

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Insulin infusion pump to be used with continuous glucose monitoring (CGM)

Device Trade Name: OneTouch Vibe™ Plus System

Device Prococode: OYC and MDS

Applicant's Name and Address: Animas Corporation 200 Lawrence Drive,
West Chester, PA 19380

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P130007/S016

Date of FDA Notice of Approval: Dec 16th, 2016

The original PMA P130007 was approved on November 25, 2014 and is indicated for continuous subcutaneous insulin infusion for the management of insulin-requiring diabetes in adults (age 18 and older) with diabetes. The Summary of Safety and Effectiveness Data (SSED) to support the indication for use is available on the CDRH website and is incorporated by reference herein. A supplemental PMA 130007/S004 was approved on December 24th, 2015, and expanded the indications for use to include pediatric patients (age 2 and older). The current supplement was submitted to replace the existing Dexcom G4® sensor and transmitter utilized in this system with Dexcom's next generation Dexcom G5® Sensor and Transmitter. Animas has a right of reference from Dexcom for the clinical data to support sensor performance that is described in the SSED for Dexcom's PMA (P120005/S018 and P120005/S031).

II. INDICATIONS FOR USE

The OneTouch Vibe™ Plus System consists of the Animas® Vibe® Insulin Pump paired with the Dexcom G5® Sensor and Transmitter.

The OneTouch Vibe™ Plus System is indicated for continuous subcutaneous insulin infusion for the management of insulin-requiring diabetes. It can be used solely for continuous insulin delivery and as part of the OneTouch Vibe™ Plus System to receive and display continuous glucose measurements from the Dexcom G5® Sensor and Transmitter.

The OneTouch Vibe™ Plus System's continuous glucose monitoring (CGM) is indicated for detecting trends and tracking patterns in persons (ages 2 and older) with diabetes, and is intended to complement, not replace, information obtained from standard home

glucose monitoring devices. CGM 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 results from the Dexcom G5® Sensor and Transmitter should be based on the trends and patterns seen with several sequential readings over time.

The System is intended for single patient use and requires a prescription.

III. **CONTRAINDICATIONS**

The following are listed in the labeling:

Contraindications for using the OneTouch Vibe™ Plus System

Insulin pump therapy is not recommended for people with diabetes who are unwilling or unable to:

- Test their blood glucose (BG) levels four to six times per day or as recommended by their Healthcare Professional (HCP).
- See their HCP regularly.
- Respond to pump alerts, warnings, and alarms because they are visually or hearing impaired.

Not following these guidelines will make it difficult for you to determine the proper amount of insulin you need based on your current health status and the foods you eat. Not seeing your HCP on a regular basis will not allow them to make proper adjustments to your pump settings and diabetes treatment plan that would be beneficial to your health. Not being able to respond to pump notifications means you may not be aware of certain health conditions or problems with your pump that require your attention.

Contraindications for using the Dexcom G5® Sensor and Transmitter

Contraindications let you know when not to use the Dexcom G5® Transmitter and Sensor; you may hurt yourself or damage the system.

- **MRI/CT/Diathermy:** Remove the Dexcom G5® Sensor and Transmitter before Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scan, or high-frequency electrical heat (diathermy) treatment. The Dexcom G5® Sensor and Transmitter have not been tested during MRI or CT scans or with diathermy treatment. The magnetic fields and heat could damage the Sensor and Transmitter, which may cause it to display inaccurate glucose readings or may prevent alerts.
- **Medications:** Taking medications with acetaminophen while wearing the Sensor may falsely raise your Sensor glucose readings. The level of inaccuracy depends on the amount of acetaminophen active in your body and is different for each person.
- The pump and any type of metallic infusion set must be removed prior to an MRI, and left outside the room during the procedure.

IV. **WARNINGS AND PRECAUTIONS**

The Warnings and Precautions can be found in the OneTouch Vibe™ Plus System System labeling.

V. **DEVICE DESCRIPTION**

The OneTouch Vibe™ Plus System (“Vibe System”) consists of the Animas® Vibe® Insulin Pump (“The Pump”) and Dexcom G5® CGM System. The Vibe® System includes an insulin infusion pump, designed to communicate via BLE technology with the Dexcom CGM transmitter to display CGM information in addition to infusion pump data, Animas 2.0 mL cartridge, infusion set, and one lithium battery. The insulin infusion pump delivers insulin through the OneTouch™ Infusion Set for continuous subcutaneous insulin infusion for the management of insulin-requiring diabetes. The Dexcom G5® CGM System sensor (“the Sensor”) provides continuous measurements of glucose in the tissue over the range of 40 to 400 mg/dL for up to seven days of use measuring and displaying glucose values and trends for patients with diabetes mellitus on the pump. The Vibe® System provides glucose trends, alerts and a low glucose alarm.

