

1. STUDY TITLE:

Extending Beta Cell Function in Newly Diagnosed Type 1 Diabetes Mellitus through Efficient Clinical Intervention and Rapid Knowledge Transfer

2. PURPOSE OF STUDY:

In contrast to proposed pharmaceutical innovations for extending beta cell function, tighter control through better diabetes management can be achieved without the toxic side effects of immune suppressant drugs. However, traditional approaches involve time intensive phone calls to patients by nurses and diabetes educators, which are simply not practical in the day-to-day clinical setting. As such, in spite of demonstrated efficacy of intensive management, there continues to be a barrier to non-pharmaceutical approaches to beta cell preservation.

We hypothesize that using the GlucoDYNAMIX diabetes intervention system for patients with new onset type 1 diabetes mellitus will rapidly increase the family/caregiver's diabetes knowledge base translating to tighter glucose control and thereby extending beta cell function during the "honeymoon phase". Using real-time technology for ensuring data integrity, automating data collection, and streamlining information access prompting provider determined interventions is believed to be the answer to wide-scale clinical adoption of intensive management without the use of costly pharmaceuticals as a method for extending beta cell function.

3. DURATION & POPULATION:

The study is designed to run for a period of 12 months. As new onset type 1 diabetes patients present to the diabetes clinic they will be offered the opportunity to participate in the study. The study is designed to monitor beta cell preservation in 30 patients; 15 with the technology and 15 using conventional management.

4. BACKGROUND:

At the pediatric endocrine unit of Atlantic Health Systems we see approximately 125 new patients with diabetes yearly and have a total diabetes population of approximately 1000 children and adolescents. We have clinical trial experience and a complete diabetes team including a research coordinator.

Effective management at the onset of type 1 diabetes is thought to prolong the honeymoon period and protect pancreas function yet is labor intensive and fraught with the potential for error. Management of the new onset diabetes patient requires collection of day-to-day data including carbohydrate intake, blood sugar data, insulin doses and symptoms of hypoglycemia. This data is routinely reviewed on a daily basis by most pediatric/adolescent diabetes care teams, a labor intensive and not always efficient task.

Under conventional circumstances, the mass of annotated glucose data is communicated to the health care team in a relatively inefficient manner. This may involve relating the values by telephone contact, FAX transmission of lists of values, or even requiring a personal visit by the patient to the medical office. The latter is particularly inefficient, since it is usually not necessary to perform the frequent reviews of the data in a face-to-face meeting; the time and expense required for an inconvenient office visit is typically not warranted.

Assuming that the medical staff is able to access the patient record as needed, a critical component of the patient record involves not only the specific blood glucose test value but also the timestamp associated with that test. While no official studies have been conducted that we are aware of, modem transferred data is quite often inaccurate due to an incorrect

setting of the internal clock of the glucose meter. And when patients self-report via manual logs, the blood glucose data as well as timestamp data are often inaccurate due to patients wanting to please the diabetes clinical staff, failure to keep an accurate logbook, simple transposition or omission of glucose data and sometimes intentionally fraudulent data for any number of reasons.

5. RATIONALE AND RELEVANCE OF THE STUDY:

According to National Standards for Diabetes Self-Management Education (NS-DSME) as published in *Diabetes Care*. Vol 28, Supplement 1, January 2005, "Clinical Practice Recommendations 2005", pgs. S72-S79, Diabetes Self-Management Education (DSME) is the cornerstone of care for all individuals with diabetes in order to achieve successful health-related outcomes. Within the comprehensive definition of DSME, the Task Force describes the proper administration of DSME to be "interactive, collaborative and ongoing." Within this process exists the need for assessment, identification, intervention and evaluation. Since the NS-DSME Task Force does not define "how" to implement the Standards, it is dependent on research in clinical practice to evaluate how to advance the delivery of care utilizing relevant available technologies to assist in the delivery of DSME.

Within the category of "creative interventions" within the Process subset of the DSME Standards, this study will examine whether using novel technology as a creative means to cost-effectively and efficiently enable proactive interventions at the teachable moment will result in improved outcomes, cost savings and greater satisfaction between the patient and the healthcare team.

6. DESCRIPTION OF RESEARCH:

Due to the way in which the GlucoMON telemetry device has been implemented as an extension of the glucose meter itself, we believe that the GlucoDYNAMIX system will overcome many of the obstacles to conventional data collection and help to cost-effectively transfer knowledge of insulin therapy to newly diagnosed patients with type 1 diabetes mellitus.

