SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name:	short term continuous glucose sensor
Device Trade Name:	DexCom™ STS™ Continuous Glucose Monitoring System
Applicant's Name and Address:	DexCom, Inc. 5555 Oberlin Drive San Diego, CA 92121
Date of Panel Recommendation:	None

Premarket Approval Application (PMA) Number: P050012

Date of Notice of Approval to Applicant: March 24, 2006

II. INDICATIONS FOR USE

The DexCom STS Continuous Glucose Monitoring System is a glucose-monitoring device indicated for detecting trends and tracking patterns in adults (age 18 and older) with diabetes. The DexCom STS System is intended for use by patients at home and in health care facilities. The device is for prescription use.

The DexCom STS Continuous Glucose Monitoring System is indicated for use as an adjunctive device to complement, not replace, information obtained from standard home glucose monitoring devices.

The DexCom STS Continuous Glucose Monitoring System aids in the detection of episodes of hyperglycemia and hypoglycemia, facilitating both acute and long-term therapy adjustments, which may minimize these excursions. Interpretation of the STS System results should be based on the trends and patterns seen with several sequential Sensor readings over time.

III. CONTRAINDICATIONS

- The DexCom STS System must be removed prior to Magnetic Resonance Imaging (MRI).
- Use of acetaminophen-containing medications when the STS Sensor is inserted may affect the performance of the device.

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IV. WARNINGS AND PRECAUTIONS

Warnings

- This device is not designed to replace a blood glucose meter. The DexCom STS System must be used with a blood glucose meter.
- Treatment decisions should not be based solely on results from the DexCom STS System. You must confirm with a blood glucose meter before making therapeutic adjustments.
- Symptoms related to low or high blood glucose levels should not be ignored. If you have symptoms of low or high glucose, use your blood glucose meter to check the STS System results.
- You should update the STS System's calibration every 12 hours at a minimum to ensure device performance. The performance of the STS System when calibrated less frequently than the recommended minimum of every 12 hours, has not been studied.

Precautions

- Always wash hands with soap and water before opening the STS package. After opening the package, avoid touching the adhesive area.
- Before inserting the Sensor, always clean the skin at the Sensor insertion location with a topical antimicrobial solution, such as isopropyl alcohol. Do not apply the Sensor until the cleaned area is dry.
- Establish a rotation schedule for choosing each new Sensor location. Avoid Sensor locations that are constrained by clothing, accessories, or subjected to rigorous movement during exercise.
- Avoid injecting insulin within 3 inches of the Sensor or 3 inches from an insulin infusion set for pump wearers.
- The Sensor must be covered with a water resistant bandage or tape prior to showering or bathing.
- The STS Sensor is sterile in its unopened, undamaged package. Do not use any STS Sensor if its sterile package has been previously damaged or opened.
- The STS System has currently only been tested in adult persons with type 1 and type 2 diabetes. The device has not been tested in children, adolescents or pregnant women.

Caution

- U.S. federal law restricts the sale of the DexCom STS System to sale by or on order of a physician.

V. DEVICE DESCRIPTION

The DexCom STS Continuous Glucose Monitoring System (STS System) is an externally worn glucose Sensor that continuously tracks and reports glucose values and trending information in real-time for up to 72 hours. The STS System is designed to provide continuous measurement of glucose concentrations over a 40-400 mg/dL range, and consists of 3 principle components; the STS Sensor, the STS Transmitter, and the STS Receiver.

Once the Sensor is inserted and the Transmitter is installed, The STS Sensor requires a 2-hour Start-up Period for Sensor equilibration. At the end of this period, the Receiver prompts the user to calibrate the System with two blood glucose fingersticks taken with the OneTouch® Ultra® Blood Glucose meter. The user then uploads the blood glucose values taken directly to the Receiver using a connection cable[1]. After calibration, the STS System provides a glucose reading and updated 1-hour, 3-hour, and 9-hour glucose trend information for viewing every 5 minutes. The STS System also has programmable High and Low Glucose Alerts and a non-changeable Low Glucose Alarm set at 55 mg/dL.

A. Description of System Components

1. STS Sensor

The STS Sensor is a sterile device, inserted into the abdominal subcutaneous tissue using a Sensor introducing system, the STS Applicator. The Applicator is adhered to the surface of the skin and facilitates the introduction of the 25-gauge introducer needle housed within the STS Applicator. After deployment of the introducer needle, the needle is retracted back into the Applicator and the Sensor remains beneath the surface of the skin, held in place by the STS Pod (Transmitter housing). The Sensor is a glucose oxidase enzyme-coated probe.

