BD Protocol #: **DBC-19BRGHT02**

Protocol Title: **An assessment of the impact of an app based diabetes training program in conjunction with the use of BD Nano 2nd Gen 4mm pen needle on diabetes self-efficacy in people with type 2 diabetes**

Current Version	Version 4.0 dated 10 January 2020
Version History	Version 1.0 dated 16 July 2019 Version 2.0 dated 16 October 2019 Version 3.0 dated 04 November 2019 Version 4.0, dated 10 January 2020
Sponsor	BD – Diabetes Care 1 Becton Drive, MC: 250 Franklin Lakes, NJ 07417
Sponsor Medical Monitor	[redacted]
Sponsor Risk Assessment	☐ Significant Risk (SR) ☒ Non-significant Risk (NSR) ☐ Minimal Risk

NCT number: NCT04090242
NCT number added post approval as per CT.gov requirement.

This study will be performed in accordance with all stipulations of the protocol and in compliance with all applicable BD Policies and Procedures. This study will be conducted in accordance with the ethical principles that originate from the Declaration of Helsinki and the Belmont Report. Study conduct will comply with regulations, and the Good Clinical Practice guidelines set forth by the International Conference on Harmonization (ICH-E6) and ISO14155.

All Study Product(s) used in this study should be considered to be for investigational use only.

SPONSOR PROTOCOL APPROVAL

Signature below indicates approval of the Protocol/Amendment as written. (Administrative changes only require signature of the Study Manager)			
Individual or function	**Name**	**Signature**	**Date**
Medical Affairs Team Representative	[redacted]	*This document is signed electronically in the eTMF system*	
Medical Monitor	[redacted]	*This document is signed electronically in the eTMF system*	
Study Statistician	[redacted]	*This document is signed electronically in the eTMF system*	
Study Manager	[redacted]	*This document is signed electronically in the eTMF system*	

INVESTIGATOR SIGNATURE PAGE

Principal Investigator	
Investigational Site	

I have read this protocol and agree to conduct this study in accordance with all stipulations of the protocol and in compliance with all applicable Good Clinical Practices and regulations.

_____ _____

Signature of Principal Investigator Date

Principal Investigator must sign each version of the protocol, including administrative changes.

Table of Contents

List of Abbreviations and Definition of Terms

ARMS-D	Adherence to Refills and Medicines Scale for Diabetes
ATD-DES	Attitudes Toward Diabetes- Diabetes Empowerment Scale
AE	Adverse event
BD	Becton Dickinson and Company
BGM	Blood Glucose Meter
BMI	Body Mass Index
cc	cubic centimeter
CFR	Code of Federal Regulations
CGM	Continuous Glucose Meter
CI	Confidence Interval
CRC	Clinical Research Coordinator
CRF	Case Report/Record Form
CRO	Contract Research Organization
DC	Diabetes Care
DDS	Diabetes Distress Screening Scale
EDC	Electronic Data Capture
FDA	Food and Drug Administration
FDAAA	FDA Amendments Act of 2007
fGM	Flash Glucose Meter (Libre, Abbott Labs)
GCP	Good Clinical Practice
HbA1c	Hemoglobin A1c
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IDD	Insulin Delivery Device
IDSRQ	Insulin Delivery System Rating Questionnaire
IM	Intramuscular(ly)
IRB/EC	Institutional or Independent Review Board/Ethics Committee
IV	Intravenous(ly)
MDI	Multiple daily injections/multiple daily insulin injections
mg/dL	Mg per deciliter
mL	Milliliter
mm	Millimeter
OAD	Oral anti-hyperglycemic drugs
OS	Operating system
PI	Principal Investigator
PHI	Personal Health Information
SC	Subcutaneous(ly)
SAE	Serious Adverse Event
SD	Standard deviation
SOP	Standard Operating Procedure
WC	Wireless Controller
WHO	World Health Organization

1.0 INTRODUCTION

Becton Dickinson (BD) has developed a diabetes care application (app) to be downloaded by a user to a mobile device. The companion app referred to as "The Diabetes Care App" or "The DC App", targets patients with type 2 diabetes mellitus who require daily insulin. The app is intended to be used as a patient education tool and data logger to augment the diabetes care team. BD has also redesigned their 4mm insulin pen needle commercialized as "Nano 2nd Gen", which is compatible with all insulin pens. The DC App can be used by patients with diabetes as a means of delivering educational content on injection therapy and lifestyle habits.

The DC App features include:

1. Curated articles identified as most relevant to the patient based on baseline criteria
2. Logging functionality for blood glucose, activity, and carbohydrates
3. Chat bot that responds to questions in real time
4. Data display to visualize logged information

Nano 2nd Gen features include:

1. A larger outer cap for easier grip and recapping
2. A larger inner shield for easier removal
3. A wider hub at the base of the needle

The Diabetes Care App is a smartphone app available on iOS and Android platforms intended to provide relevant education content and tracking capabilities for people with diabetes, specifically focusing on those with type 2 diabetes who are new to injection therapy or need a refresher on injection best practices. During enrollment users are asked to input the following but not limited to; type of therapy, most recent A1C and dietary restrictions in order for the app to map them to relevant educational content. It delivers this education through articles, step by step walkthroughs (tutorials) and video demonstrations. Some topic areas include a series of questions to confirm confidence before moving on to new areas. Users can also log blood glucose, carbohydrate consumption, and activity which can then be compiled and displayed on a user and physician report in the app. It is expected that users will access the application primarily for frequently asked questions or are ready to learn more about diabetes, drug therapy, diet, or exercise.

Nano 2nd Gen has been redesigned with a wider needle hub and revised shape and grips for the inner and outer shields. The wider needle hub surface area is intended to distribute force evenly over a greater area. This design has been shown to reduce tissue compression following insertion of the needle[1]. The redesign resulted in a true injection depth significantly less than comparator 4mm pen needles and greater consistency in achieving that depth[1]. BD Nano 2nd Gen was preferred overall for all outcomes measured on the visual analog scale and demonstrated superiority in overall preference when compared to commercially available posted hub needles of similar gauge and length[2]. BD Nano 2nd Gen demonstrated non-inferiority in all groups combined for bending, bleeding, and leakage[2].

This study will be assessing patient-reported outcomes including diabetes empowerment, diabetes distress and patient satisfaction and to understand the emotional impact of The DC App and optimized pen needle design, in addition to their impact on glycemic measures.

2.0 OBJECTIVES

The purpose of this study is to evaluate the impact of providing diabetes education through The DC App and switching to BD Nano 2nd Gen pen needles on patient reported and glycemic outcomes versus standard of care (SOC) in people with type 2 diabetes who inject insulin multiple times daily.

- The Primary objective is to evaluate changes in self-efficacy as measured by the Diabetes Empowerment Scale from baseline and study end.
- The Secondary objective of this study is to:
  - Assess for differences between Nano 2nd Gen used in conjunction with training from The DC App and standard of care on glycemic control as measured by mean 24 hour glucose.
  - Assess time in range and glycemic variability.
  - Evaluate patient reported outcomes-Diabetes Distress Screening Scale (DDS), Adherence to Refills and Medicines Scale for Diabetes (ARMS-D), Insulin Delivery System Rating Questionnaire (IDSRQ) and Patient Satisfaction on the use of DC App and Nano 2nd Gen Pen Needle (Intervention Group only).
- Exploratory objectives include frequency of hypoglycemia and patient engagement, which will be evaluated via app usage data which will also help understand which features patients utilized most frequently. Injection Technique Questionnaire will also be administered at study end.
- Subjects will be evaluated for any adverse events that may occur during their participation in the study.

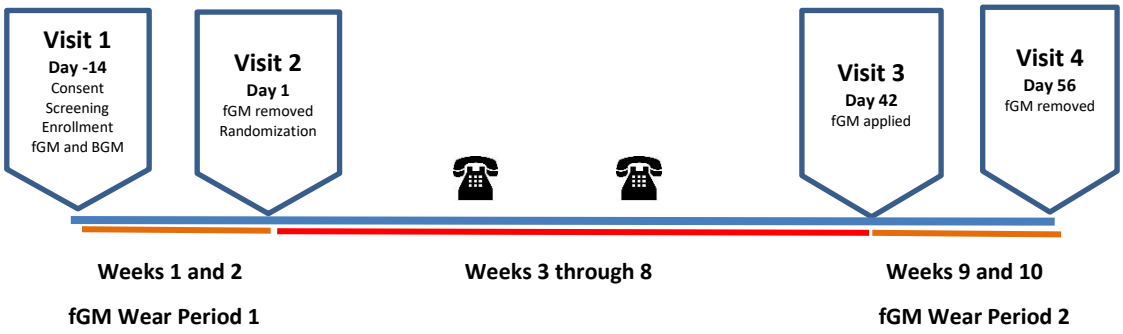
3.0 STUDY DESIGN

3.1 Overall Study Design

This is a multi-center, open-label, parallel-group, randomized controlled study in subjects with type 2 diabetes using multiple daily injection (MDI) insulin therapy. Subjects will be randomized to either receive the DC App and BD Nano 2nd Gen pen needles (intervention) or continue their standard of care using their current pen needle and diabetes management (control). The study will consist of four visits and two scheduled phone calls across a total of 10 weeks.