The GlucoMON device is an automated wireless glucose meter accessory that manages the accuracy of LifeScan®'s OneTouch® Ultra®'s internal clock, collects new glucose data from the Ultra, and transmits new glucose data to Diabetech's remote data center via long-range wireless networks. There is no cell phone, external modem or personal computer required. Upon arriving at the data center, the data is appended to the appropriate patient record and made available for use by a patient-specific Intensive Management Protocol.

The GlucoDYNAMIX intervention system manages the patient record, the patient profile, the provider profile and provider defined intensive management protocols consisting of alerts, reminders, and reports. This system includes provider defined prompts to both patients and providers to review the patient record and to take steps including real-time clinical interventions. The system may also be programmed to highlight and inform the clinical team of outlying glucose patterns and trends that may require attention. For a detailed description of the GlucoDYNAMIX system capabilities and the GlucoMON telemetry device, please refer to Addendum B – Diabetech Technology Overview.

In contrast to other medical device data transfer technologies, timely awareness of hypoglycemia and extended hyperglycemia, especially as the result of previously prescribed changes to the patient regimen by the clinical staff, is critical when managing a highly mobile adult population. In the original feasibility pilot study of the GlucoMON device in late 2002, the simple requirement for the patient to push a button on the wireless device led to infrequent transmission for all 10 patients involved in the study. Unlike conventional technologies used to manage patients with diabetes, the GlucoMON device eliminates user

interaction for transmission of glucose data thus providing a higher degree of reliability for providers interested in delivery of timely feedback after prescribing changes to the patient which could potentially result in severe near term complications.

The primary outcome variables will include:

- A blood draw for measuring C-peptide count indicating beta cell reserve will be performed both at enrollment in the study and again upon conclusion of the study timeframe.
- Mean daily glucose from the measured glucose tests including standard deviation between tests over the 12 months duration of the study.

Secondary outcome measures will include:

- A blood draw for measuring hemoglobin A1c will be performed at enrollment in the study and every 90 days through to conclusion of the study timeframe.
- Additional outcomes measures will include a work-time measure for professional staff as well as a validated questionnaire to assess quality of life and the patient's treatment satisfaction parameters.

Approximately every 3 months and at the conclusion of the study period, patients will return to the clinic for a routine diabetes follow-up encounter. At the end of the 12 month study duration, patients will return their study-issued glucose testing telemetric devices and "intervention toolset".

7. DESCRIPTION OF THE TECHNOLOGY:

See Addendum B for a detailed description of the technology

8. RECRUITMENT RATIONALE:

Patients presenting with new onset Diabetes Mellitus will be recruited from the hospital. Informed consent and child assent will be obtained from each participant.

9. RISKS, SIDE EFFECTS AND DISCOMFORTS TO PARTICIPANTS:

No significant risks are anticipated. SMBG is being performed as part of routine Diabetes management. We are not asking participants to monitor any more or less often.

10. POTENTIAL BENEFITS:

Due to more efficient and accurate communication with the patient and caregiver, we expect to see an increase in the C-peptide levels for the intervention population vs. the control group. This may be due to an increase in the rate at which provider knowledge of diabetes self-management techniques can be transferred but also represents an increase in the patient's ability to retain the knowledge transferred.

We expect to see tighter control of the glucose levels as represented by less extreme glucose excursions following hypoglycemia and hyperglycemia as measured by standard deviation between SMBG checks.

We expect to see a lesser frequency of hypoglycemia and hyperglycemia and for the follow up HbA1c to be lower than the value obtained at enrollment.

We also expect to report increased patient/family satisfaction and reduced health care provider workload compared to conventionally treated patients. Also, an increase willingness

to perform SMBG since participants are acutely aware that their data is being frequently monitored.

Additional endpoints to be evaluated will include a subjective comparison of the diabetes knowledge base between the intervention population and the control population and the need and extent of and for inpatient hospitalization both at diagnosis and subsequently.

11. CONTRAST TO PRIOR STUDIES:

Clinical Studies regarding the review of patient Self-Monitoring of Blood Glucose (SMBG) data and its use in DSME is wide-spread. However, we believe that this research is unique in the opportunity to study large amounts of self-reported patient data including real-time interaction with the health care team over an extended timeframe. Since the technology being used is itself unique in that it automates the collection and distribution of the patient SMBG data, this research will have the opportunity to evaluate the value of real-time interventions not dependent on patient self-reporting as a means of preserving beta cell function.