2. STS Transmitter

Once installed in the STS Pod adhered to the abdomen, the STS Transmitter measures the glucose signal and transmits the glucose information to the STS Receiver. The STS Transmitter consists of a Printed Circuit Board (PCB), an antenna, and 3-volt battery, all housed in a polymer-based material. The STS Transmitter contains the circuitry used to measure the electrical current signal from the STS Glucose Sensor, and the RF circuitry used to transmit the Sensor data. The antenna is used to transmit the Sensor data at 5-minute intervals to the STS Receiver via RF. The RF link that is established between the STS Transmitter and STS Receiver is for transfer of glucose data only.

[1] The STS System is currently only compatible with the OneTouch Ultra Blood Glucose Meter.

3. STS Receiver

The Receiver is a pager-like device with a re-chargeable battery. Users must keep the Receiver within 5 feet of the Transmitter to ensure Sensor-Receiver transmission. Users must enter a 5-digit Transmitter Serial Number into the Receiver to establish secure, wireless communication between the Receiver and Transmitter.

Once Receiver-Transmitter communication is established, the STS Receiver captures, stores, and converts the Sensor signal to glucose concentrations using its internally programmed algorithms after calibration. The STS Receiver is calibrated with blood glucose information uploaded directly from the OneTouch Ultra Blood Glucose Meter.

The STS Receiver acts as the primary system interface with the user. It contains an LCD screen and 4 buttons for operation. The Receiver displays the date and time information, and Sensor glucose values are updated automatically every 5 minutes. The Receiver displays the Sensor glucose values in mg/dL or mmol/L along with a 1-hour, 3-hour and 9-hour glucose trend graph to provide historical glucose information. Date and time information can be displayed in 12-hour or 24-hour format. In typical use the Receiver will last 5 days before re-charging of the battery is required.

The Receiver has High and Low Glucose Alerts that can be set by the user (as directed by their health care team) to notify users of when their current glucose level is outside of their target glucose range. The STS Receiver also has an automatic Low Glucose Alarm set at 55 mg/dL to warn users of very low glucose levels. Dashed lines on the Receiver Trend Graphs indicate the current alert level settings. The Low Alert and Alarm will vibrate/sound if the current glucose level is below the Low Alert or Low Alarm and their glucose levels are trending in the down direction. The High Alert performs in the same manner; the value and the trend information cause an Alert to occur.

The Receiver also has internal data checks to ensure the quality of the data provided to the user at all times. If the Receiver detects a problem with the Sensor signal or determines the accuracy of the value is not adequate, the Receiver will not display the reading until the accuracy is updated or the signal problem is resolved.

The Receiver contains memory to store up to 30 days of continuous glucose information. The Receiver contains a USB communication port for uploading the Sensor data stored to a PC.

VI. ALTERNATIVE PRACTICES OR PROCEDURES

Periodic glucose self-monitoring using home blood glucose meters will provide information regarding variations in glucose levels.

VII. MARKETING HISTORY

The DexCom STS Continuous Glucose Monitoring System has not been marketed in any country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Use of the DexCom STS Sensor may cause erythema at the insertion site or adhesive area, edema, and bleeding at the insertion site.

Inaccurate glucose values or inappropriate alerts and alarms provided by the STS System could result in potentially inappropriate administration of insulin or ingestion of carbohydrates.

IX. SUMMARY OF PRE-CLINICAL STUDIES

A. Laboratory Studies

1. Sterility Assurance

Sterilization of the device was validated using electron beam irradiation to ISO 11137-1994, Method 1. The results of the dose verification meet the acceptance criteria of ISO11137 – 1994, Method 1 and validate a minimum exposure of 19.3 kGy for routine sterilization with a SAL of 10-6.

2. Biocompatibility

Biocompatibility testing was performed on the Sterile STS products. This includes the Applicator, Transmitter Housing, Introducer Needle and Sensor Probe. The Transmitter is not a sterile product and does not have direct contact with the skin. Biocompatibility testing on the STS Sensor was done in accordance with ISO 10993-1:1997 Biological Evaluation of Medical Devices and with reference to FDA's memorandum "Required Biocompatibility Training and Toxicology Profiles for Evaluation of Medical Devices 5/1/95 (G95-1)". Table 1 lists the biocompatibility testing performed and the result of the testing for the Sensor, Needle, and the Adhesive Tape, respectively.