At Visit 1 (Day -14) site staff will screen and enroll qualified subjects, provide a BGM (Accu-Chek Guide) and attach a blinded flash glucose sensor (Libre Freestyle) to the back of the arm. Subjects will complete any applicable baseline Patient Reported Outcomes (PRO) questionnaires and be sent home with no changes to their current therapy. While at home Subjects will be asked to test blood glucoses using the provided BGM and continue their usual insulin dosing before returning to clinic for Visit 2. Visit 2 will consist of randomization (Interventional Group or Control Group). The control group will be continued on their current pen needle and receive standard visit education as needed. The intervention group will be trained on the use of the DC App and be switched to BD Nano 2nd Gen pen needle. During weeks 3 through 8, subjects in both groups will continue their usual insulin routine, with the control group adhering to their usual practice of managing their diabetes and the intervention group utilizing the DC app for relevant educational content and tips plus using the BD Nano 2nd Gen for all insulin injections. During Visit 3 subjects will get a 2nd fGM sensor placed and be instructed to continue their insulin routine for the final 2 weeks. Visit 4 is the last visit where subjects will have their fGM removed, return the BGM, complete applicable PRO surveys, an injection technique questionnaire and be discharged.

Figure 3.1a- Study Flow



3.2 Endpoints

1. **Primary Endpoints**
   a. **Empowerment: Attitudes toward Diabetes - The Diabetes Empowerment Scale (DES)** will be used to compare changes between groups from baseline to study end.

2. **Secondary Endpoints**
   - **24 Hour Average Blood Glucose:** Freestyle Libre Pro blinded flash glucose monitoring will be used to assess change in average 24 hour blood glucose between groups at baseline and study end. Subjects will wear Libre sensors on the backs of their arm for 14 days at a time and return to clinic with the sensors for data extraction.
   - **Time in range:** Data collected by the flash glucose monitor will also be used to calculate percent of time spent <54 mg/dL, <70 mg/dL, 70-180 mg/dL, and >180mg/dL to compare differences between groups at baseline and study end.
   - **Mean Amplitude of Glycemic Excursions (MAGE):**
     - Flash glucose monitoring data will be used to measure glycemic variability changes at baseline and study end between groups.
     - Within group comparisons will be conducted at baseline and study end for 24 hour average blood glucose, time in range, MAGE and frequency of hypoglycemia.
   - **The Diabetes Distress Scale (DDS)** will be used to compare changes between groups from baseline to study end.
   - **Insulin Delivery System Rating Questionnaire (IDSRQ)** The Insulin Delivery System Rating Questionnaire will be used to compare changes between groups from baseline to study end.
   - **Adherence to Refills and Medicines Scale for Diabetes (ARMS-D):** The Medical Adherence Questionnaire (insulin) will be used to compare changes between groups from baseline to study end.
   - **Patient Satisfaction:** a satisfaction survey with questions specific to the DC App and Nano 2nd Gen will be administered to participants in the **Intervention group only at end of study.**

3. **Exploratory Endpoints**
   - **Frequency of hypoglycemia:** The number of hypoglycemic events (<70mg/dL and <54mg/dL) as measured by blood glucose monitor (BGM) will be collected to determine frequency of hypoglycemia in each group.

- **Patient Engagement:** Engagement with The DC App will be measured by app collected usage analytics and will include assessments of time spent within app, frequency of opening the app, types of articles accessed, types of data logged, and frequency of article access or data logging.
    - Within group comparisons of highly engaged app users compared to minimally engaged users will be performed for all outcomes listed in primary and secondary endpoint sections above.
- **Injection Technique Questionnaire:** A non-validated injection technique assessment questionnaire will be used to compare injection technique between groups at study end only (no baseline assessment).

4. At each contact point, visits and phone calls, adverse events will be collected.

3.3 Acceptance Criteria

No acceptance criteria have been established for this study.

3.4 Treatment Allocation and Methods to Reduce Bias

3.4.1 Randomization

Subjects will be randomized during Visit 2 using a standard randomization technique.

3.4.2 Masking/Blinding (if applicable)

There will be no masking or blinding in this study of test products.

3.4.3 Skill and Behavior of Persons Interacting with the Device

Qualified personnel, selected to perform training of subjects on The DC App must be trained in diabetes management (e.g. Diabetes Educator, Nurse Practitioner, Nutritionist, diabetes nurse, nurse (RN), clinical research coordinator (CRC)).

3.5 Stopping Rules

No stopping rules for the study have been developed by the Sponsor. The Principal Investigator is responsible for suspending study enrollment for reasons of subject/clinician safety and well-being.

4.0 STUDY POPULATION

A minimum of 86 subjects with type 2 diabetes and currently on MDI therapy will be recruited across 3 - 6 sites. Up to 40 additional subjects may be enrolled across sites to ensure a total of 86 subjects complete the study. (Completion will be defined as a subject completing 10 weeks of study participation and can provide at least 10 days of flash glucose data at baseline (first 2 weeks) and again at study end (last 2 weeks)).

4.1 Inclusion Criteria

1. 22 years of age minimum
2. Adult subjects with **type 2 diabetes mellitus on MDI and giving themselves at least 2 injections of insulin / day <u>using a pen injector.</u>** This may include at minimum
    i. giving 1 basal injection and at least 1 meal time injection or
    ii. giving at least 2 daily injections of mixed insulins or
    iii. giving 2 meal time injections

iv. two injections of basal insulin per day will not be considered MDI for this study

v. additional OAD/non-insulin injectable therapy is acceptable

3. Must currently be on MDI insulin therapy for at least 6 months prior to enrollment and, in the opinion of the investigator, would benefit from dose optimization.
4. Willing to use the BD provided BGM for the study duration.
5. Hemoglobin A1C of 8.0 – 11% at screening (tested at enrollment unless Subject has a documented HbA1c value on file at the site that was drawn within 3 months of enrollment date).
6. In stable health status with no acute or significant illness, based on the opinion of the investigator.
7. Able to read, write and follow instructions in English (translations will not be provided).
8. Currently using an Apple iPhone with iOS Versions 13.1 or greater or Samsung phone with Android OS Versions 8 or later and able to understand the use of mobile apps. (Subject may choose to upload to the correct version themselves prior to screening visit or during the screening visit with the help of site staff).
9. Able and willing to provide informed consent.
10. Able and willing to follow study procedures.

4.2 Exclusion Criteria

Subjects with any one of the following characteristics will be excluded from participation:

1. Pregnant or breast feeding- self reported.

2. Subject on basal-only

3. Uncontrolled comorbidities or acute illness

4. Currently using Nano **2nd Gen** pen needles

5. Use of a iPhone with iOS 13.0 or lower or use of an android phone that is not a Samsung or using Android OS Versions 7.0 ”Nougat”or lower

6. If using CGM, use of CGM or fGM less than 6 months and not proficient in its use, however this may be left up to the investigators discretion.

i. Subjects may continue to wear their own CGM/fGM during their participation in this study if they adhere to the testing of blood glucose using the site provided BGM.

7. Subjects not on stable doses of concomitant non-insulin diabetes medications. Stable is defined as not requiring new non-insulin diabetes medications or any changes in dosing of current non-insulin diabetes medication during study participation (10 weeks) unless warranted by investigator for the safety of the subject.

8. Actively using one of the following diabetes management apps deemed similar and **not willing to stop** using it during participation on the study (exclusionary apps; Onedrop, Welldoc (Bluestar), Dario, Sugar Sense Glucose, Buddy, mySugr, Omada, Livongo, Accu-Check Connect, SugarIQ).