In the research performed at Children's National Medical Center in 2003, the researchers, Griffin and Henderson, report that in-office meter uploads using PC software transfers 8 to 9 minutes of time typically spent tabulating manual glucose logs instead of interacting with the patient team. Given that this phase of the office visit only totals 15 minutes, they were able to demonstrate the value of computer technology used in the delivery of DSME. However, this study was limited to a historical perspective on the SMBG data as opposed to any form of real-time review and proactive intervention.

In another body of research conducted in 2003, Klein, Malasanos and Patel at the University of Florida Department of Pediatrics studied "An Integrated Technology Approach Providing Education, Monitoring, and Communication for Children with Diabetes" as part of the Florida Initiative in Telehealth and Education (FITE). In contrast to the proposed research, this study required the patients to either possess or have ready access to an internet-connected PC, an aptitude to use the technology, and the motivation to manually and periodically upload their SMBG data. While the U of F study was novel in its use of interactive communication with the patient, it fails to address the possibility of timely interventions at the "teachable moment" This means simply that much of the context around SMBG data is lost after some short period of time thus diminishing the effectiveness of the intervention.

In summary, the proposed research expects to show a greater degree residual beta cell function especially for those patients with less access and aptitude to and for technology and self-management technique. Furthermore, this research will illustrate the value of rapid knowledge transfer through a system which permits the clinician to educate patients in the remote home setting while leveraging the context of the situation.

Attachment A – Patient’s Guidelines for Proactive Care

Manual logging of data as prescribed in the Standard Care Guidelines remains a very important requirement within the Proactive Care Guidelines.

It is not possible to replace or recreate the detailed information which is possible to acquire from a handwritten log with only that data which is captured from the toolset, primarily glucose test data and its accompanying timestamp.

Diabetech, a company based in Dallas, Texas supplies the GlucoMON device as well as the diabetes management technology for the trial. This system complies with security and privacy regulations to protect your medical information. From their computer center in Dallas, the company automates the reporting of your blood glucose to the medical team.

Within the otherwise “normal-looking” glucose meter case resides a glucose meter docking station connected by a small wire to a small long-range wireless computer hidden inside the case (See Diagram 1.) Whenever the meter is docked in the case, the computer compares the clock time to the atomic clock, corrects the meter’s internal clock, then reads the meter’s blood glucose stored data and copies the new data to the local computer’s database. SMBG data is then automatically transmitted via the wireless network to a secure computer accessible only to the investigators.

This automatic time keeping method used to synchronize the current generation glucose meter clock to the world’s most accurate atomic clocks results in the world’s most accurate blood glucose data. Unfortunately, other systems do not have this automatic data integrity check which then results in unusable data, data that is hard to work with or even worse, decisions made without realizing that the timestamps are not accurate. For many reasons, the internal clock of these glucose meters is often times incorrect due to user error and/or mechanical design flaws which allow the clock time to change due to static electricity, dropping, etc...With the GlucoMON, the meter’s clock is always accurate and the data is reliable.



Diagram 1. GlucoMON® device including the hidden wireless computer (shown with OneTouch® Ultra® from LifeScan, Inc.)

Once received at Diabetech’s computer datacenter, the blood glucose data is added to the patient record and various messages (e-mail, text messages, pager alerts) and reports are sent to the medical team. The data will be reviewed approximately every three days or in some cases more often. This can be triggered by patient initiated contact with the care team, critical event occurrence, or suspected trends that require

prompt review of the patient record. Staff review of the patient data is logged. See Diagram 2. for a picture of the system.

