin data vs. channel
5) Standard deviation of Diasensor skin data vs. channel
6) Diasensor skin absorbance data vs. channel (every 100th row)
7) Mean Diasensor skin absorbance data vs. channel
8) Standard deviation of Diasensor skin absorbance data vs. channel
9) Raw Reference data vs. channel
10) Mean Reference data vs. channel
11) Standard deviation of Reference data vs. channel
12) Reference absorbance data vs. channel
13) Mean absorbance of reference data vs. channel
14) Standard deviation of reference absorbance data vs. channel
15) Dark spectra vs. channel
16) Temperature sensors vs. time

4.2.3 The software will calculate and display the standard deviation of the HemoCue readings.

Software Requirement: 3.1.6

Use the D1000 data re-formatted into the Diasensor 2000 format. Build a .hc object from the HemoCue readings in this file. Use the .hc object to test the D2000 software.

We are unable to compare the D1000 and the D2000 software because it differs in a crucial area. The D1000 software translates each session into a format that makes it appear as a sitting. Each session has a HemoCue number assigned to it, so there are multiple occurrences of each HemoCue number, depending on the number of valid sessions in each sitting. This causes different weights for the HemoCue results, depending on the number of valid sessions in a sitting. The D2000 software only puts one reading in the .hc file for each sitting, so all HemoCue readings have the same weight. Therefore, the standard deviation of the HemoCue as calculated by the D1000 software and the standard deviation of the HemoCue as calculated by the D2000 software will be different.

Because the software uses the standard S-Plus function to calculate standard deviation, which has been confirmed in the past, we do not need to re-test this function. Use the D2000 software to calculate standard deviation.

1. Confirm that the HemoCue standard deviation is displayed to the user.
2. Confirm that for every HemoCue listed in the .hc file, there is at least one matching HemoCue reading in the D1000 data.

4.2.4 The software will perform a Standard Deviation check and remove the subsessions that do not pass. It will then check to ensure that less than or equal to 30% of the data was removed due to Standard Deviation errors.

Software Requirement: 3.1.5

Use the Diasensor 1000 S-Plus spectral data and the data re-formatted into the Diasensor 2000 format.

Run the Diasensor 1000 PDA software, then run the D2000 format of the same data through the Diasensor 2000 PDA software.

1. Confirm that .ska objects containing only the subsessions that passed the Standard Deviation check are created, and that the results are quite similar. The results may not be identical because the D1000 software creates subsessions based on a time break, the D2000 software creates subsessions based on the number of spectra (16). The D1000 software may throw out some subsessions that the D2000 software does not.

2. Confirm that a message containing the total number of subsessions, the number of subsessions that failed, and whether this data set passed the Standard Deviation check is output, and that the results are quite similar, as stated above.

4.2.5 The software will check to see if there is sufficient Calibration data to continue forming a Calibration.

Software Requirement: 3.1.7

Use the Diasensor 1000 S-Plus spectral data and the data re-formatted into the Diasensor 2000 format.

Run the Diasensor 1000 PDA software, then run the D2000 format of the same data through the Diasensor 2000 PDA software.

Perform tests to check the Sufficient Calibration Data Criteria, which are:

The number of countable Calibration sessions must be greater than or equal to 600.

The number of countable Calibration sittings must be greater than or equal to 108.

The number of days with at least 1 countable Calibration sitting must be greater than or equal to 54.

1. Confirm that the software displays messages indicating how many of each item in each criteria there were in the Calibration, and how many were still needed to pass each criteria.
2. Confirm that the number of days and countable sessions and sittings are very similar for the D1000 and D2000 data. The results may not be identical because the D1000 software creates subsessions based on a time break, the D2000 software creates subsessions based on the number of spectra (16). The D1000 software may throw out some subsessions that the D2000 software does not. If there is any question about the results, calculate each: sessions, sittings and days.

4.2.6 The software will average the skin spectra in each subsession, so there will be a maximum of four skin spectra per session. The software will convert each average skin spectrum to absorbance units.

Software Requirement: 3.1.8

Use the Diasensor 1000 S-Plus spectral data and the data re-formatted into the Diasensor 2000 format.

Run the Diasensor 1000 PDA software, then run the D2000 format of the same data through the Diasensor 2000 PDA software.

1. Compare the averaged absorbance objects and confirm that they are quite similar. The results may not be identical because the D1000 software creates subsessions based on a time break, the D2000 software creates subsessions based on the number of spectra (16). The D1000 software may throw out some subsessions that the D2000 software does not.

4.2.7 The software must be capable of producing a Calibration vector using Slope Intercept Corrected (SIC) Calibration method.