9. Known sensitivity to adhesives.

10. Currently using the DC app.

11. Employed by, or currently serving as a contractor or consultant to BD or study site

12. Any other condition the investigator deems to pose a risk to the Subject in the study

5.0 DESCRIPTION OF STUDY PRODUCTS

5.1 Test Product(s)

- **The Diabetes Care Application**

  The DC App is a mobile app that enables people with diabetes to make smarter choices and provides personalized resources and expert content, helping to empower the patient to have meaningful conversations with their health care team. This is the first digital diabetes solution from BD that delivers personalized support and empowers you to feel confident and in control of your diabetes management, whenever and wherever you are. BD Diabetes Care has the ability to identify trends beyond your blood glucose numbers, learning and growing with the patient, offering personalized insights and helpful tips to keep healthy behaviors on track.

- **BD Nano™ 2nd Generation**

  4mm x 32G XTW 5-bevel pen needle (available in the US under this brand name) /BD Nano Pro 4mm x 32G XTW 5-bevel pen needle (available in Canada under this brand name). The BD pen needle to be used in this study has a 32G extra-thin walled cannula with a nominal length of 4mm, and a 5-bevel tip.

5.2 Control products

For this study, subjects in the Control group will use their current pen needle, injector, and insulin and receive standard guidance on diabetes management provided by the HCP.

5.3 Ancillary Products

Ancillary products are materials that are critical to the use of the study product or execution of the protocol, such as certain concomitant medications or critical device components which are used with the study device (or drug) and must be used exactly as specified in this protocol.

- **Accu-Chek Guide BGM (Roche)**

The Accu-Chek Guide Blood Glucose Monitoring System quantitatively measures glucose in fresh capillary whole blood from the fingertip, palm, and upper arm as an aid in monitoring the effectiveness of glucose control. The blood glucose values can 1) be downloaded and viewed using Accu-Chek Connect Portal or 2) since the Guide will communicate directly with the DC App, BG can be either viewed on the mobile device or a report can be run.

- **Freestyle Libre Pro (Abbott)**

A blinded flash glucose monitor. It consists of 2 components: 1) a clinician reader that can activate multiple sensors at the same time and download sensor data 2) the sensors that are applied for 2 weeks at a time to the back of the arm and continuously measure interstitial glucose levels.

- **Torbot Skin Tac (for use with Freestyle Libre Pro Sensor)**

Skin Tac liquid adhesive barrier is a Latex-free, hypo-allergenic, clear, non-rubber liquid adhesive. Prepares the skin for application of tapes, dressings, infusion sets, and much more. This unique “tacky” skin barrier, being latex-free and hypo-allergenic, makes it ideal for patients with sensitive skin. It is recommended by Abbot to help the sensor remain in place for up to 14 days (see Appendix 1).

5.4 Product Labeling

Only approved products will be used in this study. Commercial products will be supplied as labeled by the manufacturer.

5.5 Maintenance and Storage of Study Products

Investigational study products should be stored according to manufacturer’s recommendations.

6.0 STUDY METHODS

6.1 Training of Site Staff by Sponsor

- Qualified personnel (trained in the operation of The DC App) will train site staff or designee on the use of The DC App (install, creating an account, navigation, and operation).

6.2 Schedule of Activities

Activity	Visit 1	Visit 2	Phone 1	Phone 2	Visit 3	Visit 4
	Day -14	Day 1 (+/- 2 day)	Day 14 (+/- 2 day)	Day 28 (+/- 2 day)	Day 42 (+/- 2 day)	Day 56 (+/- 2 day)
Informed Consent	X[1]					
Demographics	X					
Body measurements (height, weight)	X					
Pregnancy (self-reported)	X					
Diabetes History and Current Therapy	X					
Point-of-Care A1c (if previous testing performed greater than 3 months)	X					
Confirm Inclusion and Exclusion Criteria	X					
Apply and activate Freestyle Libre Pro sensor	X				X	
Training on BD provided BGM and instructions on BG testing	X					
Randomization: Site staff will instruct as required per 1. Intervention Group (App/Nano Group) 2. Control Group (SOC Group)		X				
Follow-Up-Depending on the randomization perform either SOC education or prompt subject to complete required training modules within the app			X	X	X	
Scan and remove Libre, upload data		X				X
Download BGM		X				X
Administer Diabetes Empowerment Survey (DES)	X					X
Administer Diabetes Distress Survey (DDS)	X					X
Administer Insulin Delivery System Rating Questionnaire (IDSRQ)	X					X
Administer Medication Adherence (Insulin)	X					X
Administer Patient Satisfaction						X Intervention Group Only
Administer Injection Technique Questionnaire						X
Inquire and evaluate AEs		X	X	X	X	X
Discharge from Study						X

[1] Informed consent must be obtained before any study related activities take place.

6.3 Recruitment and Informed Consent

Subjects may be (pre-) screened prior to the Visit 1 - Screening: the Investigator or other site staff may reach out to potential subjects and inform them about the study requirements as well as do a high-level check of the inclusion and exclusion criteria. However, no study-related procedures will be performed prior to a study subject signing the Informed Consent Form.

Subjects will be recruited by the study site. Prior to study participation, every potential subject must provide written informed consent (See Section 15.2 for Informed Consent requirements). After being presented with an overview of the study procedures and use of the App, each subject will be given ample time to review the Informed Consent Form and ask any questions about the procedures. If the subject agrees to participate in the study he or she will sign the Informed Consent Document.

6.4 Visit 1 Screening (Day -14)

Subjects will be screened during Visit 1 to ensure they meet all inclusion and none of the exclusion criteria for participation in the study. The screening consists of the procedures indicated in the table above and briefly described below.

Demographic Data and Physical Assessment

1. **Demographics:** Subjects will be asked a number of background and demographic questions to ensure they meet the study-specific eligibility criteria. Information collected will include, but is not limited to:
    - Age
    - Gender
    - Ethnicity/Race
    - Height and Weight and BMI (sponsor will calculate BMI)
2. **HbA1c:** If the subject has not had a documented HbA1c in the past three months they will be given a point-of-care A1C test.
3. **Pregnancy: Self-Reported:** Subjects (females of child bearing potential) will need to attest they are not pregnant and not breast feeding at screening.
4. **Diabetic History and Current Therapy** Information collected will include, but is not limited to:
    - When were they diagnosed with diabetes (month and year)?
    - How long have they been on insulin (year and month)
    - Current method of administration (pen, syringe, pump, other),
    - Current pen needle usage (Brand, Gauge and Length (mm))
    - Current insulin type (basal, bolus, mixed),
    - Type of insulin (brand).
    - Current Insulin regimen (includes insulin and concomitant diabetes medication)
    - Do they currently use a diabetes app, if so
        - Which one?
        - How long have they been using it?
    - Do they use CGM, if yes, how long have they used it and what do you use?
5. Confirm smartphone make and model and software version.
6. **Confirm Inclusion and Exclusion Criteria**
    - Subjects who do not meet the criteria will be dismissed at this point.
    - Subjects who do meet the criteria will be enrolled.

Enrollment, Training and Libre Application

1. Once eligibility has been determined subjects will be provided and trained on the BGM (Accu-Chek Guide BGM) and have a Freestyle Libre Pro sensor (blinded to subject) placed on the backs of their arms by site staff who will then activate the sensor before sending the subject home. To aid in helping the sensor stick for the 10-14 days, the use of a skin prep will be used, Torbot Skin Tac. (See Appendix 1).
2. Applicable baseline surveys and questionnaires will be administered during this visit.
3. Subject will be instructed to continue on their current insulin therapy (unless instructed to change per the investigator).
4. Subjects will be instructed to test their blood glucose using the site provided BGM.

6.5 Visit 2 (Day 1 +/- 2 Day)

- Subjects will return to the clinic at their scheduled time.
- Subjects will be evaluated for any adverse events.
- Site will confirm subject continues to meet inclusion and exclusion criteria to include ensuring the subject has made no changes in their non-insulin diabetes medication and significant changes in their insulin regimen. If changes occurred, site will document the nature of the change according to the rules in Section 6.9.
- Site staff will download Libre data and remove sensor and confirm a minimum for 10 days of BG data.
- Site staff will download the BGM data using Accu-Chek Connect (or equivalent)
- Subjects will be randomized to receive The DC App and Nano 2G pen needles (intervention group) **or** to continue their current therapy and receive standard visit education (control group).
    a. Intervention Group: Site staff will introduce the subject to the app and how it works. Site staff will assist them in downloading the app, creating an account, reviewing the app functionality, highlighting required modules, and connecting the Accu-Chek Guide meter (this is optional). In addition, they will be provided with BD Nano 2nd Generation pen needle to use during their participation in the study.
    Note: to maintain confidentiality a separate account will be created for each subject using an anonymized user name/email account and password based on their unique subject number. The app will be removed at the end of the subject's participation in the study.
    b. Control group will be instructed to continue their current insulin therapy using their current pen needle and injector.
- Subjects will be instructed to measure their BG using the supplied Accu-Chek Guide meter
- Subjects will be instructed to bring their phone, if applicable, BGM and fGM to the next clinic visit.