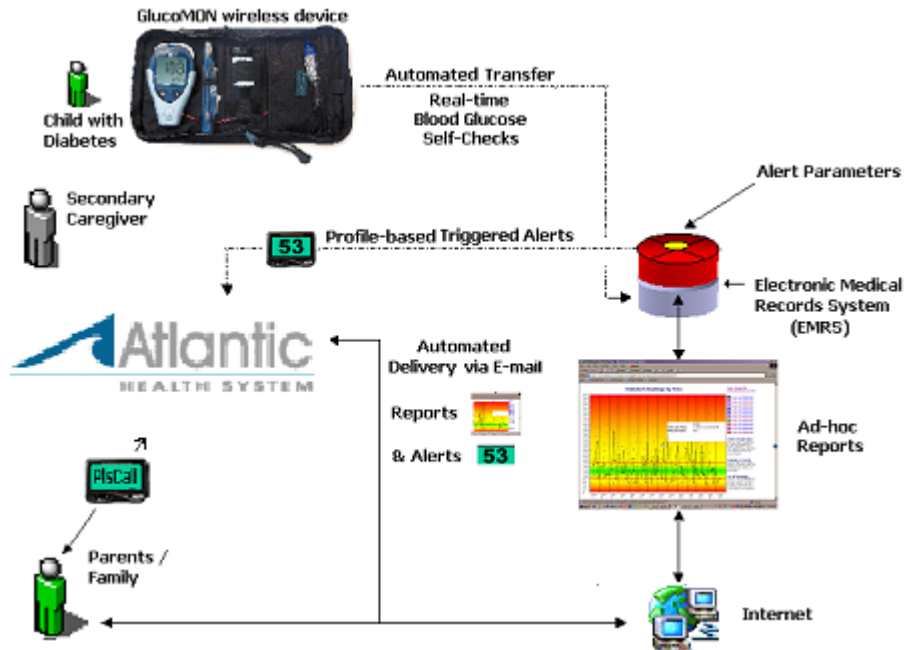


Diagram 2. Diabetes Intervention Schematic

The following scenarios are foreseen in the Intervention Group that will require new methods and procedures for both the patient and the AHS Staff. They are set out below. While significant effort has been spent attempting to predict the optimal process in each case, we are sure to identify ways to further streamline these procedures during the trial period based on actual experience. Capturing office efficiency is one of the primary objectives of the study, any optimization or enhancement to the following procedures are not only encouraged but must be documented so as to capture the root cause of the change and to understand the implications of proactive intervention. Any changes to these Proactive Guidelines that affect the patient will be distributed to you via email if practical or regular mail if email is not practical.

SMBG test data collection – Using the GlucoMON device and testing as normal as described in the materials included with the OneTouch Ultra glucose meter, first undock the meter from the cradle, test, remove the test strip then re-dock the meter (detailed instructions are include in Attachment C and in the GlucoMON Pocket User Guide which comes with the GlucoMON device. A successful test and transmission procedure will result in the meter showing “PC” within a few seconds of the re-dock and the eventual return of the GlucoMON LED from a double flashing green to a single flashing green every 4 seconds.

Remember to recharge the device with the included electric wall mount charger at least every other day for a full 6 hours. Please refer to the GlucoMON instruction booklet that comes with the device for further instructions.

DO NOT USE ANY ELECTRIC CHARGER OTHER THAN THE ONE THAT COMES WITH THE GLUCOMON DEVICE. IF YOU LOSE YOUR CHARGER, PLEASE CALL THE OFFICE OR DIABETECH (877.MyGluco) AND A NEW CHARGER WILL BE SENT TO YOU. THE DATA ON YOUR METER WILL CONTINUE TO STORE SAFELY ON YOUR METER UNTIL YOUR GLUCOMON IS READY TO SEND.

SMBG review initiated by AHS Staff – At the discretion of the AHS Staff, patient glucose numbers are reviewed to see if there are indications for intervention. Should they decide to take action on the patient's record, they will contact the patient or their primary caregiver by phone, email, or pager. Please reply directly to the communication, as this will make the communication tracking easier and more accurate. In other words, try not to send a new email but rather, use the reply feature in your email account. Phone calls will be simply logged by the medical staff.

SMBG test data review requested by Study Participant – At any time the patient or patient caregiver feels the need, you may contact the AHS Staff according to the standard office guidelines. In the event that the Staff require a review of your blood glucose history, the medical staff may access the patient's GlucoMON stored record. It is also possible that they will request a faxed log from the patient team in order to obtain additional detail prior to advising the patient or caregiver.

Proactive contact initiated by AHS Staff – As the patient's blood glucose is automatically collected by the GlucoMON device, the medical staff may review the data from time to time. In the event that they have a question for the patient or patient team, they may contact you by any number of methods (phone call, email, page, etc...) as they determine to be appropriate.