Table 1. STS System Biocompatibility Results

Test Requirement	Standard/ Test Method	Sensor	Needle	Adhesive Patch	Test Result
ISO MEM Elution Using L-929 Mouse Fibroblast Cells	ANSI/AAMI/ ISO 10993-5:1999	X	X		Non-toxic
ISO Guinea Pig Maximization Sensitization Test Method for Biomaterial Extracts	ANSI/AAMI/ISO 10993-12; ANSI/AAMI/ISO 10993-12	X	X		Non-sensitizer
ISO Intracutaneous Reactivity Test	ISO 10993-10 (2002)	X	X		Non-irritant

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Test Requirement	Standard/ Test Method	Sensor	Needle	Adhesive Patch	Test Result
ISO Acute Systemic Injection Test	ISO 10993-11 (2002)	X	X		Non-toxic
Subacute (14-Day) Intravenous Toxicity Study in Mice Five Repeat Dose Exposure	ISO 10993-11 (1993)	X			Non-toxic
Bacterial Mutagenicity Test (Ames Assay)	ISO 10993-3 (1993)	X			Non-mutagenic
ISO Intramuscular Implant Test 28-day Duration in Rabbits	ISO Test Method for implantation in muscle, ANSI/AAMI/ ISO 10993-6 (1995) (28 day)	X			Non-irritant for wear period.
Repeated Patch Dermal Sensitization Test	ISO 10993-10 (2002)			X	Non-sensitizer
Cytotoxicity Study Using the ISO Agarose Overlay Method	ISO 10993-5			X	Non-toxic
ISO Skin Irritation Study	ISO 10993			X	Non-irritant

3. Accuracy

   Each manufactured Sensor is evaluated for in-vitro accuracy, oxygen tolerance, and glucose sensitivity against its predetermined acceptance criteria. Sensors must meet these requirements prior to Sensor manufacture release.

4. System Level Functional Testing

   Operation of the DexCom STS System at the system level was evaluated by exercising major functions of the system confirming that the system operated in accordance with its predetermined acceptance criteria to ensure that the design input meets the design output requirements. Design verification activities including all safety testing, are conducted in in-vitro

and in-vivo environments and, where appropriate, FDA- and ISO-approved standards are utilized to conduct the testing performed.

5. Shelf-life Stability

   Sensor stability was evaluated at the end of an 8-month period after being stored under controlled temperature conditions at 22 ± 3°C. All results were within stability specifications.

6. Interferences

   Sensor response to acetaminophen was evaluated by placing Sensors in phosphate buffered saline (PBS) solutions containing physiologically relevant concentrations of the potentially interfering substance. The Sensor output current was monitored and evaluated for significant changes in signal. These studies indicated that STS Sensor signal changes with exposure to acetaminophen and therefore this interfereing substance has been listed as a contraindication.

7. Electromagnetic Compatibility

   Transmitters, receivers, and associated cabling were tested for electromagnetic emissions in accordance with the following test standards

   - EN55011 (Radiated and Conducted Emissions)
   - EN61000-4-3 (Electric Field Immunity
   - EN61000-4-4 (Electrical Fast Transients)
   - EN61000-4-5 (Surge)
   - EN61000-4-6 (Conducted Immunity)
   - EN61000-4-8 (Magnetic field Immunity)
   - EN61000-4-11 (Voltage Dips, Drop Outs and Variations)
   - MIL-STD-461E (Magnetic and Electric Field Immunity)
   - FCC Part 95 (Medical Implant Communication Service)

   All devices met the requirements of these standards.

8. Electrostatic Discharge

   Receivers and Transmitters were subjected to electrostatic discharge testing in accordance with the requirements of EN61000-4-2. Contact (±2, ±4, ±6 kV) and air (±2, ±4, ±8 kV) discharges were applied to multiple points on the receivers and transmitters. All test samples passed functional testing performed following exposure to these discharges.

9. Environmental Testing

(a.) Mechanical Vibration

Receivers were subjected to mechanical vibration testing for 90 minutes equally divided between 3 mutually perpendicular directions at a frequency of 5-150 Hz and an acceleration of $0.1g^2$/Hz. Functional testing performed after vibration exposure confirmed that no units were damaged by this testing.

Transmitters were subjected to mechanical vibration testing for 90 minutes equally divided between 3 mutually perpendicular directions at a frequency of 5-150 Hz and an acceleration of $0.1g^2$/Hz. Functional testing performed after vibration exposure confirmed that no units were damaged by this testing.

(b.) Mechanical Drop

Receivers were dropped from a height of 1 meter onto a solid wood block. All samples passed functional testing after the drops.

Transmitters were dropped from a height of 1 meter onto a solid wood block. All samples passed functional testing after the drops.

(c.) Temperature Shock

Receivers were exposed to temperature shock of 10°C per minute with a temperature range of 0°C to 45°C. All samples passed functional testing after temperature shock testing.

Transmitters were exposed to temperature shock of 2°C per minute with a temperature range of 0°C to 45°C. All samples passed functional testing after temperature shock testing.