Description of System Components

The OneTouch Vibe™ Plus System is comprised of the following components:

Animas Vibe Insulin Pump

The Animas® Vibe® Insulin Pump delivers insulin through an infusion set for continuous subcutaneous insulin infusion for the management of insulin-requiring diabetes.

The Animas® Vibe® Insulin Pump is an external cartridge (syringe) pump and delivery system for ambulatory use by patients with insulin requiring diabetes who would benefit from continuous insulin infusion. The pump delivers a prescribed dosage of insulin as a single programmable bolus or at multiple programmable basal rates.

In addition to CGM data, the Animas® Vibe® Insulin Pump will also display established Animas platform insulin-delivery information: set up information, dosage history, alarms, error and warning messages, device status and self-test capabilities. The Animas® Vibe® Insulin Pump will not use the continuous glucose monitoring (CGM) data to calculate insulin doses. The CGM data is being provided on the pump screen only as a convenience to the user.

The Animas® Vibe® Insulin Pump consists of the following subsystems:

- A disposable insulin cartridge for storage of insulin.
- Battery compartment for holding a battery (the pumps energy source).
- Electronics, drive mechanism, software and display which form the core of the pump.

The insulin cartridge is a proprietary syringe comprised of a barrel and a plunger. The cartridge is filled with insulin by the user and is placed in a dedicated housing inside the

pump. Within this housing, the cartridge plunger interfaces with a piston, a component of the pump drive mechanism. During the pump delivery sequence, a brushless dc motor drives a speed-reducing gear train and precision lead screw. The lead screw's rotational motion is translated to a linear motion by the (non-rotating) piston. The forward motion by the piston applies a force to the cartridge plunger, which results in the delivery of insulin into the infusion set to the patient via the cannula. The volume of insulin delivered is directly dependent on the displacement of the plunger.

The Animas® Vibe® Insulin Pump is a prescription device intended for home use and has been designed to withstand the environment typically seen by the patient in the home environment. The Animas® Vibe® Insulin Pump includes a light emitting diode color display with an adjustable brightness. The design provides protection against fluid ingress (rated IPX8) and has also been designed to conform to relevant electromagnetic compatibility, drop-testing and electrostatic discharge (ESD) standards for performance in the home environment.

The pump software provides the intelligence for key functionality such as user interface, error monitoring, status reporting and history recording.

Calibrations are performed by the patient using standard commercially-available blood glucose meter devices and entered manually by the patient into the Animas® Vibe® Insulin pump through a data entry menu. After calibrating the system, the Pump automatically displays the current glucose value, trend graphs of recent glucose values and rate of change arrows once every five minutes. The Animas® Vibe® Insulin Pump also contains circuitry to provide audible or vibratory alerts for high and low glucose values. The user can configure the Pump to provide audible, vibratory or combined audible and vibratory alerts. The pump also contains a non-configurable low glucose alarm at 55 mg/dL to provide users additional warning of hypoglycemia.

Dexcom G5® Sensor

The Dexcom G5® Sensor is comprised of a sensor applicator, an adhesive pad and transmitter mount and the sensor probe. The G5 Sensor is a sterile device inserted by the user into the abdominal subcutaneous tissue using the applicator. The applicator is adhered to the surface of the skin with a standard medical grade adhesive pad. The applicator contains a 26-gauge introducer needle that contains the sensor probe. The needle is not exposed, or even visible, to the user during the insertion process. After deployment of the introducer needle, the needle is retracted back into the applicator. The applicator is then detached and disposed by the user, exposing a transmitter mount ready for placement of the transmitter.

The sensor probe remains beneath the surface of the skin and uses the enzyme glucose oxidase to convert the glucose in the interstitial fluid around the sensor into an electrical current proportional to the ambient glucose concentration. The sensor continuously measures glucose in the interstitial fluid every five minutes. The flexible sensor has an

adhesive to adhere the sensor to the skin. The sensor that is adhered to the skin is replaced every seven days.

Dexcom G5® Transmitter

The Dexcom G5® Transmitter makes continuous measurements of the user’s glucose level in conjunction with a Dexcom G5® sensor. The transmitter sends the measured electrical glucose signal wirelessly to the Animas® Vibe® Insulin Pump at regular 5-minute intervals. The transmitter is programmed with a unique identification serial number that is manually entered into the corresponding pump by the user in order to establish a secure wireless communication link between the two hardware components. The transmitter is reusable and can be used for repeated 7-day sessions by a single-user over the lifetime of the battery encased in the device.

Model (Catalog) numbers

The following is a list of catalog numbers of the full product line for the Animas Vibe pump the model, as well as compatible accessories.