Study Participant contact with AHS following a request by AHS Staff – When the Staff contact you, please follow up with any requests for information in a timely manner. In the event that there is a technical question with the GlucoMON device, optional pager issue or otherwise, either the Staff or an authorized member of the Diabetech Support Team may contact you. You will be notified of the official contact info for authorized individuals so as to ensure the patient's safety and privacy.

If you have any questions regarding the Intervention Technology Toolset, please call Diabetech Customer Support at 877.MyGluco and they will be happy to answer your questions.

If you require medical advice in the care of the patient's diabetes, please contact the AHS Staff.

If you have a medical emergency, call 911.



Addendum B – Diabetech Technology Overview

The technology being proposed to enable the outcomes from this study had its beginnings in May 2001. Of course there had to be a systematic way to enhance the clinical process. However, unlike every diabetes management system developed before and since, Diabetech was keenly aware of the importance of timely and accurate data collection as the most critical element. Without reliable access to timely, accurate data, information becomes suspect and the ability to make decisions – compromised. Technology which requires patients to change behavior or assuming a tech savvy individual with technology at his/her disposal was estimated to be the primary obstacle to the advancement of clinical diabetes management. This was validated in Diabetech's first clinical study, End-to-End Wireless Diabetes Management System, which began in late 2002 and concluded in April 2003.

During that early study the team was able to validate several critical points including the fact that patients are generally unwilling to take on any extra work beyond their current glucose testing and insulin regimen. The pilot version of a wireless-enabled glucose meter was small in size, self-contained, easy to operate and only required the patient to press a button to initiate the collection and automated wireless transfer of their glucose meter data to the remote data center.

Patient's placed the highest value from using the system on unprompted wireless email messages and phone calls from the diabetes team at the diabetes center. The team at the diabetes center placed the highest value on being effortlessly presented with factual patient record and certain report formats, which helped them to focus in on problem areas, which required changes to the patient regimen.

GlucoDYNAMIX Design Requirements

- ✓ Patient technology should be transparent to the user without introducing new requirements over and above current self-test requirements. This includes battery charging, button pushing, logging in to a website, etc;
- ✓ Patient biometric machine data, primarily glucose, should be accurate and reliably available to the appropriate member(s) of the team at the right time and in the preferred format;
- ✓ A Field support function should be capable of managing the patient technology remotely and in real-time to ensure high quality data and availability;

Diabetech has accomplished the above objectives using current generation technology, at low cost, an ability to scale up to address large volumes and to begin the process of optimizing a wireless medical sensor device platform, highly tuned communications & remote device management protocols and clinically oriented Intensive Management Protocols (IMPs) without introducing burdensome obstacles to patient and/or clinical adoption.

The current system can be described at a high level as including the following elements:

- ✓ Machine Data Collection & Device Management (GlucoMON wireless device)
 - ReFlex networks in North America for greater digital coverage and reliability
 - Lower cost for development and airtime
 - Self-contained wireless computing platform for small size and behavioral transparency
- ✓ Subjective Data Collection, Messaging & Device Management
 - Highly Reliable 2Way text messaging devices for real-time Interactive Services
 - Server based applications for easy management and rapid changes
 - Guaranteed & Reliable Wireless Protocol
 - Cell Phone text messaging & email for less reliable, outbound messaging
- ✓ Outpatient Diabetes Clinical Informatics Module
 - Enhances existing clinical information systems/patient management systems
 - Provider-defined, Automated Analysis of the Patient Record
 - Real-time Alerts, Reminders and Requests for Patient Information

Addendum B – Diabetech Technology Overview (Cont'd)

- IMP specific web-based Reports & Physician Dashboard

GlucoDYNAMIX System Overview

Since clinicians typically are most interested in what it is that they will be working with, we have positioned the descriptions of the profile management and intensive management protocols at the beginning. Diabetes Intervention Technology is only possible because of ready access to accurate data. A detailed description of how the system collects timely and accurate patient data is located toward the end of this section. Without a high degree of reliability on the data, any analysis is circumspect.

- **Patient Profile Management**

Each patient enrolled in the intervention group will have a profile which describes relevant information that may be interesting during the real-time intervention process and/or historical analysis. This includes patient information, authorized caregivers, contact numbers, email addresses, patient handle for abstract labeling of the patient record designed to protect privacy, specific Intensive Management Protocols being used to manage the patient, etc...