(d.) Temperature Humidity Exposure

Sensor Systems were tested in an environmental chamber at 95+5% to -10% humidity and 37±2°C for 72 hours to evaluate the effects of extreme temperatures and humidity on the STS Sensor and Transmitter. All systems passed the pre-specified requirements after exposure.

Receivers were exposed to temperature and humidity profiles from 0°C to 45°C and 10% RH to 95%RH for 24 continuous hours. All samples functioned continuously during testing and passed all functional testing after temperature and humidity testing.

Transmitters were exposed to temperature and humidity profiles from 0°C to 45°C and 10% RH to 95%RH for 24 continuous hours. All samples functioned continuously during testing and passed all functional testing after temperature and humidity testing.

(e.) Temperature Storage

Receivers were exposed to -26°C for 24 hours followed by 52°C for 24 hours. All samples passed functional testing after exposure to these storage temperatures.

(f.) Atmospheric Pressure

Receivers were exposed to 70kPa for 1 hour, followed by 150kPa for 1 hour. All samples passed functional testing after exposure to these pressures.

Transmitters were exposed to 70kPa for 1 hour, followed by 150kPa for 1 hour. All samples passed functional testing after exposure to these pressures.

10. Device Integrity Testing

(a.) Needle Insertion Force

STS Sensors were deployed through a moistened chamois to evaluate the needle insertion force. All samples demonstrated an insertion force less than the predetermined acceptance criteria.

(b.) Needle Bond Strength

Needle assemblies were tested to evaluate the bond strength between the needle and needle carrier. All samples demonstrated bond strength greater than the predetermined acceptance criteria.

(c.) Contact Resistance

STS Sensors and STS Transmitters were evaluated to determine the maximum change in contact resistance during a 72 hour period. All samples demonstrated a contact resistance less than the predetermined acceptance criteria.

11. Package Integrity/Shipping Testing

(a.) Sensor Packaging

Sensor packaging sterile barrier was evaluated per ASTM D 4169-04a (Standard Practice For Performance Testing Of Shipping Containers And Systems) and ASTM F2097-01 (Guide For Design And Evaluation Of Primary Packaging For Medical Products) standards. All units were evaluated in testing and passed the testing requirements of all distribution tests.

(b.) STS Starter Kit Packaging

Starter Kit packaging configurations were tested according to ASTM D 4169-04a (Standard Practice For Performance Testing Of Shipping Containers And Systems) and ASTM F2097-01 (Guide For Design And Evaluation Of Primary Packaging For Medical Products) standards. The STS Sensors (sterile product) are housed in their sterile barrier packaging

and then inserted in the Starter Kit packaging. All units passed the testing requirements of all distribution tests.

12. Software Validation

Comprehensive testing is performed to ensure the performance of each of the manufactured devices has met the software design specification and software requirements specifications established for each item. The verification and validation activities are completed according to the FDA guidance entitled "General Principles of Software Validation: Final Guidance for Industry and FDA Staff" released January 11, 2002.

Verification and Validation of the software implementation is accomplished through software code reviews, unit testing, and system level testing. These evaluations verify that the software implementation satisfies the design implementation as defined in the Software Design Document and validate that the software conforms to user needs and intended uses.

B. Animal Studies

In-vivo testing of the DexCom STS Sensor has been performed in numerous studies to assess Sensor and system functionality throughout the development process. In addition to functionality, the animals were observed for clinical signs of adverse events (infection, skin irritation). Over 300 STS Sensors have been implanted in *in vivo* studies. Additional *in vivo* studies were performed to assess the effect of other minor manufacturing changes on functionality during the development process. All studies were guided by Title 21 CFR Part 58.

Summaries of some of the studies are included in Table 2:

Table 2. Animal Study Summary

Study Name and No.	No. of Animals	No. of Sensors Used	Purpose
In Vivo Feasibility (RPT2633)	14	Up to 2 per animal	The Sensors were tested for their ability to track glucose followed daily by performing glucose tracking studies (GTS) and for their ability to communicate with the Receiver. The Sensors remained inserted for 1-8 days.
Effect of Sterilization (RPT2628)	9	1 per animal	The Sensors were tested for function and longevity (up to 3 days) following sterilization.

Study Name and No.	No. of Animals	No. of Sensors Used	Purpose
Beta Configuration (RPT2656)	13	Up to 2 per animal	The safety and function of the Sensor after e-beam sterilization were evaluated in three studies. Output of all implanted Sensors was tracked in the rats over a 72-hour period.
Improved Sensitivity and Automated Skiving (RPT9560)	11	Up to 2 per animal	The safety and function of the beta configuration of electron beam sterilized STS Sensors with varying sensitivities and Sensor processing differences were evaluated in two studies.