Table 1. Description of Pump Models and Accessories.

Description	Catalog number
REVENUE KIT	
Rev, Kit, Vibe Adult Blu, mg, US	11751000
Rev, Kit, Vibe Adult Blk, mg, US	11751100
Rev, Kit, Vibe Adult Sil, mg, US	11751200
Rev, Kit, Vibe Adult PGL, mg, US	11751400
Rev, Kit, Vibe Adult LGN, mg, US	11751500
REPLACEMENT KIT	
Rep, Kit, Vibe Adult Blu, mg, US	11720000
Rep, Kit, Vibe Adult Blk, mg, US	11720100
Rep, Kit, Vibe Adult Sil, mg, US	11720200
Rep, Kit, Vibe Adult PGL, mg, US	11720400
Rep, Kit, Vibe Adult LGN, mg, US	11720500
Pump Supplies	
Lithium Batteries (1.5V)	100-155-00
Cartridges	100-124-01
Infusion sets	100-181-00, 100-006-00, 100-240-04, 100-396-00, 100-905-00
Battery cap	100-158-01
Cartridge Cap	100-159-01
Pump Accessories	
Pump Skins	100-496-00, 100-496-01, 100-496-02, 100-496-03, 100-496-04, 100-496-05, 100-496-06, 100-496-07
Bra Pocket	100-023-00, 100-023-01
Low Profile Clip	100-195-01

Clip-N-Go™	100-030-00
Dexcom CGM	
Dexcom G5 Sensor/Transmitter	9438-09

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the control of diabetes. Control of diabetes can be achieved through a combination of methods and behaviors. Self-behaviors include healthy eating, taking medications, as appropriate, and being active. Persons with diabetes may also administer insulin by injection or by using other insulin infusion pumps as prescribed by his/her physician. Methods of controlling glucose levels (glycemic control) have been shown to reduce severe diabetes-related complications. Methods of monitoring glycemic control include periodic measurement of Hemoglobin A1c (HbA1c), which reflects average blood glucose levels over a three month period. Self-monitoring of blood glucose using glucose meters and test strips provides quantitative measurements of fingerstick blood glucose at a single point in time for patients and their healthcare providers to monitor the effectiveness of glycemic control and make more immediate treatment modifications.

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The OneTouch Vibe™ Plus System is available to patients in the United States (original FDA approval November 25, 2014 followed by approval as currently indicated December 24, 2015) and has been commercially available outside the United States in the following regions since 2011; European Union and Asia Pacific. The OneTouch Vibe™ Plus System was approved in Canada in August 15, 2014 and was subsequently introduced into that market.

The device has not been withdrawn from marketing for any reason related to safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

Potential device-related non-serious events related to CGM or insulin pump use include:

- Skin irritation or redness
- Infection
- Pain or discomfort
- Bruising
- Edema

- Rash
- Bleeding
- Allergic reaction to adhesives
- Hypoglycemia from over-delivery of insulin
- Hyperglycemia and ketosis possibly leading to ketoacidosis due to pump malfunction, or problems with the cannula, needle, or insulin infusion set tubing resulting in cessation of insulin delivery
- Loss of communication between the pump and the sensor resulting in CGM values, alarms, and alerts not being available to the user
- Catheter occlusion resulting in missed insulin dosing
- Catheter dislodgement or fracture during infusion set insertion resulting in injury and/or inability to administer insulin
- Failures of the infusion set or at infusion site resulting in inability to administer insulin
- Mechanical or battery failures resulting in interruptions in insulin delivery or incorrect insulin delivery

Sensor breakage with fragments retained under the skin and catheter fracture during infusion set insertion are potential procedure-related complication. Based on post-market experience with similar devices and the results observed in this clinical study, the occurrence and severity of these events do not raise major concerns.

One potential risk of combining the CGM and the pump is that the user might be more inclined to use the CGM data in an unapproved way to determine their insulin dose. Inaccurate sensor results, if used to make dosing decisions, may lead to hypo- or hyperglycemia. However, no further complications are expected due to the pump being combined with the CGM as a system beyond the potential complications of the pump or CGM alone.

Like other insulin pumps, there is an inherent risk that patients who do not use the system as instructed (nonadherence) could harm themselves. Patients should be informed that sensor interstitial glucose values should not be used to make insulin dose decisions and that all threshold alerts and alarms should be confirmed with a blood glucose measurement.

The risks of actions taken based on false positive hyperglycemic readings include inappropriate or excessive administration of insulin and failure to treat hypoglycemia. These inappropriate treatments could result in or prolong hypoglycemia and result in seizures, loss of consciousness, or death. The risks of actions taken based on false positive hypoglycemic readings include failure to administer insulin and failure to treat hyperglycemia. False positive high alerts and low alerts and alarms may increase the number of unplanned blood glucose checks; and disrupt patient activity and sleep. If the false positive rate is too high it can result in ‘alarm fatigue’ and patients may deactivate these alerts/alarms.