6.6 Phone Calls (Day 14 +/- 2 day and Day 28 +/- 2 day)

- The site will follow up 2 times over the middle 6 weeks.
- Subjects will be evaluated for any adverse events.
- Site will confirm subject continues to meet inclusion and exclusion criteria to include ensuring the subject has made no changes in their non-insulin diabetes medication and significant changes in their insulin regimen. If changes occurred, site will document the nature of the change according to the rules in Section 6.9.
- During these calls the site will inquire about the subject's diabetes management, provide recommendations if needed and ask about any adverse events.
- If participating in the Intervention group the site will prompt the subject to visit the app regularly (daily) and utilize the app related tools and review the diabetes education material.
- If participating in the Control group questions will be addressed as usual.

6.7 Visit 3 (Day 42 +/- 2 day)

- Subjects will return to the clinic at their scheduled time.
- Site will confirm subject continues to meet inclusion and exclusion criteria to include ensuring the subject has made no changes in their non-insulin diabetes medication and significant changes in their insulin regimen. If changes occurred, site will document the nature of the change according to the rules in Section 6.9.
- Site staff place a new fGM sensor on subjects arm.
- Subjects will be evaluated for any adverse events.
- Subject will schedule their next visit and be reminded to bring their BGM and fGM (if it falls off) to the next clinic visit.
- Subjects will be instructed to continue to measure their BG using the supplied site provided BGM.
- Staff should remind intervention group subjects who have not completed the recommended modules to view them in the app.
- Any questions the subject has regarding their therapy may be addressed as usual.

6.8 Visit 4 (Day 56 +/- 2 day)

- Subjects will return to the clinic at their scheduled time.
- Subjects will be evaluated for any adverse events.
- Site will confirm subject continues to meet inclusion and exclusion criteria to include ensuring the subject has made no changes in their non-insulin diabetes medication and significant changes in their insulin regimen. If changes occurred, site will document the nature of the change according to the rules in Section 6.9.
- Site staff will download Libre data and remove the sensor.
- Site staff will download the BGM data.
- Site staff will collect BGM and fGM.
- Study end surveys
    a. All Subject: DES, DDS, ARMS-D, IDSRQ and Injection Technique Questionnaire
    b. Intervention Group only-Patient Satisfaction survey
- Staff will perform standard discharge procedures (remove App from phone) and address any questions the subject has regarding their therapy.

6.9 Additional Information

- Rules applying to changes in diabetes medication (insulin)
    a. The following would not be considered a change in medication (Insulin) and would **not** need to be documented on the Medication Change CRF
        i. Daily changes in insulin dosing to cover a meal (calculated prior to each meal based on carb intake)
        ii. A correction dose delivered on a single day (to cover a trending increase in BG)
    b. The following would be considered a change in medication/insulin regimen and would need to be documented on the Medication Change CRF
        i. Titration in basal or prandial insulin dose and plan to continue it every day (e.g. basal dose is increased by 3 units due to elevated fasting blood glucose levels)
        ii. Add/Remove a dose, bolus or basal (not a correction dose) during the day and plan to continue it every day (for example: go from 2 injections a day to 3 injections per day, or 3 injections to 2 injections per day)
        iii. Change in insulin type resulting in a new regimen (change from bolus only to/from basal/ bolus, change from basal/bolus to/from a mixed insulin) and instructed to continue this regimen.

- Rules applying to changes in diabetes medication (non-insulin)
    a. Stable is defined as not requiring new non-insulin diabetes medications or any changes in dosing of current non-insulin diabetes medication during study participation (10 weeks) unless warranted by investigator for the safety of the subject.
- The subjects in the Intervention Group will be instructed to call the site if they have any problems with the app as it might be easily and quickly fixed remotely.
- Libre flash Glucose Meter
    - If a sensor comes off after day 10 but before day 14 the sensor should be saved and returned to clinic at the regularly scheduled visit for data collection and download.
    - If a sensor falls off before day 10, the subject should return to the clinic to have another sensor placed.
    - Subjects should be reminded to bring a ALL sensors back to the clinic
    - If at Visit 2
        - It was noted that the sensor failed to collect BG data or if the sensor fell off before the required 10-14 days and subject DID NOT return to the clinic for a replacement sensor, the subject may be discontinued. At the Investigators discretion the subject may be re-screened and re-enrolled.
    - Visit 4
        - IF sufficient fGM data has been collected (minimum of 10 days), sensor can be removed and subject may complete all visit related procedures as applicable (i.e. Patient Reported Outcome Surveys and Questionnaire, Subject Disposition/End of Study).
        - IF sufficient fGM data HAS NOT been collected and additional fGM data is required, the subjects will be asked to extend their conduct duration to allow for collection of the necessary fGM data, this includes continued use of the provided BGM.
            - Site will complete all visit 4 related procedures as applicable for the initial fGM download and the subject will complete the Patient Reported Outcome Surveys and Questionnaire. A new sensor will be placed and subject will be sent home for the additional days of fGM wear to obtain the 10 day minimum of fGM data. The subject will return for an unscheduled visit and complete any procedures not completed during the preceding visit (i.e. Subject Disposition/End of Study, uninstall App, etc.).

- Subjects are to be reminded to bring their BGM, fGM and phone, if applicable to every appointment.
-

7.0 INTERRUPTION OR DISCONTINUATION OF PARTICIPATION/TESTING

7.1 Discontinuation of study subjects

Subjects may request withdrawal from the study at any time or may be withdrawn at the discretion of the Principal Investigator for any of the following reasons:

- Adverse Event/Concurrent Illness
- Noncompliance with study requirements or restrictions
- Failure to meet ongoing inclusion criteria, or development of an excluding condition
- Protocol deviation
- Withdrawal of consent

- Subject is lost to follow up
- Administrative issues
- Any other reason which, in the opinion of the PI, makes the subject's participation in the study not in his or her best interest.

7.2 Replacement of Subjects

Each site will plan to enroll approximately 10-40 subjects. If one site cannot meet their goal, enrollment may shift to one or two of the other sites until 86 subjects have completed the study.

7.3 Retention of Data from Discontinued Subjects

All study data collected from the subject up to the point of discontinuation will be recorded on the Case Report Form, entered into the study database, and included in subsequent analyses, as appropriate. No data will be collected from subjects after the point of discontinuation except as needed to follow ongoing adverse events.

7.4 Discontinuation Visits and Follow-up Procedures

For subjects discontinued due to adverse events, the clinical course of the event will be followed according to accepted standards of medical practice until the event resolves, stabilizes, or in the opinion of the Investigator, is no longer considered clinically significant.

7.5 Management of Study-Specific Signs and Symptoms

The PI and their qualified designees are responsible for ensuring that all study-related medical conditions are managed in the subjects according to accepted medical practice. Unless specified otherwise, the clinical course of any such signs or symptoms will be followed according to accepted standards of medical practice until they resolve, stabilize, or, in the opinion of the PI, are no longer considered clinically significant. At any time the PI may undertake more aggressive treatment measures than described above when he or she believes them necessary to protect the well-being of study subjects.

8.0 RISK / BENEFIT ASSESSMENT

8.1 Potential Risks

The risks to the subjects are non-significant and the findings may reveal information that may improve medical care for persons with diabetes. The potential benefit to medical practice outweighs the non-significant differential risk compared with current standard of care, experienced by the study subject.

Risks associated with insulin titration and daily injections of insulin:

- Hypoglycemia
- Hyperglycemia

Risks associated with placement of a Libre sensor

- Discomfort or pain
- Fainting
- Bleeding
- Bruising
- Redness
- Infection
- Allergic reaction to adhesive

8.2 Potential Benefits

The data collected in this study will contribute to optimizing the app in order to maximize potential benefits to providers and patients with future iterations.