- **Provider Profile Management**

Likewise, a provider office consists of many people with various specialties and roles. The system needs to know exactly how a provider office intends to distribute the work load as it relates to phone encounters, information review, who wishes to receive alerts, which person is responsible for reviewing different reports, etc...

- **Operational Patient Record**

In its simplest description, this is the database where all of the information is stored. Unlike a typical medical management system, it also requires a front-end transaction-processing engine in order to handle the wireless messaging and real-time analysis and intervention.

- **Intensive Management Protocols (IMPs)**

Knowing what to do with the data when it arrives at the Diabetech data center as well as defining the characteristics of the system depends on the configuration of provider-defined IMPs. In the case of this specific study, we are configuring the system with best practices for managing information designed to introduce tighter glycemic control and extending beta cell function .

- ✓ **Real-time Analysis**

Analysis may be triggered by the passage of time, the receipt of new data, the lack of new data or by ad-hoc analysis of the data. It can also relate to a specific patient, a demographic subset of the population, or an entire population.

- ✓ **Real-time Interventions**

Intervention can take on many forms. Historically, diabetes management intervention is typically thought of in terms of a phone call from the diabetes nurse to a patient. Unfortunately, it is difficult for a healthcare provider to understand when an intervention is most appropriate as well as having the relevant patient data and thoughtful analysis available in order to support an efficient and effective patient encounter.

The technology at task within this study has taken on the role of a provider's assistant by performing many of these same functions inherent in the historical definition of intervention. The IMP considers all of the possibilities for intervention and draws upon different mechanisms, timings, analysis, media types, delivery possibilities, etc... in arriving at the appropriate intervention at the appropriate time. We describe 4 categories of system intervention: Alerts, Reminders, Reports and Requests. The Request intervention is slightly different than the others in that it combines aspects of the IMP intelligence in knowing what

Addendum B – Diabetech Technology Overview (Cont'd)

to request, where to make the request while at the same time increasing the likelihood of a successful data collection event.

- **Alerts (example)**

A copy of the glucose reading and timestamp can be sent to any number of destinations including cell phones, email or pagers. High and Low filters as well as time of day and day of week may also be applied to the blood sugar reading as a way to automatically filter which alerts are sent.

- **Reminders (example)**

Based on the patient profile or assessment of the dynamic patient record, messages can be sent or scheduled for future delivery to remind the patient of certain information or prescribed actions. An example of this feature would be a text message to the patient's cell phone or email reminding them of the clear-cloudy / cloudy-clear rule for drawing a syringe with both short-acting and long-acting insulin.

- **Reports (example)**

There are two main categories of Real-time reports. Reviewing the Practice at a glance is necessary for efficient practice management and for identifying relative risk in efficiently determining the priority ranking for timely provider intervention.

Otherwise, once focused on an individual patient, real-time reports can help to quickly understand trends for easy isolation of troubled times of day which require immediate attention in order to maintain tight glucose control.

- **Requests (examples)**

An additional form of intervention may focus on the need for very specific data. We refer to this as a data request message. Based on real-time system analysis of the patient profile, the dynamic patient record and the applicable intensive management protocol, certain information may be expected, anticipated or desired. When the system discovers this condition, it sends a message to the patient's mobile device asking the patient for a specific response. In some cases, the patient's reply may be as simple as answering a question with a carbohydrate count for a recent meal. In others, the system may be attempting to clarify an out of range blood sugar result exceeding a certain standard deviation from an expected range.

For this more complicated patient response to a system request message, a number of most probable explanations or annotations are presented to the patient in menu format. This method has the benefit of minimizing the number of button pushes for the patient as well as standardizing response types. If none of the embedded replies are appropriate, the patient is able to type a custom reply using short codes or free form comments. As before, the data is sent to the Diabetech data center where it is appended to the patient record. Real-time Analysis is now able to consider the new data. This enhanced analysis might then cause a message to prompt a member of the provider team to intervene or it may simply result in additional entry into the patient record without a requirement for proactive intervention.

- ✓ **Dynamically Scheduled Interventions**

In contrast with Real-time Intervention, Dynamically Scheduled Interventions are able to leverage real-time data and based on analysis, automatically schedule a future intervention. In

Addendum B – Diabetech Technology Overview (Cont'd)

some cases, the system is able to cancel the scheduled intervention when new data arrives, which mitigates the need for the scheduled intervention.