The risks of actions taken based on false negative hyperglycemic readings include failure to administer or insufficient administration of insulin and inappropriate administration of extra carbohydrate. These inappropriate treatments could prolong or induce hyperglycemia. The risks of actions taken based on false negative hypoglycemic readings include inappropriate administration of insulin or failure to administer or insufficient administration of extra carbohydrate. These inappropriate treatments could result in or prolong hypoglycemia and result in seizures, loss of consciousness, or death. False negative high alerts and low alerts and alarms will prevent the patient from having the opportunity to perform unplanned blood glucose tests and treat as instructed by their healthcare providers.

The CGM component is to be used only for tracking and trending glucose levels. The risk related to either an inaccurate sensor value outside of the patient's normal range or a false alert or alarm is the risk of performing an unnecessary additional blood glucose test to confirm the erroneous sensor reading. The risk of medical harm may be mitigated through labeling which emphasizes that patients should confirm all CGM readings prior to making treatment decisions.

The risks of the device failing to alert an asymptomatic user to a high or low blood sugar is no greater than that associated with traditional blood glucose monitoring.

IX. SUMMARY OF NONCLINICAL STUDIES

The Dexcom G4® CGM component was submitted to FDA by Dexcom and approved for patients aged 2 years and older (P120005/S018 and P120005/S031). The Dexcom G5® was also submitted by Dexcom (P120005/S033) and approved. Animas has received a right of reference from Dexcom to leverage the data in these submissions to support the change from the Dexcom G4 CGM to the Dexcom G5 CGM in OneTouch Vibe™ Plus System. As such, no new preclinical or clinical studies using the CGM device as part of the OneTouch Vibe™ Plus System were necessary to demonstrate safety and effectiveness. See the SSED for the original P130007 for the performance of OneTouch Vibe™ Plus System.

Laboratory Studies

The following pre-clinical testing was performed on the OneTouch Vibe™ Plus System and on the Animas® Vibe® Insulin Pump. See the SSED for P120005/S018 and P120005/S031 for additional pre-clinical testing that was referenced to support the Dexcom G5® CGM System.

The changes in this submission were validated by performing appropriate software and hardware testing, as described in Table 2, below.

Protocols, test reports and acceptance criteria have been reviewed and found to be acceptable.

The following functionality of the Animas® Vibe® Pump and System was tested:

- Case integrity testing
- Dual vent functionality
- Display functional testing
- Keypad button functional testing
- Vibrator motor functional testing
- Audio piezo functional testing
- Real time clock functional testing
- Infrared interface functional testing
- RF CGM interface functional testing
- Pump rewind
- Load cartridge
- Prime and fill cannula functional testing
- Occlusion detection functional testing
- Loss of prime functional testing
- Low insulin functional testing
- Delivery functional testing

Design Verification Activities

Product and component verification testing was completed to demonstrate that the finished device performs in accordance with design specifications and is further described in the table below.

Pump and System Qualification

Insulin pumps were subjected to environmental and functional testing to ensure they continue to function normally even when exposed to extreme environmental conditions. Qualification testing of the pump and accessories, including cartridge, consisted of environmental stress conditioning including drop testing, pump cleaning, electrostatic discharge, mechanical vibration, storage temperature, humidity and atmospheric pressure and mechanical rigidity and strength. Environmental exposure testing confirms the pump remains functional after temperature, vibration and shock exposures are applied to the pump. Basal and Bolus delivery performance met the accuracy specifications at the minimum, intermediate, and maximum settings.

System level testing was conducted to verify that the system components worked together, and communication was maintained between components per specifications.

Pump and system level testing occurred over a range of environmental and test conditions. In some cases, devices were pre-stressed before undergoing additional functional testing.

Table 2: Summary of Laboratory Studies

Test	Purpose	Acceptance Criteria	Results
RFI Testing EMI/EMC Compliance	Pump complies with RFI, magnetic field requirements.	IEC 60601-2-24 criteria for RFI, magnetic field used.	Pass

FCC	Verify pump adheres to FCC limits.	FCC CFR Title 47, part 15	Pass
CGM Data Reception	Verify communication with single, recognized CGM transmitter.	Communication with pump is activated and maintained as intended without interference from other devices.	Pass
ESD Stress Test	Verify functional performance after being subjected to high voltage levels of ESD.	No permanent degradation, loss of function or data loss.	Pass
CGM Transmission Interference	Verify system recovers from EMI.	Communication re-established or error displayed within 45 minutes.	Pass
CGM Range Test	Verify BLE communication between CGM and pump.	BLE communication when CGM and pump are within 12 feet, line of sight.	Pass
Battery Life Testing	Verify system meets requirements for battery life and battery alarms.	Minimum battery life: 3 weeks with recommended battery under normal use. Replace battery alarm at least 30 minutes prior to battery depletion.	Pass
History Data	Verify non-volatility of pump history data and CGM history data.	Pump history data and CGM history data will not be lost due to loss of power caused by removal of battery.	Pass

For a description of prior laboratory testing leveraged in support of this submission, see the SSED for both P130007 and P130007/S004.