Software Requirement: 3.1.9

Use the Diasensor 1000 and Diasensor 2000 average absorbance objects created in 4.2.6.

Run the Diasensor 1000 PDA software for SIC Calibration. Then, run the D2000 format of the same data through the Diasensor 2000 PDA software.

1. Confirm that the D2000 software saves three files: one for the calibration vector and constant, one for the PLS loadings, and one for the Load Vector.
2. Confirm that a parameter is used to indicate how many of the PLS loadings should be saved. Set the parameter to 25.
3. Confirm that the files are in the correct format, as follows:

- The Calibration constant and Calibration vector are stored in an object named: cal.vec. The first column in cal.vec is the Calibration constant, the Calibration vector is stored in columns 2 through 65.
- The PLS Loadings are stored in an object named: pls.load. There is one row for each rank up to the parameter number. The first column in each row of pls.load is the constant, the PLS Loadings are stored in columns 2 through 65.
- The SVD Load vector is stored in an object named: svd.load, in columns 1 through 64.

4. Compare the calibration vectors and calibration constants of the D1000 and D2000 software, and confirm that they are quite similar. A difference may occur because for the D1000 software, we used a time-based break on subsession. For the D2000 software, we break based on the number of spectra in a subsession, which are 16.
5. Confirm that the PLS loadings and the Load Vector of the D1000 and D2000 data are quite similar. A difference may occur for the same reason as stated above.

4.2.8 The software will print an Error Grid of Calibration Self-predictions.

Software Requirement: 3.1.10

Use the Diasensor 1000 and Diasensor 2000 average absorbance objects created in 4.2.6.

Use the D1000 and D2000 Calibration vectors and constants created in 4.2.7.

Run the Diasensor 1000 PDA software for SIC Calibration. Then, run the D2000 format of the same data through the Diasensor 2000 PDA software.

1. Compare the D1000 Error Grid with the D2000 Error Grid. They should be similar, although they may not be identical because the D1000 software creates subsessions based on a time break, the D2000 software creates subsessions based on the number of spectra (16). The D1000 software may throw out some subsessions that the D2000 software does not.
2. Compare the correlation coefficient, the RMSEC (Root Mean Square Error of Calibration, a.k.a. SEP), and the slope. They should be similar, although they may not be identical for the same reason as above.
3. Compare the Quality Monitoring Cutoff printed on the D2000 error grid with the Quality Monitoring Cutoff of the D1000 data, which should be $(2 * RMSEC_{D1000})$.
4. Compare the QM Cutoff value, stored in the file qm.cutoff with the QM Cutoff printed on the D2000 error grid. They should be identical.

4.2.9 The software must enable the analyst to create a patient skin library, which contains the patient's Calibration coefficients.

Software Requirement: 3.1.11

Use the Diasensor 1000 and Diasensor 2000 average absorbance objects created in 4.2.6.

Use the D2000 Calibration vector and constant created in 4.2.7.

Use the D2000 PLS Loadings and Load Vector created in 4.2.7.

Use the D2000 file qm.cutoff, containing the QM Cutoff Value created in 4.2.8

Use the D1000 and D2000 S-Plus spectral data (.ska objects).

1. Confirm the accuracy of the control average absorbance. Calculate the absorbance of two randomly chosen control spectra. Calculate the average of the two absorbance records. Create a subset of the data that contains the same two control readings. Run this file through the D2000 software. Compare to the hand calculated data, both absorbances and average absorbances. They should be identical.
2. Confirm the accuracy of the average absorbance of the sensor readings collected at the same time as the control. Calculate the absorbance of two randomly chosen control sensor spectra. Calculate the average of the two absorbance records. Create a subset of the data that contains the same two control sensor readings. Run this file through the D2000

software. Compare to the hand calculated data, both absorbances and average absorbances. They should be identical.

3. Confirm that the Calibration Vector, Calibration Constant, PLS Loadings, Load Vector, and QM Cutoff value were correctly stored.
4. Compare the D1000 and D2000 Mean of the Calibration Skin Spectra. They should be similar, although they may not be identical because the D1000 software creates subsessions based on a time break, the D2000 software creates subsessions based on the number of spectra (16). The D1000 software may throw out some subsessions that the D2000 software does not.
5. Confirm that the following were stored correctly:

- The Calibration Date, the date the file was created.
- The Sensor Ranges (rangeSensors), low and high point pre-set to 99.
- Leverage tolerance, pre-set to 1.
- LOF tolerance, pre-set to 1.
- Distance tolerance, pre-set to 0.
- A slope correction number, pre-set to 1.
- A bias correction number, pre-set to 0.
- The channel numbers to be used, default = 1-57
- The total number of channels, default = 64
- The *Diasensor 2000* Valid Measurement Range. (Default is 0-400)
- The patient Alert Range. (Default is 40-400)
- The deviation that the current Control pixel measurements may drift from the maximum and minimum values of the Control average absorbance. The default is 0.003.
- The rank number (default = 25), and rank weight (default = 1)
- The Quality Monitoring flag, default = "T"

4.3 Requirements for Evaluation Data

4.3.1 The software must check if there is sufficient Evaluation data to verify the success of the Calibration, and inform the user of the result.