A specific example of a Dynamically Scheduled Intervention would be a night-time hypoglycemia recheck reminder. In this scenario, the system is set to monitor the incoming glucose results from a specific patient. The protocol can be configured to watch for any test after a given time in the evening to flag low blood sugar test results under a certain threshold and begin a timer which can only be cancelled upon receipt of a subsequent blood sugar result.

For example, between the hours of 10pm and 6am, any test result received by the system below 60mg/dl begins a timer. If a recheck of the blood glucose is received by the system within 20 minutes, the reminder intervention is cancelled. If, however, a recheck of the blood glucose is not received by the system within 20 minutes, a reminder message is sent to the caregiver's cell phone or a digital recording is placed via telephone to the home number reminding the caregiver to retest. This cycle is repeated for any result occurring before 6am.

The system is highly configurable to support differences in patients and the differing guidelines applied by the diabetes provider community.

✓ **QuickTips Educational Reinforcement**

QuickTips helps diabetes educators to deliver on the often talked about promise of "intervention at the teachable moment". In contrast to other technologies, which send a series of generic "Tip of the Day" messages, QuickTips are part of a completely automated patient-specific diabetes-training program. Based on the IMP, patients receive pointed, relevant educational messages on their 2Way text messaging device, cell phone or email. Intelligent software compares what's happening in the patient record and determines which message(s) to send.

For example, as part of the New Onset Type 1 Beta Cell Preservation IMP, providers can define specific educational messages that introduce concepts such as troubleshooting infusion sites, glycemic index as it affects glucose control, etc... When post-prandial blood sugars are elevated outside of the normal range, a mini training module around glycemic index might be warranted. The patient then automatically receives a detailed wireless email message introducing them to the subject and assists the CDE to transfer knowledge as life happens. The patient also has the option to request more information about glycemic index or select from up to 5 other categories of diabetes education. This self-paced training course takes advantage of the fact that people are rarely sitting in front of a PC.

Leveraging Diabetech's unique perspective on the intelligent delivery of timely and relevant content, diabetes educators and physicians can now touch the patient between visits and reinforce the most important messages via mobile text messaging. QuickTips uses relevant and timely feedback to influence patient behavior and thus outcomes.

✓ **Historical Analysis and Reporting**

The main difference is that the GlucoDYNAMIX patient record is accurate and complete. The clinical staff can rely on resulting GlucoDYNAMIX information as compared to self-reported, unchecked patient logbooks.

Likewise, systems that allow manual uploads of glucose meter data are inherently less reliable. And, because there are so many steps involved between patient upload and provider review, only historical analysis is possible, long after the context of the situation has passed.

Historical reporting may be a valuable tool however when attempting to compare various populations or diabetes center best practices.

✓ **Real-time Data Collection**

Of course, without the data, analysis and intervention do not happen or if it does it can be ineffectual and a waste of time. What's even more dangerous than not having the data is sometimes having the wrong data, inaccurate data or even fraudulent data which are all commonplace in traditional clinical review of patient logbooks and even with computer downloads from patient glucose meters.

Within a very short window of time, the clinical staff understands their ability or inability to rely on certain kinds of data.

○ **Telemetric Medical Device Data Collection**

Within the patient's otherwise "normal-looking" glucose meter case, the GlucoMON includes a glucose meter docking station and a small long-range wireless computer. Whenever the meter is returned to the docking station, the GlucoMON computer reads the meter and copies the new data to the computer's database. The GlucoMON's 2way radio feature then automatically transmits (SMBG data including an accurate timestamp in an encrypted format) to a secure server and is not accessible to anyone outside of specific Diabetech technical personnel.

Once received at the computer data center, the data is appended to the patient record. Depending on analysis of the data just received, analysis of the data and the patient record may or may not result in an automated system action. The Intensive Management Protocol and the Patient Profile also help to define when to take action which can be driven by the receipt of new data, the transpiring of time, analysis of the new data, and analysis of the patient record.

○ **Short Code Driven Interactive Virtual Logbook**

This section describes the system capability as it relates to alerts, reminders, requests and reports which form the balance of the technology being used to conduct this research. While there are many ways for patients and team members to log information, the GlucoDYNAMIX system is unique in its use of automated messaging and distribution considering the mobile environment.

Patients are rarely sitting in front of a telephone or computer and are usually away from home. Therefore, educational interventions, which leverage mobile devices such as, cell phones and pagers are believed to enhance the training program for raising one's awareness and proficiency regarding diabetes management techniques. The following categories are used to define system interaction for performing the data collection function.