Software Verification and Validation Testing

Comprehensive verification testing was conducted to confirm that the software used in the Animas Vibe Pump System meets all specified requirements and that the software will operate reliably and safely under normal or abnormal use conditions.

Software development activities included establishing detailed software requirements, linking requirements with associated verification tests, software code reviews, unit testing, system level testing and defect tracking and dispositioning to ensure the software conforms to patient needs and intended uses.

Since, except for the hardware and software updates to accommodate the Dexcom G5 BLE communication protocol, and the removal of pediatric warnings as appropriate with

use of Dexcom G5, the OneTouch Vibe™ Plus System is unchanged from the device approved under P130007, non-clinical studies for these devices were limited to validation activities for the software modifications required to accommodate the BLE communications.

This validation testing confirmed that the hardware and software change did not adversely impact any other aspects of device operation.

Package and Shipping Testing: No changes were made to packaging. Packaging shipping and handling testing performed in support of P130007/S004 was leveraged to support this submission. Please see the SSED for P130007/S004 for more information.

Human Factors Testing: A task/use error analysis performed by the sponsor in support of this submission indicated that there is no potential for serious harm to the user from the updates described in this submission, and no new critical tasks have been created. This included usability testing and labeling comprehension on pump and CGM tasks. Therefore the previous validation testing of the critical tasks described in the SSED for P130007/S004 has been leveraged to support this submission. This testing is adequate to demonstrate that the system is safe and effective.

A. Animal Studies

No animal studies were conducted using OneTouch Vibe™ Plus System.

B. Additional Studies

None.

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

Dexcom performed clinical studies in both adult and pediatric subjects to establish a reasonable assurance of safety and effectiveness with the Dexcom G4® CGM System for detecting trends and tracking patterns when used as an adjunct to blood glucose testing in subjects with diabetes mellitus. Please see P120005/S018 and P120005/S031 for details on this clinical study, including study design, age ranges of subjects, safety and effectiveness results, and financial disclosure information.

The algorithm utilized in the Dexcom G4® was approved for use in the Dexcom G5® in P120005/S033. A retrospective analysis was conducted to verify and validate the change.

This submission leverages (by right of reference from Dexcom) the clinical studies performed in submissions P120005/S018 and P120005/S031. No additional clinical study was conducted using the OneTouch Vibe™ Plus System.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Clinical Chemistry and Clinical 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.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The results of the pivotal clinical study performed in P120005/S018 establish a reasonable assurance of safety and effectiveness with the Dexcom G4® Platinum CGM System for detecting trends and tracking patterns when used as intended, adjunctively with blood glucose testing in subjects with diabetes mellitus. The results of the clinical studies performed in P120005/S031 further support the use of this device for pediatric patients aged 2 and up. These clinical studies were leveraged to support the performance of the Dexcom G5 CGM System, reviewed and approved under P120005/S033. See P120005/S018 and P120005/S031 for additional information.

No additional clinical study was required for the OneTouch Vibe™ Plus System. The preclinical data presented above (Section IX) as well as that described in P130007/S004 establish a reasonable assurance of safety and effectiveness for the OneTouch Vibe™ Plus System.

The clinical data referenced from Dexcom's PMA P120005/S018 and P120005/S031, from previous supplements to this PMA, and with the pre-clinical testing provided in support of this supplement demonstrate that the OneTouch Vibe™ Plus System complies with the applicable voluntary standards for biocompatibility, sterilization, electromagnetic compatibility and safety.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory data of OneTouch Vibe™ Plus System (described above) as well as data collected in a clinical study conducted to support PMA approval of the Dexcom CGM System as described in Dexcom's PMA P120005/S018 and P120005/S031.