X. SUMMARY OF CLINICAL STUDIES

1. Pilot Study of the Effectiveness and Safety of the DexCom™ STS Glucose Sensor (Feasibility Study - PTL9000)

The purpose of this study was to evaluate the initial safety and effectiveness of the DexCom STS System in subjects with diabetes mellitus requiring insulin. This study was a nonrandomized, retrospective feasibility study conducted at three clinical centers in the United States. Following screening, subjects participated in a 12-hour in-clinic day in which up to 2 Sensors were inserted into the abdomen. Fingersticks were performed every 20 minutes for the duration of the in-clinic study to compare the Sensor results to a home blood glucose meter and a clinical blood glucose analyzer (HemoCue Analyzer). The Sensors were removed at the end of the in-clinic day. A subset of subjects continued to wear the Sensors for an additional 12 hours after completion of the 12-hour in-clinic day. Subjects returned to the clinic between 24 and 72 hours after device removal to examine the insertion site and document any adverse events. A phone call was made to the subjects 7-10 days after removal to document any subsequent adverse events.

The clinical study population consisted of 31 persons with diabetes mellitus requiring injectable insulin that met the inclusion and exclusion criteria. Fifteen (15) (48%) of the subjects were female. The average age was 42(±13) years. Twenty-seven (27) (87%) were Type 1 subjects and 4 (13%) were Type 2 requiring insulin. Sixteen (16) (52%) subjects wore the device for 12 hours and 15 (48%) subjects wore the device for 24 hours.

Nineteen (19) adverse events were reported in 14 study participants. These events consisted of 1 report of bleeding at the insertion site, 1 report of

bruising, 2 reports of blisters, 1 report of edema (swelling), and 14 reports of erythema (redness). All were mild and required no treatment.

The retrospective mean absolute relative difference (MARD) of the Sensor compared to the OneTouch Ultra meter was 13.8% and the average R-value (Pearson correlation coefficient) was 0.93.

Results from this pilot study showed that this device was safe for use up to 24 hours.

2. 72-hour Study of the Effectiveness and Safety of the DexCom™ STS Glucose Sensor (Feasibility Study - PTL9001)

This study evaluated the Sensor over multiple 72-hour sessions during home use and in the clinic in people with diabetes mellitus requiring insulin. Each 72-hour study included one in-clinic day. Each participant wore up to two Sensors and participated in the in-clinic day on either the first, second or third day of the Sensor wear period. The remaining days of the study, subjects were able to go home, to work, and to do what they would do in a normal day. A minimum of 10 subjects had to be enrolled with a blinded glucose display on the devices. Once the first 10 subjects were completed, if DexCom and the Investigator deemed it safe, subsequent persons in the protocol could be unblinded to the continuous data of one of the Sensors.

During the in-clinic study day, subjects took fingersticks three times an hour for 12 hours using the One Touch® Ultra meter and a subset of subjects had blood draws taken for the YSI analyzer. While at home, subjects were asked to take ~8 fingersticks per day.

The subjects returned to the clinic at the end of the 72-hour insertion period for Sensor removal, examination of the Sensor site and documentation of any adverse events. The subjects had a final clinic visit 7 days after the Sensor removal (Study Day 10) to document any subsequent adverse events.

The clinical study population consisted of 42 persons with diabetes mellitus that met the inclusion and exclusion criteria. Demographic data was provided for 41 of the 42 subjects. Sixteen (16) (39%) subjects were female. The average age was 43(±12) years. Thirty-three (33), 80% of those enrolled, were people with Type 1 diabetes and 8 subjects (20%) enrolled had Type 2 diabetes mellitus, requiring insulin.

The first 14 (33%) enrolled subjects were blinded to the continuous glucose data, and the data was analyzed retrospectively. The 28 (67%) later subjects were able to view the continuous glucose data, trend information, and high and low glucose alerts from one of the STS Sensors in real-time. The data from both Sensors of the 28 subjects was analyzed prospectively.

Eighteen (18) adverse events were reported in 11 study participants. These events consisted of 1 report of bleeding at the insertion site, 1 report of a blister, 1 reports of edema (swelling), 15 reports of erythema (redness). All were mild and required no treatment.

For the 28 Sensors inserted in the 14 blinded subjects, all 28 were analyzed. Retrospective analysis of the data reported a mean absolute relative difference (MARD) across the 72 hour period for all Sensors of 20.3% and an average R-value (Pearson's correlation coefficient) of 0.88.

For the 56 Sensors inserted in the 28 unblinded subjects, 51 produced analyzable prospective data. Prospective analysis of the data reported an overall mean absolute relative difference (MARD) across the 72 hour period of 18.95%, and a median ARD of 15.42%. The traditional Clark Error Grid showed overall 97.71% of the matched pairs were in Region A or B. When further broken down by SMBG range, Region A or B accounted for about 90% in the 40-80 range and about 97% in the >240 range.