Benefits associated to use of the App:

- Subjects will be exposed to a diabetes management mobile application that they may have access to in the future should they find it useful.

Benefits associated with the use of the App and Nano 2nd Gen pen needles:

- Improved glycemic control in part due to improved technique.

9.0 ASSESSMENT OF SAFETY AND ADVERSE EVENTS

9.1 Adverse Event Definitions

Adverse Event (AE): Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease in a subject that is temporally associated with the use of an investigational product or participation in an investigation, even if the event is not considered to be related to the study product or procedures.

This includes events not seen at baseline and events that have worsened if present at baseline. The term AE will refer to all adverse events (serious and non-serious) occurring during participation in a study of either investigational devices and/or drugs.

Serious Adverse Event (SAE): An SAE is any AE occurring during study participation that results in any of the following outcomes:

- Death
- Life Threatening (refers to any event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe)
- Hospitalization or prolongation of a hospital stay
- Persistent or significant disability or incapacitation (refers to any event which results in a substantial and/or permanent disruption of the subject's ability to carry out normal life functions)
- Required intervention to prevent permanent impairment/damage
- Congenital anomaly/birth defect
- Important medical event that may require intervention to prevent one of the preceding conditions.

Unanticipated Adverse Device Effect (UADE): Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. Refer to Protocol Section 8.1 (Potential Risks) for a list of *anticipated* adverse events, signs or symptoms. (21CFR-812.3(s))

9.2 Adverse Event (AE) Management

At each study contact, subjects will be questioned in an open-ended manner regarding any new or worsening undesirable signs or symptoms they may have experienced since the previous contact. Elicited signs and symptoms must be comprehensively documented on the appropriate source documentation.

Each sign, symptom, disease or illness reported must be evaluated by the Investigator or designee to determine if it meets the definition of an Adverse Event.

The clinical course of the event will be followed according to accepted standards of medical practice until the event resolves, stabilizes, or in the opinion of the Investigator, is no longer considered clinically significant. The Investigator must supply the Sponsor with information concerning the follow up and/or resolution of the AE.

9.2.1 Study-Specific Exceptions to AE reporting:

Some signs and symptoms are inherent to the conditions under study (i.e., diabetes) and are likely to occur transiently for nearly all subjects in this study. Episodes of hyperglycemia and hypoglycemia as determined by the BGM (not fGM), occurring after subject enrollment and exposure to study product and/or study procedures, should be reported as adverse events based on the following criteria:

- All blood glucose values <54 mg/dL (hypoglycemia) that require 3rd party (defined as, assistance of another person to administer carbohydrates or glucagon (because person is not physically able)) or medical assistance for recovery will be recorded as an AE (severe hypoglycemia) and assessed for seriousness.
- Any self-identified hypoglycemia or hyperglycemia without a BG reading that requires 3rd party assistance because subject is not physically able or requires medical assistance for recovery will be recorded as an AE and assessed for seriousness.
- BG > 400 mg/dL that requires 3rd party assistance (medical assistance) for treatment will be recorded as an AE and assessed for seriousness
- BG >400 mg/dL (and no symptoms of ketosis, defined as nausea, vomiting, fatigue, excessive thirst) will not be considered an AE.
- All blood glucose values <54 mg/dL, or self-identified as hypoglycemia that resolves with standard carbohydrate self-administration will not be recorded as an AE unless otherwise determined by the Principal Investigator.
- Mild, self-limited pain, swelling, or brief and minimal bleeding at the injection sites, at sites of sensor placement or sites used for blood glucose testing (lancets).

The above signs and symptoms will not be reported on the Adverse Event CRF as long as they occur in the same circumstances, extent and severity as described above.

However, these signs and symptoms ***must be reported as AEs*** should any of them occur in such a way that the extent or nature of the experience exceeds that normally associated with the procedure, as judged by the PI, or the event meets the criteria for a Serious Adverse Event (SAE). Subject will be asked to return to the clinic if any of these circumstances occur during the wear periods.

9.3 Assessment of Adverse Events (AEs)

All AEs must be assessed for Seriousness, Severity, and Relationship. All AEs, regardless of classification, must be comprehensively documented in the CRF and on the SAE form, if applicable, and reported to BD. This includes AEs related to marketed study products. The following information about the event is to be reported on the AE CRF:

- Seriousness, classified as: Non-Serious or Serious
- Severity, classified as:
  - Mild: Transient symptoms, easily tolerated, no interference with daily activities
  - Moderate: Marked symptoms, moderate interference with daily activities, tolerable

- Severe: Considerable interference with daily activities, intolerable

- Relationship
  - Each AE will be assessed for its relationship to the study device or procedure according to the following guidelines.
  - Assess each AE for its relationship to the device or procedure.
    - Device Related: This category should be restricted to AEs directly attributable to the study device used
    - Procedure: A procedure includes any study-related activity performed

The following categories shall be used for assigning the certainty of the relatedness.

Relatedness	Description
Not Related	Event is independent of study intervention and/or evidence exists that the event is related to another etiology. There must be an alternative etiology documented by the clinician.
Unlikely Related	Event in which the temporal relationship to study intervention makes a causal relationship improbable (e.g., the event did not occur within a reasonable time of the study device use) and in which underlying disease provides plausible explanations (e.g., the participant's clinical condition other concomitant treatments).
Likely Related	Event in which there is evidence to suggest a causal relationship and the influence of other factors is less likely. The event occurs within a reasonable time after use of the study device and is less likely to be attributed to concurrent disease.
Related	Event in which there is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out. The event occurs in a plausible time relationship to use of the study device and cannot be explained by concurrent disease.

In addition, the following should be recorded for each AE:

- Action(s) taken to remedy the AE, including change in study treatment or participation, or medical/surgical treatments
- Duration of the AE from onset through resolution, as applicable
- Cause (including suspected product/procedure and/or other cause)
- Outcome of the event, including resolution and sequelae, as applicable

9.4 Additional procedures for Assessing & Reporting Serious Adverse Events (SAE)

SAE criteria are specified in Section 9.1. All SAEs must also be assessed by the Investigator and Sponsor Medical Monitor to determine whether an SAE is expected or unexpected. An adverse event will be considered unexpected or unanticipated if the nature, severity or frequency of the event is not

consistent with the risk information previously described in the protocol, Informed Consent, or Investigator's Brochure (if applicable).

Any adverse event meeting the criteria for 'Serious', regardless of the Investigator's opinion of expectedness or relationship to the study product, must be reported to BD within 24 hours. The Investigator or designee must report the event by telephone or email to the Study Monitor. In addition to reporting the SAE to the Study Monitor, the Investigator must also submit a completed SAE form to the BD Trial Safety Dept. via email listed below within 24 hours of receipt of the information.

- Safety Email: BD_Trial_Safety@BD.com

Medical questions about study safety issues and serious adverse events can be directed to the Sponsor Medical Monitor.

9.4.1 Reporting Obligations to IRB/EC and Health Authorities

The Investigator must report any adverse events which are serious, unanticipated/unexpected and probably or possibly related to the study product or procedures to the reviewing IRB/EC. This report must be submitted as soon as possible, but in no event later than 10 working days after the Investigator first learns of the event.

The Investigator may also have additional responsibilities for AE reporting to their governing Health Authority which they are responsible for identifying and fulfilling.

The Sponsor will provide results of any evaluation of an unanticipated/unexpected adverse device effect to appropriate Health Authorities, to all Investigators, and to all reviewing IRB/ECs within 10 working days after the Sponsor is notified of the event. If the Investigator wishes to assume responsibility for filing reports of evaluation results to their own IRB/EC in lieu of the Sponsor, they must notify the Sponsor in writing of this preference and must retain evidence of their compliance with this requirement.

BD will comply with all other Sponsor safety reporting requirements and timelines for other entities (e.g., Data Safety Monitoring Boards) and local health authorities in other countries where this study or other studies with the same product are being conducted, in compliance with study procedures and applicable local regulatory requirements and BD Standard Operating Procedures.

10.0 INCIDENTS

A Clinical Study Incident is defined as any problem or issue involving the investigational product(s), reference methods, associated procedures or equipment, or represents a product-related injury (or potential for injury) to study subjects or personnel as a result of execution of this protocol. Clinical Study Incidents may adversely (or potentially adversely) affect human safety, the integrity of the evaluation data, or the operation of devices or systems, and warrant prompt attention.