Potential device-related non-serious events related to CGM or insulin pump use include:

- Skin irritation or redness
- Infection
- Pain and discomfort
- Bruising
- Edema

- Rash
- Bleeding
- Allergic reaction to adhesives
- Inadvertent or unintended insulin dosing (e.g., from rolling onto the pump while sleeping or tampering by young children)
- Hypoglycemia from over-delivery of insulin
- Hyperglycemia and ketosis possibly leading to ketoacidosis due to pump malfunction, or problems with the cannula, needle, or insulin infusion set tubing resulting in cessation of insulin delivery
- Loss of communication between the pump and the sensor resulting in CGM values not being available to the user
- Catheter occlusion
- Catheter dislodgement or fracture during infusion set insertion
- Failures of the infusion set or at infusion site
- Mechanical or battery failures resulting in interruptions in insulin delivery or incorrect insulin delivery

Sensor breakage with fragments retained under the skin and catheter fracture during infusion set insertion are potential procedure-related complication. Based on post-market experience with similar devices and the results observed in this clinical study, the occurrence and severity of these events do not raise major concerns.

One potential risk of combining the CGM and the pump is that the user might be more inclined to use the CGM data in an unapproved way to determine their insulin dose. Inaccurate sensor results, if used to make dosing decisions, may lead to hypo or hyperglycemia as the CGM sensor has not been approved to be used to dose insulin. However, no further complications are expected due to the pump being combined with the CGM as a system beyond the potential complications of the pump or CGM alone.

Like other insulin pumps, there is an inherent risk that patients who do not use the system as instructed (nonadherence) could harm themselves. Patients should be informed that sensor interstitial glucose values should not be used to make insulin dose decisions and that all threshold alerts and alarms should be confirmed with a blood glucose measurement.

A pump malfunction may lead to a clinically significant hypoglycemic event, ketosis or ketoacidosis. A patient should respond with carbohydrate or insulin therapy, hydration, or other medical assistance as necessary. If unaddressed, severe hypoglycemia, severe hyperglycemia and ketoacidosis can result in serious harm and death. Failure of the user to reset the insulin on board feature when indicated after a pump battery change may also lead to a clinically significant hypoglycemic event.

There is a risk of inadvertent insulin bolusing by young children playing with the buttons on the pump or by people rolling over in the night on the pump and inadvertently pushing the buttons on the pump. This pump contains an auto-locking feature to help mitigate accidental button pushing.

The risks of actions taken based on false positive hyperglycemic readings include inappropriate or excessive administration of insulin and failure to treat hypoglycemia. These inappropriate treatments could result in or prolong hypoglycemia and result in seizures, loss of consciousness, or death. The risks of actions taken based on false positive hypoglycemic readings include failure to administer insulin and failure to treat hyperglycemia. False positive high alerts and low alerts and alarms may increase the number of unplanned blood glucose checks; and disrupt patient activity and sleep. If the false positive rate is too high it can result in ‘alarm fatigue’ and patients may deactivate these alerts/alarms.

The risks of actions taken based on false negative hyperglycemic readings include failure to administer or insufficient administration of insulin and inappropriate administration of extra carbohydrate. These inappropriate treatments could prolong or induce hyperglycemia. The risks of actions taken based on false negative hypoglycemic readings include inappropriate administration of insulin or failure to administer or insufficient administration of extra carbohydrate. These inappropriate treatments could result in or prolong hypoglycemia and result in seizures, loss of consciousness, or death. False negative high alerts and low alerts and alarms will prevent the patient from having the opportunity to perform unplanned blood glucose tests and treat as instructed by their healthcare providers.

The CGM component is to be used only for tracking and trending glucose levels. The risk related to either an inaccurate sensor value outside of the patient’s normal range or a false alert or alarm is the risk of performing an unnecessary additional blood glucose test to confirm the erroneous sensor reading. The risk of medical harm may be mitigated through labeling which emphasizes that patients should confirm all CGM readings prior to making treatment decisions.

Clinical studies performed for the Dexcom G4 Platinum reported several non-serious adverse events. In a study of 79 adult subjects (P120005/S031) there were ten (10) adverse events. Seven (7) adverse events were Erythema affecting 7 subjects; two (2) adverse events were Edema affecting 2 subjects; one (1) adverse event was reported as a study procedure-related adverse event (IV insertion issues during clinic session). All adverse events were deemed Mild and Probably Related to Study. In a study of 51 pediatric subjects (P120005/S018), thirteen (13) adverse events were reported, affecting 10 subjects. Twelve (12) adverse events were related to skin irritation related to the device (erythema at adhesion area or needle insertion site). All of these were rated as ‘Very slight’. One (1) adverse event was categorized as ‘Other’, possibly related to study. All adverse events were resolved or were stable at study termination. No serious adverse effects or unanticipated adverse device effects were reported in the clinical studies.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study(ies) as referenced above. Additional factors to be considered in determining probable risks and benefits for this device are discussed below:

Benefits:

This device includes placement of the glucose conversion algorithm onto the transmitter (not on the receiver as in the Dexcom G4 Platinum CGM) and incorporates a smart-device based app that allows smart devices to act as a primary display for the system (to input calibrations and other associated diabetes management information) and link the CGM system to Dexcom Share. The use of the Animas Vibe with Dexcom G5 System provides the added benefit for patients to use their smart device as the primary display without having to carry an additional device (the CGM receiver) with them. Additionally, the Animas Vibe with Dexcom G5 System utilizes the updated Dexcom 505 software which improves the overall accuracy of sensor glucose values displayed on the Vibe pump.