The precision of the Sensor was evaluated on 20 of the 28 subjects where the Sensor and Receiver algorithm were the same as the device used in the Pivotal Study (PTL9002). The reproducibility of two Sensors worn simultaneously in the abdomen was evaluated. Precision was estimated by comparing the glucose readings from the two STS Systems. In this study 631 paired STS Sensor values were obtained. Reproducibility of the Sensors was evaluated using Mean Relative Difference (MRD) and MARD (absolute relative difference) between corresponding Sensor values in each subject. The data was collected over a 3-day (72 hour period). The data was collected in the Clinic on Day 1 of the study (12 hours) and from home use on Days 2 and 3. The MRD was –3.9% and the MARD was 21% between Sensors.

There were no moderate or severe irritation events or Unanticipated Adverse Device Effects associated with use of the STS System during this study, indicating that subjects can use this device in a safe manner for up to 72 hours.

3. Safety and Efficacy Study of the DexCom STS Continuous Glucose Monitoring System (PIVOTAL STUDY – PTL9002)

(a) Overview

To evaluate safety and effectiveness of the STS System, 91 participants were enrolled at 4 centers. All participants had Type 1 or Type 2 diabetes mellitus, and required insulin to manage their diabetes. About 80% of participants had Type 1 diabetes and about 20% had Type 2 diabetes. Subjects ranged in age from 18 to 79 years of age.

Participants used the STS System for approximately nine days. Each subject participated in 3 consecutive periods of 3-day STS system use. STS Receivers were calibrated approximately 3-4 times per day using the OneTouch Ultra meter. Approximately half of the participants used the STS System in a controlled clinic environment for 2 of the 9 days. The remainder of the study took place at home.

The study was intended to collect additional Adverse Device Event information as well as collect accuracy measures to establish Sensor accuracy against a laboratory reference (Yellow Springs Instrument 2300 STAT Plus Glucose Analyzer) and a home blood glucose meter (LifeScan OneTouch Ultra Blood Glucose Meter). Subjects were randomized to a "Control Group"

or "Display Group" to gather information on the clinical effectiveness of continuous glucose data and alerts when compared to a control group where continuous glucose readings and alerts were not provided to the user.

(b) Demographics

Of the 91 study subjects, 75 subjects were persons with type 1 diabetes and 16 subjects were persons with type 2 diabetes, all required insulin therapy for diabetes management. Fifty-eight percent (58%) of subjects enrolled were male (42% female) and the mean age of the enrollment population studied was 44±13 years. Ninety-three percent (93%) of subjects were Caucasian, 3% African American or Black, 2% Asian and 1% where American Indian or Alaska native. Fifty-six (56%) percent of the population used CSII for insulin therapy, and the remaining subjects were on MDI therapy. The mean Body Mass Index was 27.9±5.51. Mean duration of diabetes was 21±12 years, and the average A1c was 7.6%±1.1% for the Control Group and 8.0%±1.4% for the Display Group. There was no significant difference between the Control Group and Display group populations in average A1c ($p = 0.16$, two-tail t-test).

(c) Study Procedures

Following screening, subjects were randomized using a block randomization method, to a Control group (n=44) or Glucose Display group (n=47). All participants wore three (3) DexCom STS Sensors for three (3), 72-hour periods for a total time of nine (9) days or 216 hours. The Control group was blinded to the continuous Sensor data for all three wear periods (Period 1, 2, and 3), and the glucose display group was blinded on Period 1, and unblinded to the continuous glucose data for Periods 2 and 3. For periods that the study groups were blinded (Periods 1-3 for the Control group and Period 1 for the Display group) subjects were asked to take fingersticks for calibration and comparative means while at home. When unblinded, the Display group was only required to take fingersticks for calibration purposes and to confirm the hyperglycemia and hypoglycemia alerts. Subjects also completed a daily diary for each 3-day insertion period. Subjects in the Control group also participated in two in-clinic days on Day 1 (the 1st day of the first Sensor insertion period) and on Day 3 (the 3rd day of the first insertion period) of the study. During these in-clinic days, meals and insulin levels were adjusted during the In-Clinic Day to obtain a full range of glucose values. All insertions were done at the clinic by the subjects. Sensor insertion sites were examined after removal of each Sensor. Study staff documented any irritation and/or adverse device effects. A follow-up phone call occurred 6-10 days post-removal of the last Sensor.

(d) Devices Utilized

Of the 91 subjects, 287 STS Sensors were evaluated across the 9-day period (3 insertion periods) for either the in-clinic portion of the study or the home use portion of the study.