Incidents involving injury to study subjects will also be reported as Adverse Events (refer to Section 9). Examples of Clinical Study Incidents that are not Adverse Events might be **mislabeling or adulteration of the investigational device, equipment or device malfunctions, and errors in the device instructions, damage to devices caused by shipping or handling or improper storage, or injury to study personnel due to execution of the protocol**. If appropriate, an Incident may also be documented and reported as a protocol deviation.

Study-specific procedures for reporting Incidents, as well as adverse events and protocol deviations, will be provided to the study site prior to study execution. The Monitor should be contacted immediately when site becomes aware of or suspects any defective or malfunctioning product. This includes:

- Products that are involved in Study Incidents,
- Products that are found to be expired, damaged or defective,
- Products that are possibly the cause of an adverse effect, regardless of whether the product was believed to be damaged, defective or malfunctioning.

Such products (whether investigational or marketed) should be segregated and returned with appropriate documentation to the BD address below, unless instructed otherwise by BD. The Study Monitor should be contacted with any questions regarding return of study products. BD will supply mailing kits specifically intended for product contaminated with potentially bio-hazardous material.

11.0 RETURN OR DESTRUCTION OF STUDY PRODUCT

At the conclusion of the study, and as appropriate during the course of the study, any products, supplies or BD equipment that are required to be returned will be shipped to BD at the address below, unless instructed otherwise:

DC App will be removed from subject's phone at the end of the study with the option to re-install under the subjects personal account if desired.

All unused or used Nano 2nd Gen, failed or not failed, damaged or otherwise involved in an Incident or Adverse Event should be returned to BD.

12.0 DATA COLLECTION AND MANAGEMENT

12.1 Source Documents

Source data includes all information in original records (and certified copies of original records) of clinical findings, observations, or other activities (in a clinical study) used for the reconstruction and evaluation of the study. Source data are contained in source documents (original records or certified copies) and are used to verify the authenticity of information recorded on the Case Report Form (CRF). Typical source documents include the hospital chart, medical office file, laboratory report, clinician notes, patient record, recorded data from automated instruments or other documentation prepared and maintained by the investigator/staff or ancillary services which contains a record of all observations and other data pertinent to the investigation on a study subject.

The investigator is required to maintain original source documents at the site. Should an original source document (e.g., an instrument printout, direct entry CRF) need to be forwarded to BD for data entry, the site must retain a clearly designated certified copy. The Study Monitor will confirm that procedures for copy certification have been established at the site prior to transmittal of any original source documents. In this study the following CRFs may serve as original source documents: provide all 5 questionnaires/surveys

1. Diabetes Empowerment Survey (DES)
2. Diabetes Distress Survey (DDS)
3. Attitude towards Refills and Medication Survey-Diabetes (ARMS-D)

4. Insulin Delivery System Rating Questionnaire (IDSRQ)
5. Patient Satisfaction Survey
6. Injection Technique Questionnaire

12.2 Case Report Forms (CRF)

The case report forms (CRF) will be provided by the Sponsor. The term "CRF" as used in this protocol may refer to traditional paper CRFs, or electronic case report forms for electronic data capture (EDC), as determined by the Sponsor. Electronic data collection in the eCRF is based on the use of Oracle software and is developed, supported and allocated by the Sponsor.

The Investigator may delegate CRF completion to study personnel. However, the Sponsor must be apprised in writing of the name of such persons and the scope of their authority. The Principal Investigator or designee is obligated to review each CRF page and sign or initial the indicated pages using ink or for EDC provide an electronic signature. An individual record will be kept for each subject that provided informed consent.

All entries to a paper CRF should be made clearly in black or dark blue indelible ballpoint pen to ensure the legibility of self-copying or photocopied pages. Corrections are made by placing a single horizontal line through the incorrect entry, so that the original entry can still be seen, and placing the revised entry beside it. The revised entry must be initialed and dated by a member of the Investigator's research team authorized to make CRF entries. Correction fluid must not be used.

CRF entries will be compared to source documents by the study monitor or designated personnel. Unless specified otherwise, all information on the CRFs must be traceable to original source documents.

12.2.1 CRF/Data Transmittal

Instructions for CRF Transmittal will be provided to the Investigator at Study Initiation. Specific procedures may be described in a study-specific Monitoring Plan.

12.3 Electronic/Device Source Data

In this study the following will be collected electronically and uploaded to secure BD network:

- Blood glucose-Abbott Libre fGM
- Blood glucose-Accu-Chek Guide BGM
- App engagement summary-DC App

12.4 Data Management and Storage

Data Management will be performed by the Sponsor. Electronic data capture is being utilized for this study as the electronic records entered at the site will be entered directly into the controlled database. Data security is ensured through password protection, limited access, audit trails, and regular backups of the data. Upon completion of the study and verification of data, data will be screened for accuracy and completeness, after which the database will be locked from any additional changes. A copy of the locked database will be provided to the BD Corporate Statistics Department for statistical analysis.

All documents containing personal information of the study participants must be stored at the study site. The data collected during the course of the study will be entered into the CRF. The study participants will be identified by the study participant code. Patient confidentiality will be maintained throughout the study, including the publication of the study results. The Investigator or designee will review and sign the CRFs as applicable with the system recording the date it was signed. The Investigator's signature is confirmation that clinical and laboratory data are entered in the eCRF are complete and accurate.

The data obtained and entered in the CRF is the property of the Sponsor.

The study data, copies of the study material and the medical documents will be provided to authorized bodies for internal audit should it be conducted, and on the audit demand. All data obtained in the course of the study will be stored confidentially after the end of this trial as applicable.

13.0 STATISTICAL METHODS

13.1 Sample Size Determination

The sample size calculation is based on showing significant difference between the two study arms for patient reported outcome for Diabetes Empowerment Survey (DES) at end of study. Assuming the baseline DES is similar for the two arms, the difference between control and test arms at end of study is 0.4 (about 10% of baseline), the standard deviations for pre- and post-intervention DES are 0.8 and 0.6, respectively, and the correlation coefficients between pre- and post- measurement pairs for both arms is 0.6, a sample size of 43 per arm (86 subjects in total) has >80% power of detecting a significant difference between the two arms at end of study (based on a 2-sided t-test with confidence level of 95% for the difference of DES between two groups). If a 10% buffer is added (to compensate for subject attrition or unusable data), it will lead to a planned enrollment number of 96 subjects.

13.2 Data Evaluability

All data collected will be analyzed, subject to review for possible exclusion based on significant protocol deviations.

13.3 Statistical Methods

Statistical methods will be detailed in a Statistical Analysis Plan which will be finalized and approved before database lock. Summary statistics will be provided for all exploratory study endpoints. For categorical data, count and percentage with 95% confidence interval will be calculated. For continuous measure, average, standard error, 95% confidence interval, median and inter quartiles will be provided.

Primary endpoint:

The difference of DES between two groups (test arm - control arm) at end of study with two-side 95% confidence interval will be calculated using a linear mixed effects model adjusting for baseline DES. The results will be tested for statistical significance.

Secondary endpoints:

Generally, for quantitative endpoints, the within-group difference between baseline and study end and between-group difference between baseline visits to study end changes with two-sided 95% confidence interval will be calculated; for binary endpoints, the within-group and between-group difference in proportion of favorable outcome with two-sided 95% confidence interval will be calculated.

13.4 Interim analysis

None

13.5 Additional analyses

None

14.0 QUALITY CONTROL AND ASSURANCE

14.1 Accountability of Study Products

Investigational study products will be only be released for use to Investigators who have obtained written IRB/EC approval (as required) for participation in this study, who have completed all required

study documentation, and who have been qualified by the Sponsor. Investigators must maintain control over all study products, and ensure they are used in accordance with this protocol. Failure to do so may result in the Sponsor suspending or terminating the study at the Investigator's site.

The Investigator will ensure that study products are only dispensed to subjects (or used for specimens) properly enrolled in the study. The Investigator must maintain records of receipt, disposition, return and/or destruction of all study products. All investigational study products released to the site must be accounted for at the unit level prior to study close out, regardless of disposition. The Study Monitor will regularly review all records regarding study product accountability.

The Sponsor will maintain records that document the shipment, receipt, disposition, return and/or destruction of study products.

14.2 Monitoring

BD, the study sponsor, will designate trained and qualified personnel to monitor the progress of this clinical study in accordance with BD Monitoring SOPs and the study-specific Monitoring Plan. A pre-study site qualification visit will be conducted to assess the adequacy of the site facilities and staff with respect to study requirements.