Design changes were made to the Animas Vibe Pump to be compatible with the Dexcom G5 BLE transmitter. Additionally, the pump incorporates an auto lock feature and specialized pump “packs” to help prevent pediatric patients (age 7 and below) from accessing the bolus and basal deliveries.

Compared to using only self-monitored blood glucose (SMBG) values to manage diabetes, the Animas Vibe with Dexcom G5 System can provide extra monitoring for hyper- and hypoglycemia and facilitate a more comprehensive understanding of glucose trends and patterns in response to activities of daily living.

Use of sensor values, alarms, or alerts have the potential to alert users to glucose values outside their target range and can be especially valuable in individuals who have hypoglycemic unawareness or do not recognize the signs and symptoms of hypoglycemia.

Benefits of an insulin pump include the ability to administer insulin in a manner that is more consistent with the normal physiologic release of insulin and that corresponds to their specific needs and lifestyles. The insulin pump of OneTouch Vibe™ Plus System provides a method of insulin delivery that is more consistent with the physiologic release of insulin in a person without diabetes. Both basal and bolus rates of insulin release incorporate factors such as insulin sensitivity, age, weight, usual activity, and typical diet and can be individualized to maximize insulin effectiveness. The integration of the Dexcom G5 CGM with the Animas Vibe insulin pump can provide opportunities to prevent hypoglycemia and hyperglycemia especially in young children (who are unable to self-manage) and adolescents (who may have erratic eating habits and risky behavior).

PotentialRisks:

Potential risks of combining the CGM and the pump is that the user might be more inclined to use the CGM data in an unapproved way to determine their insulin dose. Use of inaccurate glucose concentration data can result in an incorrect dose of insulin being delivered leading to hypo- or hyperglycemia. Another potential risk is that of young children deliberately or inadvertently altering insulin dosage/administration by pushing buttons or dislodging insulin infusion catheter and/or sensor.

• **Specific risks of the CGM and sensor include:**

- Missed alerts, false negative and false positive alerts with corresponding actions or lack thereof.
- Skin irritation or redness, inflammation, pain or discomfort, bruising, edema, rash, bleeding, infection, or allergic reaction due to either the sensor needle or the adhesive
- Sensor breakage leaving a sensor fragment under the skin

• **Risks of the pump include the following:**

- Tampering with pump buttons may result in inadvertent delivery of insulin resulting in hypoglycemia might occur more frequently with young children.
- Inadvertent dislodgement of insulin tubing from the infusion site might occur more frequently in children.
- Hypoglycemia from over-delivery of insulin due to a pump defect
- Cessation of or decreased insulin delivery resulting in hyperglycemia and possibly ketoacidosis due to pump failure, problems with the cannula, or insulin infusion set tubing, or failure of the user to reset the IOB feature after changing the pump battery. Catheter dislodgement or fracture during infusion set insertion resulting in injury and/or inability to administer insulin
- Mechanical or battery failures resulting in interruptions in insulin delivery or incorrect insulin delivery
- Catheter occlusion resulting in missed insulin dosing
- Skin irritation, or redness, inflammation, pain or discomfort, bruising, edema, rash, bleeding, infection, or allergic reaction at the infusion site
- Failure of the infusion set or at the infusion site resulting in inability to administer insulin

Risks of the sensor augmented pump include both false positive and false negative readings with the following potential consequences:

- False positive hyperglycemic readings:
 1. Inappropriate or excessive administration of insulin and failure to treat hypoglycemia
 2. Loss of consciousness, seizures, or death related to severe or prolonged hypoglycemia.
- False positive hypoglycemic readings:
 1. Failure to administer insulin or a sufficient amount of insulin
 2. Failure to treat hyperglycemia.
- False positive high alerts and low alerts and alarms:
 1. Needless increase in SMBG
 2. Disruption of patient activity or sleep.
 3. Alarm fatigue with subsequent deactivation of alarms & alerts
- False negative hyperglycemic readings:
 1. Failure to administer or insufficient administration of insulin and inappropriate administration of carbohydrates, thus increasing the risk of prolonging or inducing/exacerbating hyperglycemia.
- False negative hypoglycemic readings:

1. Inappropriate administration of insulin
 2. Failure to administer or insufficient administration of extra carbohydrate.
 3. Inappropriate treatments could result in or prolong hypoglycemia and result in seizures, loss of consciousness, or death.
- False negative high alerts and low alerts and alarms:
 1. Failure to recognize need to intervene with additional SMBG and indicated interventions.
 - Use of sensor values, alarms or alerts
 3. Inaccurate alarms and alerts may increase the risk of performing unnecessary capillary glucose measurements.