(e) Adverse Events

Twenty-one (21) adverse events were reported in 16 of 91 study participants. These events consisted of 2 blisters, 2 reports of edema (swelling), and 17 reports of erythema (redness). All were mild and required no treatment.

(f) Subject Discontinuations

None of the subjects withdrew from the study.

(g) Results

Development of the STS System, including the final Sensor design and algorithm was completed prior to initiation of the PTL9002 study. Performance statistics were calculated using the OneTouch Ultra meter for calibration during real-time use. No post-processing of the data was done on the dataset for calculation of the STS System glucose results.

For the in-clinic dataset of 14 participants, the mean and median absolute relative difference (ARD) were 26±21% and 23%, respectively when OneTouch Ultra meter values were used as calibration and the STS values were compared to YSI analyzer measurements. For the glucose measurement range of 40-350 mg/dL, the STS Sensor had 51% of its values within 20%, and 70% of its values within 30% of the YSI value.

The data were further broken down by glucose ranges. The following table shows the percent of STS System readings within 20%, 30% and 40% of YSI values (or within 20 mg/dL for values ≤80 mg/dL):

Table 3. STS Readings within 20%, 30% and 40% of YSI readings by Range

YSI Readings (mg/dL)	Number of Paired Readings	% of STS Readings Within 20%*	% of STS Readings Within 30%*	% of STS Readings Within 40%*
40-80*	140	56	74	88
81-120	133	44	63	75
121-240	314	46	67	86
241-350**	89	65	81	93

*The absolute difference from the OneTouch meter is measured in mg/dL if the meter reading is ≤ 80 mg/dL.

** There were no YSI readings above 350 mg/dL observed in these studies.

To evaluate the High Glucose Range performance of the STS System (performance above 300 mg/dL), the Home Use portion of the data was evaluated looking at the percentage of STS readings with an ARD ≤ 20%, ≤30%, and ≤40% of the OneTouch Ultra Meter. This information is presented in Table 4.

Table 4. Percentage of STS Readings within 20%, 30%, and 40% of the OneTouch Ultra Meter

Blood Glucose Meter Readings (mg/dL)	Number of Paired Readings	% of STS Readings Within 20%*	% of STS Readings Within 30%*	% of STS Readings Within 40%*
>300-350	121	84	98	100
>350-375	32	91	100	100
>375-400	12	83	83	100

The Clarke Error Grid Analysis indicated that 90% of the STS System readings were within the clinically acceptable Zones A and B when the STS was calibrated with the OneTouch Ultra meter and compared to the YSI analyzer.

The following table (Table 5) shows the percentage of points falling within each zone, stratified according to the range of glucose concentrations.

Table 5. Stratified Clarke Error Grid

Glucose Range	Number of Paired Readings	A+B %	A %	B %	C %	D %	E %
<=80 mg/dL	156	69%	52%	17%	0%	31%	0%
81-120 mg/dL	137	99%	44%	55%	2%	N/A	N/A
121-240 mg/dL	314	98%	46%	51%	3%	N/A	0%
>240 mg/dL	126	87%	57%	29%	14%	0%	0%
Total (40-400 mg/dl)	733	90%	49%	41%	4%	7%	0%

*N/A means that the Clarke Error Grid does not consider the possibility of these zones in that concentration range.

Low and High Glucose Alerts

The ability of the STS System to detect high and low glucose levels is assessed by comparing STS Sensor results to YSI analyzer results at low and high glucose concentrations, and determining if the STS System would have captured the low or high event. There were 733 pairs of matched STS System and YSI analyzer results evaluated.

The Low Glucose Alert

Estimates of how well the adjustable Low Glucose Alert performs are presented in Table 6, below. Results show that if the STS Low Glucose Alert is set at 70 mg/dL, the STS System will alert when glucose levels drop below 70 mg/dL as determined by the YSI, 57% of the time. At this alert setting, the percentage of times the STS System would alert and the glucose is above 70 mg/dL is 24%. If you set the STS System to 90 mg/dL, the STS System will detect a glucose value of 90 mg/dL or less 68% of the time. At the 90 mg/dL alert level, approximately 9% of alerts received would be false.

Table 6. Hypoglycemic Alert (Low Alert) Evaluation

STS Alert Level	True Alert Rate*	False Alert Rate**
60 mg/dL	54%	36%
70 mg/dL	57%	24%
80 mg/dL	62%	13%
90 mg/dL	68%	9%

*True Alert Rate is the % of time when the glucose level was at or below the alert setting and the alert would have sounded.

**False Alert Rate is the % of time when the device would have alarmed but the blood glucose level was above the alert setting.