One of the most basic challenges for providers and diabetes educators is collecting timely and accurate patient diabetes data. As previously discussed, using a telemetric-style device for keeping accurate time on the glucose meter and providing a more reliable and efficient method of glucose data collection already goes a long way toward solving this problem. Extending this technology to the task of collecting additional forms of timely and relevant data (i.e. – insulin dosing, carbohydrate intake, activity levels, etc...) presents yet another challenge, which needs to be overcome.

A systematic approach to data marking has been developed in support of this research that will allow people to work together through the use of a universal

Addendum B – Diabetech Technology Overview (Cont'd)

diabetes library of ‘short codes’. This allows people to quickly and easily add data and information to the patient record via mobile devices and email.

Each short code has been tested to ensure a simple and accurate user experience. For example, when a patient wishes to add a carbohydrate intake event to their patient logbook, they use the short code ‘ca’ followed by the number of grams of carbohydrate eaten. Likewise, for adding insulin dosing to their record, they use ‘mb’ for meal bolus, ‘cb’ for correction bolus or ‘sb’ for snack bolus followed by the number of milligrams of insulin administered. In the insulin example, not only are we able to collect the insulin quantity but also additional context around the insulin event such as whether or not there was food involved in the patient’s decision to dose insulin. The mobile device handles the approximate time stamping automatically for the user based on the time of the transmitted wireless message. A short code is also available to allow the user to mark the data with a different timestamp in the event too much time has lapsed since the actual event.

Once the message has been entered into the mobile device and the patient presses the ‘Send’ command, the data is transmitted via a guaranteed wireless messaging protocol to the Diabetech data center where it is identified, authorized and appended to the patient record.

GlucoDYNAMIX Technology Roadmap

While the current system makes the best of currently available technology, future iterations of the system and its components are already in research & development. The system is positioned to assist patients and diabetes clinicians in the active role of intervention as opposed to a more passive design of collection and management as a simple web-accessible repository of data.

- ✓ **Devices**
Diabetech is positioning the current GlucoMON wireless device as one of many designs in a suite of medical devices, which integrate sensor technology with advanced data collection and remote device management functionality. This includes design and integration of software and hardware for implantable devices, localized on-body/near-body and remote medical and non-medical devices.
- ✓ **Intensive Management Protocol Strategy**
Diabetech’s IMPs are designed with the goal of being able to tie a specific intervention to its direct consequence, which will often be an improved outcome. Only by having a real-time go anywhere system, which is capable of assessing the probabilities of each and every data point, is it possible to maximize the opportunity for a meaningful intervention and to positively influence a beneficial outcome. We believe this approach may increase the likelihood of securing reimbursement for the delivery of intensive management by qualified medical personnel.
- ✓ **Disease States**
Beyond diabetes, Diabetech has been asked by several organizations including hospitals, sensor companies and universities to consider applying the Diabetech design concepts and platform technology to create similar solutions in the fields of cardiopulmonary, cardiology and the growing health & wellness category.

Study Site: Morristown Memorial Hospital
Principal Investigator: Harold Starkman, MD FAAP
Nurse Coordinator: Fran Melchionne

β -Cell Preservation Study Protocol
in Pediatric Type 1 Diabetes

Addendum B – Diabetech Technology Overview (Cont'd)

Diabetes Intervention Technology

Between glucose meters, insulin pens, insulin pumps, pedometers, heart rate monitors, blood pressure monitors, PDAs, PCs, cell phones, wireless data, internet, email, text messaging, diabetes management software and clinical information systems, there has to be cohesive platform for making it all work together. We've chosen to work from that perspective and to focus on building a platform for developing and managing these devices as a key element of clinical protocols which all have their own unique requirements.

Diabetech is fluent across many forms of communication standards including short-range wireless, long-range wireless and wireline networks as enabling technology to facilitate the automation and management of remote devices. We consider all of the possibilities before arriving at a final design for any given element of the solution. Our team's credentials include current membership in the Bluetooth Special Interest Group, former contributing member of the CDMA Steering Committee (including current wireless carriers such as SprintPCS, Verizon, etc...) and contribution to the product design and launch of the short and long-range wireless versions of the iPAQ PDA from Compaq, now Hewlett-Packard.