The risks of the device failing to alert an asymptomatic user to a high or low blood sugar is no greater than that associated with traditional SMBG. Moreover, the sponsor has mitigated the risk of inappropriate interventions and severe adverse events (SAEs) through labeling that emphasizes patients should obtain capillary glucose measurements to confirm all CGM readings prior to making treatment decisions.

Every insulin delivery method carries some degree of risk of a harmful event. However, health care providers (HCPs) generally will not prescribe insulin pumps to patients or parents/caregivers who do not demonstrate that they are checking glucose levels frequently (4-6 times/day), can recognize and treat the symptoms of both hypo- and hyperglycemia, and have some knowledge of sick day “rules”. Likewise, HCPs are not likely to prescribe sensors or sensor-augmented pumps to patients or parents/caregivers who are not engaged in care, demonstrate adequate self-management/management skills and willingness to perform finger stick blood glucose measurements twice daily for sensor calibration, and/or are seeking ways to improve glycemic control.

Adolescents often have high risk behaviors or developmental tasks, e.g. acceptance by peers, which may interfere with self-management skills regardless of insulin delivery method. The use of an insulin pump, however, can be programmed with basal rates that can limit the severity of hyperglycemia, thus preventing diabetic ketoacidosis (DKA). Pre-set pump settings can also insure that basal rates and bolus doses do not exceed the recommended total daily dose (TDD), thus reducing the risk of hypoglycemia. Therefore, although non-adherence to instructions and misuse of the pump or pump malfunction has the potential to result in hypo- or hyperglycemia, the pump has built in features that can mitigate these risks.

Additional safeguards in young children (which include pre-set pump settings, activating an auto lock feature which would prevent additional boluses or changes to pre-set settings, documentation of basal and bolus amounts of insulin delivered {TDD}, placement of infusion sites and sensors in sites that are out of reach, adequately securing the infusion site and tubing, and placing the device in pump “packs”) can reduce the risk of deliberate or inadvertent tampering with device or insertion sites that may result in over or under-delivery of insulin in children or dislodgment of the tubing from the insertion site.

There is a risk of inadvertent insulin bolusing by children playing with the buttons on the pump or by people rolling over in the night on the pump and inadvertently pushing the buttons on the pump. This pump contains a locking feature, which will prevent accidental button pushing; however, this feature must be enabled.

Summary of Other Factors:

Successful use of the device among users is facilitated by the training that is available on the Animas and Dexcom websites, certified Animas trainers, and comprehensive and illustrated user manuals and quick reference guides.

Labeling in User Manuals and Quick Start Guides clearly states that glucose sensors are adjunctive to SMBG and should not be used independent of SMBG to make treatment decisions. The labeling also advises patients to perform a finger stick blood glucose when their sensor readings do not correspond to their symptoms of hyper- or hypoglycemia. Users are further advised to recalibrate their sensor if there is a discrepancy between the sensor and the finger stick glucose levels. Additional risks are mitigated by careful patient selection and education. Only patients/parents/caregivers willing to perform the necessary blood glucose checks, sensor changes and calibrations should be prescribed the system.

Risk mitigations associated with use of insulin pump therapy include labeling and training with a healthcare provider who has been certified as a pump/CGM trainer. Risk mitigations that prevent children, especially young children, from altering basal and bolus rates include activating an auto-locking feature after setting basal rates and bolus doses and labeling that emphasizes the potential risk of and strategies to reduce the risk of inadvertent or deliberate tampering with pump settings. Users are also instructed to have a backup plan for therapy (e.g. insulin pen or syringe) in case they are unable to use their pump. However, there is still some risk of inadvertent button pushing that could lead to over-bolusing of insulin.

1. Patient Perspectives:

Patients want a variety of devices to aid and inform them and their healthcare practitioners regarding their glucose control. This device provides a consolidated option for conveniently integrating CGM use with insulin pump use. This information was gathered during patient oriented conferences and face-to-face meetings with patients.

Conclusion:

In conclusion, given the available information above, the data support that for the indication for use of the device the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The benefits of using the OneTouch Vibe™ Plus System outweigh the risks.

XIII. CDRH DECISION

CDRH issued an approval order on December 16th, 2016.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

XV. REFERENCES

None.