The High Glucose Alert

Estimates of how well the adjustable High Glucose Alert performs are presented in Table 7. Results show that if the STS High Glucose Alert is set at 200 mg/dL, the STS System will alert when glucose levels rise above 200 mg/dL as determined by the YSI, 98% of the time. At this alert setting, the percentage of times the STS System would alert and the glucose is below 200 mg/dL is 31%.

Table 7. Hyperglycemic Alert (High Alert) Evaluation

STS Alert Level	True Alert Rate*	False Alert Rate**
140 mg/dL	99%	21%
180 mg/dL	98%	24%
200 mg/dL	98%	31%
240 mg/dL	96%	43%
300 mg/dL	97%	67%

*True Alert Rate is the % of time when the glucose level was at or above the alert setting and the alert would have sounded.

**False Alert Rate is the % of time when the device would have sounded but the blood glucose level was actually below the alert level.

Calibration Stability

The STS System should be calibrated every 12 hours. To demonstrate performance of the STS System over a 12-hour calibration period 91 Sensors were evaluated to verify that performance remains consistent over the 12 hour calibration period, a portion of STS Systems are evaluated in 3 hour increments after calibration. Performance is assessed by comparing the % of STS Sensor readings falling within 20, 30, and 40 % of the One-Touch reading in each 3 hour period. Minimal deterioration in performance is noted. See Table 8, below.

Table 8. Percentage of STS Readings Falling Within 20, 30, and 40% of OneTouch Readings With Data Stratified in Three Hour Increments After Calibration

Time After Calibration (hours)	% of STS Readings Within 20%*	% of STS Readings Within 30%*	% of STS Readings Within 40%*
0-3	62	79	89
3-6	63	79	88
6-9	59	81	91
9-12	58	74	85

*The absolute difference from the OneTouch meter is measured in mg/dl if the meter reading is ≤ 80 mg/dL.

The performance of the STS System when calibrated less frequently than the recommended minimum of every 12 hours has not been studied.

Sensor Stability

The STS Sensor provides glucose information for up to 72 hours (70 hours after initial calibration). Performance of the STS System was evaluated according to length of time from Sensor insertion. From the home use data set, the percentage of STS System values with an ARD within 20%, 30% and 40% were evaluated at 12 hour increments from insertion. Results in Table 9 indicate that there is no significant decrement in accuracy with increase in wear time.

Table 9. Percentage of STS Readings Falling Within 20, 30, and 40% of OneTouch Readings With Data Stratified in 12 Hour Increments After Sensor Insertion

Time After Insertion (hours)	% of STS Readings Within 20%*	% of STS Readings Within 30%*	% of STS Readings Within 40%*
0-12	64	82	91
12-24	63	79	88
24-36	59	76	86
36-48	63	79	88
48-60	58	77	87
60-72	62	81	91

*The absolute difference from the OneTouch meter is measured in mg/dl if the meter reading is ≤ 80 mg/dL.

Sensor Life

Ninety-one (91) of 94 Home Use Sensors calibrated successfully on Day 1 and were evaluated for Periods 2 and 3 of the Home Use portion of the study. Three (3) additional Sensors applied were "replacement Sensors" and therefore were not included in the analysis. Seventy-one (71) of the 91 Sensors (78%) lasted more than 60 hours and up to 72 hours in duration and 75%of the Sensors lasted at least 65 hours and up to 72 hours. Of the 24 Sensors that shut-off prior to the last 5 hours of use approximately two-thirds shutoff due to the signal failure shutoff and one-third fell off the subjects.

Of these Sensors evaluated, 3% of the devices provided less than 60 readings per day, and 66% percent of the Sensors provided 200 or more readings per day. The majority of the missing readings (17%) were lost due to transmission data gaps between the Receiver and Transmitter. Other reasons for loss of readings were due to signal problems, which caused a data gap and STS System re-calibration requirements, which are elicited by the algorithm or were user related.

XI. CONCLUSIONS DRAWN FROM STUDIES

The results of the pre-clinical verification/validation testing and clinical trials to assess the performance of the DexCom STS Continuous Glucose Monitoring System with real-time glucose readings and trend information establish reasonable assurance that this system is safe and effective for its intended use when utilized in accordance with product labeling.

XII. PANEL RECOMMENDATIONS

In accordance with the provisions of section 515(c)(2) of the act as amendment by the Safe Medical Devices Act of 1990, this PMA was not referred to the Clinical Chemistry and Toxicology Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

FDA issued an approval order on March 24, 2006.

The applicant's manufacturing facilities were inspected on August 3, 2005, August 19, 2005 and found to be in compliance with the Quality Systems Regulation (21 CFR 820)

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, precautions and Adverse Events in the labeling.

Postapproval Requirements and Restrictions: See approval order.