Prior to study start, a study initiation visit will be conducted to provide training to site staff with regard to the protocol, the completion of study documentation and Case Report Forms (CRFs), the monitoring schedule, and all regulatory requirements. During the study, routine monitoring visits will be conducted to assure the site continues to adhere to the protocol, the investigator agreement, and regulations regarding conduct of clinical studies. Assessments will be made regarding the subjects' protection and safety, when relevant, as well as the quality, completeness, and integrity of the data. The Study Monitor will assist the investigative site with query resolution and will perform site close-out activities once all queries have been resolved.

Additional visits may be carried out depending upon site activity and performance. The Investigator must agree to the inspection of all study related records and give direct access to source documents for verification of data on CRFs.

The Investigator is responsible for ensuring that any site-owned equipment required for use in the study is properly installed and maintained (e.g., inspected, calibrated, alarmed). Documentation of equipment maintenance procedures must be available for review by the Monitor.

14.3 Audits and Inspections

If the study is selected for audit by the Sponsor or if there is an inspection by the appropriate Health Authorities, then the Investigator and his team will make themselves available during the visit. The Investigator must agree to the inspection of all study related records and give the auditor/inspector direct access to source documents for verification of data on CRFs. The subject's anonymity must be safeguarded and data checked during the audit remain confidential.

As soon as the Investigator is aware of an upcoming inspection/audit by the Health Authorities, he/she will promptly inform BD. As agreed with the Investigator, BD personnel may be present at the site during the inspection.

14.4 Protocol Deviations

Protocol deviations are not permitted and should be implemented prospectively as a protocol amendment whenever practical or appropriate, unless required to protect the safety and well-being of the subject. The Investigator must notify the Sponsor immediately of any such deviation resulting from the need to protect a subject.

Protocol deviations (other than those required to protect the safety and well-being of a subject) may impact the evaluability of study data, and may place subjects at risk. If the Investigator or their staff inadvertently deviates from the study plan, the Investigator should implement appropriate corrective

and preventive procedures, and should notify the Sponsor at their earliest convenience. Significant deviations may also need to be reported to the IRB/EC and local health authority.

The Study Monitor will evaluate records of study conduct at the site to identify any deviations, and will also report them to the Sponsor. Upon evaluation by the Sponsor, actions may be required to prevent additional deviations, such as retraining of the site, implementation of additional site procedures, and more frequent monitoring. If these steps fail, more serious measures, up to and including termination of the site and withdrawal of study product may be necessary.

15.0 ETHICAL AND REGULATORY STANDARDS

15.1 IRB/EC

An appropriate IRB/EC must review this protocol, the Informed Consent Form (if applicable), and any other supporting study documents which affect subject or study personnel safety, prior to study initiation at an investigational site. No investigational site may begin the study until the IRB/EC has given its written approval, signed by the IRB/EC chairperson or authorized personnel, and a copy of the approval letter and the approved Informed Consent Form (if applicable) has been provided to the Sponsor.

15.2 Informed Consent

Prior to giving informed consent, each candidate will have the opportunity to review the study procedures, risks and benefits and ask any questions he or she may have regarding the study. Before enrolment, each subject must give informed consent, documented by signing a written form, created and approved in compliance with 21 CFR Part 50.25 and 21 CFR Part 56. Each subject should be given a copy of the signed informed consent document.

15.3 Confidentiality of Data

Subject confidentiality is strictly held in trust by the participating investigators, their staff, and BD and their agents. This confidentiality is extended to cover testing of biological samples in addition to the clinical information relating to participating subjects. Subject confidentiality and anonymity will be maintained at all times by removal of all identifiers from any data, clinical samples or documentation submitted for this study.

Any data collected meeting the definition of PHI will be collected and maintained using the designated authorizations and following all privacy procedures as specified in the applicable health authority regulations.

BD will maintain the security and confidentiality of all clinical study data sent to BD. BD clinical study databases will not be shared with any third party without the express written consent of the Principal Investigator and/or Site.

The Study Monitor or other authorized representatives of BD may inspect all documents and records required to be maintained by the Investigator. The Site will permit access to such records. BD and the Site may be required to provide regulatory agencies access to clinical study data and records, as well as source documents.

All other agreements as to confidentiality by BD, the Principal Investigator, and the Site may be found in the Confidential Disclosure Agreement and the Clinical Trial Agreement.

15.4 Protocol Modifications

Amendments to the protocol will not be implemented without agreement from the Sponsor and prior submission to and written approval from the governing IRB/EC, except when necessary to eliminate an immediate hazard to the subject. Notice of an emergency modification shall be given to the Sponsor and the reviewing IRB/EC as soon as possible, but in no event later than 5 working days after the

emergency occurred. Protocol amendments may affect Informed Consent Forms for current and future subjects.

Minor changes to the protocol, such as correction of typographical errors or changes in personnel names (other than the PI) or contact information will be processed as administrative changes. Administrative changes will be submitted to the governing IRB/EC but implementation of the administrative change may proceed without prior IRB/EC approval, unless so required by the IRB/EC or site SOPs.

15.5 Study Discontinuation

BD reserves the right to temporarily suspend or prematurely discontinue the study at a single site or at all sites at any time and for any reason. If such action is taken, BD will discuss the reasons with all Investigators (the Investigator). If the study is terminated or suspended due to safety reasons, the sponsor will inform the health authorities as required, and provide the reason(s) for the action. Investigator(s) must inform their IRB/EC promptly and provide the reason(s) for the suspension or termination.

15.6 Clinical Study Registration

In compliance with Title VIII of Public Law 110-85, known as FDA Amendments Act of 2007 (FDAAA), BD will register all applicable studies and disclose study results in a publicly accessible database, e.g. the ClinicalTrials.gov web site. Applicable studies will be registered no later than 21 days after commencing enrollment. Study results for applicable studies will be posted to the website within 12 months of the last subject visit for collection of primary outcome data, or after health authority approval for previously unapproved devices. BD has responsibility for determining whether this study qualifies as an “applicable” study under the law, and if so, will take responsibility for registration and disclosure as required by law.

15.7 Publication of Results

BD believes that results of applicable clinical studies of our products should be published in peer-reviewed literature in a timely, accurate, complete and balanced manner, regardless of study outcomes. BD is committed to making information public whenever it relates to the safety and efficacy of its marketed products.

Should this study be considered an “applicable study,” any formal presentation or publication of data collected from this study will be considered as a joint publication by the investigator(s) and the appropriate personnel of BD. Authorship will be based on generally accepted criteria of the ICMJE (International Committee of Medical Journal Editors) and determined by mutual agreement. For multi-center studies, it is mandatory that the first publication is based on data from all centers, analyzed as stipulated in the protocol by BD statisticians, and not based on data from single sites or a subset of sites. Investigators participating in multi-center studies agree not to present data gathered from one center or a small group of centers before the full, initial publication, unless formally agreed to by all other investigators and BD (the sole exception being an unanticipated adverse event that is product-related and which might have clinically significant safety implications for a marketed product or a class of products).

BD must receive copies of any intended communication in advance of publication as specified in the Clinical Study Agreement. In a timely manner, BD will review the communications for accuracy (thus avoiding potential discrepancies with submissions to health authorities), verify that confidential information is not being inadvertently divulged and to provide any relevant supplementary information to the investigators.

15.8 Record Retention

If the Principal Investigator or Clinical Center withdraws from the responsibility of keeping the study records, custody must be transferred to a person or entity who will accept the responsibility. BD must be notified in writing of the name and address of the new custodian.

Federal regulations require that a copy of all essential study documents (e.g., IRB/EC approvals, signed informed consent forms, source documents, CRF copies, safety reports, test article dispensing records, etc.), must be retained in the files of the responsible Investigator for a minimum of 2 years following notification by BD that all investigations are completed, terminated, or discontinued, or that the FDA has approved the application (21 CFR 812.140).

16.0 BIBLIOGRAPHY/REFERENCES

Christopher J. Rini; Bruce Roberts; Rick Klug, Benjamin Selvage; Ronald J. Pettis: New BD Nano™ PRO Pen Needle Hold Down Force vs. Depth Poster presented at: ADA 78th Scientific Sessions; 2018 June 22-26th; Orlando, FL

2. Whooley S, Briskin T, Gibney MA, Blank LR, Berube J, Pflug BK. Evaluating the User Performance and Experience with a Re-Engineered 4 mm × 32G Pen Needle: A Randomized Trial with Similar Length/Gauge Needles. Diabetes Ther. 2019; 10(2):697-712.