Software Requirement: 3.1.12

Run the software using the reading (.rdg) file created in section 4.1.2 (see table 3 for the data format).

1. Confirm that the following are displayed to the analyst: the number of countable Evaluation sittings, the number of days with at least 1 countable Evaluation sitting, and the number of each still needed to pass the sufficient Evaluation data criteria.
2. Calculate the numbers to ensure they match the software. Remember: Sittings with a status code other than zero(0), eighteen(18), and nineteen(19) are not countable. The sufficient Evaluation data criteria are as follows:

- Number of days with at least one (1) countable Evaluation sitting should be greater than or equal to twenty five (25).
- Number of countable Evaluation sittings should be greater than or equal to forty-nine (49).

4.3.2 The software shall calculate the mean of the absolute values of the differences between the paired *HemoCue* and *Diasensor 2000* measurements. The software shall calculate a 95% confidence interval and compare the result to a threshold of 90, beyond which the Evaluation is said to have failed.

Software Requirement: 3.1.13

Run the software using the reading (.rdg) file created in section 4.1.2 (see table 3 for the data format).

1. Confirm that the threshold parameter and output file name parameter can be used.
2. Create a subset of data. Using this subset, hand calculate the mean of the absolute values of the difference between the paired HemoCue and D2000 measurements. Calculate a 95% confidence interval and compare the result to a threshold of 90. Run the D2000 software that performs this function also using the subset of data. Compare the results. They should be identical.
3. Confirm that the calculated upper boundary of the confidence interval is displayed.
4. Confirm that a Pass or Fail status is displayed.
5. Confirm that a text file is created in the correct directory which contains the following:

- Distributor ID, User ID
- .rdg file name
- Threshold used
- Confidence Interval calculated
- "Evaluation Status:" (Pass or Fail)

4.3.3 The software must enable the analyst to create a Physician's report containing the results of the Evaluation.

Software Requirement: 3.1.14

Run the software using the reading (.rdg) file created in section 4.1.2 (see table 3 for the data format).

Because most of the data stored are created using standard S-Plus functions that have been confirmed in the past, we do not need to re-test them.

1. Hand calculate the relative error between the average Diasensor 2000 and HemoCue readings, and compare to the output of the software. They should be identical.
2. Hand calculate the Standard Error and compare to the output of the software. They should be identical.
3. Confirm that the number of glucose readings is correct.
4. Confirm that the following are output to a file:

- The relative error between the average Diasensor 2000 and HemoCue readings.
- The Correlation Coefficient, Standard Error, Slope, Intercept, and the number of glucose readings.
- A plot displaying the Diasensor 2000 vs. HemoCue individual readings.

5. Confirm that the output file is named according to the naming convention and is in the correct directory.

4.4 Miscellaneous Software

4.4.1 Software Used to Attach to the Correct Patient Directory

Software Requirement: N/A. This software attaches the analyst to the directory where the patient data is stored. It was developed to reduce the risk of the analyst accidentally using the wrong data or storing a file in the wrong directory. This software is fully described in the SDD.

Use a test master list, which has the following file format:

Table 5: d2k.master.list Structure Format

Column	Field Name	Description	Range
1	distributorId	First 4 digits of the Bico_user_id	numeric, 4 digits max., 0-4294
2	userId	Last 6 digits of the Bico_user_id	numeric, 6 digits max. 0-967295
3	BicoLogin	A translated form of the device Serial Number	8 alphanumeric
4	TopLevelDir	Top level directory	Alphanumeric, length varies

1. Confirm that the following parameters can be used, and that the software attaches to the correct directory based on the parameters.

- Distributor ID, a parameter.
- Patient ID, a parameter.
- Subdirectory, an optional parameter defaulted to null. Test both null and "src" subdirectory.
- Return directory, a parameter defaulted to "F". If the parameter is used as "T", do not attach to the directory, just return it to the calling program. Test both "T" and "F".

2. Confirm that, if there are multiple BICO login ID's for the Distributor ID/User ID combination, a list of the available BICO login ID's is displayed and the user is asked to choose one.