17.0 PROTOCOL REVISION HISTORY

Protocol Revision history/Version #	Rationale for Change	Section or Page affected	Description of change
1.0	New Protocol		
2.0	Up-versioned protocol	Page 1 and headers on all pages	Original Version 1.0 dated 16 July 2019 Revised Version 2.0 dated 16 October 2019
2.0	Updated Medical Affairs Representative	Page 2	Original [redacted] Revised [redacted]
2.0	Providing restrictions on type of phone and version of operating system.	Inclusion Criteria	Original Currently using a smartphone and able to understand the use of mobile apps.

			Revised Currently using an Apple iPhone with iOS Versions 13.1 or greater or Samsung phone with Android OS Versions 8 or later and able to understand the use of mobile apps.
2.0	Providing restrictions on type of phone and version of operating system.	Exclusion Criteria	Original Use of a smartphone with iOS 10.0 or lower or with Android OS 5.0 “Lollipop” or lower Revised Use of a iPhone with iOS 13.0 or lower or use of an android phone that is not a Samsung or using Android OS Versions 7.0 ”Nougat” or lower
3.0	Up-versioned protocol	Page 1 and headers on all pages	Original Version 2.0 dated 16 October 2019 Revised Version 3.0 dated 04 November 2019
3.0	To allow the subject, if they choose, to update their phones with the correct OS during their screening visit.	Section 4.1, Inclusion criteria	Original Currently using an Apple iPhone with iOS Versions 13.1 or greater or Samsung phone with Android OS Versions 8 or later and able to understand the use of mobile apps. Revised Currently using an Apple iPhone with iOS Versions 13.1 or greater or Samsung phone with Android OS Versions 8 or later and able to understand the use of mobile apps. (Subject may choose to upload to the correct version themselves prior to screening visit or during the screening visit with the help of site staff).
3.0	Clarification – subject does NOT have to be using CGM to qualify	Section 4.2, Exclusion Criteria	Original If using CGM, use of CGM or fGM less than 6 months and not proficient in its use, however this may be left up to the investigators discretion. Revised If using CGM, use of CGM or fGM less than 6 months and not proficient in its use, however this may be left up to the investigators discretion.
3.0	Allow the use of a secondary adhesion to ensure Freestyle Libre remains in place for the required 10-14 days.	Section 5.3 Ancillary Products	Added Torbot Skin Tack (for use with Freestyle Libre Pro) Skin Tac liquid adhesive barrier is a Latex-free, hypo-allergenic, clear, non-rubber liquid adhesive. Prepares the skin for application of tapes, dressings, infusion sets, and much more. This unique “tacky” skin barrier, being latex-

			free and hypo-allergenic, makes it ideal for patients with sensitive skin. It is recommended by Abbot to help the sensor remain in place for up to 14 days (see Appendix 1).
3.0	Request for site to confirm phone model and OS version as this is critical to App functionality	Section 6.4 - Screening	Added Confirm smartphone type and software version.
3.0	Allow the use of a secondary adhesion to ensure Freestyle Libre remains in place for the required 10-14 days.	Section 6.4 – Libre Application	Original Once eligibility has been determined subjects will be provided and trained on the BGM (Accu-Chek Guide BGM) and have a Freestyle Libre Pro sensor (blinded to subject) placed on the backs of their arms by site staff who will then activate the sensor before sending the subject home. Revised Once eligibility has been determined subjects will be provided and trained on the BGM (Accu-Chek Guide BGM) and have a Freestyle Libre Pro sensor (blinded to subject) placed on the backs of their arms by site staff who will then activate the sensor before sending the subject home. To aid in helping the sensor stick for the 10-14 days the use of a skin prep will be used, Torbot Skin Tac. (See Appendix 1)
3.0	To ensure there is a minimum of 10 days of BG data before subject leaves the site.	Section 6.5 – Visit 2 and Visit 4	Original Site staff will download Libre data and remove sensor. Revision Site staff will download Libre data and remove sensor and confirm a minimum for 10 days of BG data.
3.0	To document how to handle potential device failures and adhesive failures during Libre use and ensure a minimum of 10 days of BG data is collected in support of the secondary objective.	Section 6.9 – Additional Information	Libre flash Glucose Meter If a sensor comes off after day 10 but before day 14 the sensor should be saved and returned to clinic at the regularly scheduled visit for data collection and download. If a sensor falls off before day 10, the subject should return to the clinic to have another sensor placed. Added Subjects should be reminded to bring a ALL sensors back to the clinic. Visit Specific Rules for Libre Sensor, If at Visit 2 • It was noted that the sensor failed to collect BG data or if the sensor fell off before the required 10-14 days and subject DID NOT return to the clinic for a replacement sensor, the subject may be discontinued. At the Investigators discretion the subject may be re-screened and re-enrolled.

			Visit 4 • IF sufficient fGM data has been collected (minimum of 10 days), sensor can be removed and subject may complete all visit related procedures as applicable (i.e. Patient Reported Outcome Surveys and Questionnaire, Subject Disposition/End of Study). • IF sufficient fGM data HAS NOT been collected and additional fGM data is required, the subjects will be asked to extend their conduct duration to allow for collection of the necessary fGM data, this includes continued use of the provided BGM. ○ Site will complete all visit related procedures as applicable for the initial fGM download and the subject will complete the Patient Reported Outcome Surveys and Questionnaire. A new sensor will be placed and subject will be sent home for the additional days of fGM wear to obtain the 10 day minimum of fGM data. The subject will return for an unscheduled visit and complete any procedures not completed during the preceding visit (i.e. Subject Disposition/End of Study, uninstall App, etc.).
3.0	Removed statement as subjects will receive an autotomized user name and password for this study.	Section 6.9 – Additional Information	Removed Subject will be required to utilize their password for downloading of app from app stores.
4.0	Amendment	Title Page and Headers on each page	Updated Version number and date throughout protocol
4.0	Due to 1) slow enrollment due to difficulty identifying subjects who meet the inclusion and exclusion criteria, 2) larger than expected number of subjects who select of Early Terminations and 3) Libre sensor adhesion issues (ability for senor to remain intact for 10-14 days); sponsor would like to 1) add additional sites and 2) increase the number of subjects enrolled to enable the sponsor to meet their target of 86 completers. Definition of completers Completion will be defined as a subject completing 10 weeks of study participation and can provide at least 10 days of flash glucose data at	Section 4.0 Study population	ORIGINAL A minimum of 86 subjects with type 2 diabetes and currently on MDI therapy will be recruited across 2-3 sites. Up to 10 additional subjects may be enrolled across sites to ensure a total of 86 subjects complete the study. (Completion will be defined as a subject completing 10 weeks of study participation and can provide at least 10 days of flash glucose data at baseline (first 2 weeks) and again at study end (last 2 weeks)). CHANGED TO A minimum of 86 subjects with type 2 diabetes and currently on MDI therapy will be recruited across 3-6 sites. Up to 40 additional subjects may be enrolled across sites to ensure a total of 86 subjects complete the study. (Completion will be defined as a subject completing 10 weeks study participation and can provide at least 10 days of flash glucose data at baseline (first 2 weeks) and again at study end (last 2 weeks)).

	baseline (first 2 weeks) and again at study end (last 2 weeks)).		
4.0	Updated enrollment numbers based on above	Section 7.2	ORIGINAL Each site will plan to enroll approximately 30 subjects. If one site cannot meet their goal, enrollment may shift to one or two of the other sites until 96 subjects have been enrolled or 86 subjects have completed the study. CHANGED TO Each site will plan to enroll approximately 10-40 subjects. If one site cannot meet their goal, enrollment may shift to one or two of the other sites until 86 subjects have completed the study.

18.0 APPENDICES

18.1 Sensor Adhesion Guide

Signature Page for VV-TMF-166844 v1.0

Reason for signing: Finalize	Name: [redacted] Role: M Date of signature: 21-Jan-2020 18:16:41 GMT+0000

Reason for signing: Finalize	Name: [redacted] Role: M Date of signature: 21-Jan-2020 21:05:42 GMT+0000

Reason for signing: Finalize	Name: [redacted] Role: C[redacted]ct Management Date of signature: 22-Jan-2020 14:23:53 GMT+0000

Reason for signing: Finalize	Name: [redacted] Role: S[redacted]rogramming Date of signature: 24-Jan-2020 11:09:30 GMT+0000

Signature Page for VV-TMF-166844 v1.0