A Guideline for Smart Implant Systems Supporting Patients with Diabetes Type 1
Tristan Brugman
University of Twente
P.O. Box 217, 7500AE Enschede
The Netherlands
t.w.r.m.brugman@student.utwente.nl

ABSTRACT
There are several applications for smart implant systems in supporting patients with diabetes type 1. While the different components of these systems have been studied and compared, the requirements of the system from an application level have not yet been determined. In this study, possible requirements of several main categories of applications are listed. Finally, new developments are considered of components that currently do not fulfill the requirements of a specific application, the closed-loop system.

Keywords
Implantable Device, Diabetes Type 1, Continuous Glucose Monitoring, Artificial Pancreas Device System, Threshold Suspend Device System

1. INTRODUCTION
Blood glucose levels are controlled by release of insulin by the pancreas. Insulin enables the cells to take up glucose from the blood to use for energy. When the supply of insulin is too low, the cells will not be able to absorb the glucose from the blood. The cells get a lack of fuel and the blood glucose levels increase. The pancreas of diabetes 1 patients is not able produce enough insulin on its own. Therefore, insulin has to be injected to regulate glucose levels. The amount of insulin that has to be applied shall be in balance with the glucose intake (by food) or glucose consumption (by physical activity). Ideally the glucose level should be kept in a narrow range.

At present, for the majority of people with diabetes, self-monitoring of blood glucose (SMBG) and manual injection of insulin is the most common approach to glucose level monitoring and control.

For this study, applications that support diabetes type 1 patients making use of smart implants will be investigated. The main goal of these systems is to help the patient in keeping the blood glucose levels within a narrow range. Other possible functions are warning the patient in case of too low or too high glucose levels and informing physicians about the condition of the patient.

Smart implant systems for supporting diabetes 1 patients consist of a Continuous Glucose Monitoring (CGM) sensor, a wireless transmitter and a receiver [10]. The receiver can be connected to a variety of devices, such as a handheld device that displays data or an insulin pump. The transmitter and receiver can be connected by a variety of communication techniques. There are many possible implementation choices for each of these components and techniques, each with different limitations.

Main limitations of CGM sensors are suboptimal accuracy, reliability, lag time between change in glucose levels and their measurement [4] and limited lifetime [11]. Insulin pumps may undermedicate or overmedicate if they malfunction or are used improperly. Device problems that have been reported include alarm problems, loosening and/or occlusion of the catheters, bent cannula, and screen display problems [36]. Since these pumps are sometimes remotely controllable [21], and misuse could severely impact the patient’s health, security must also be considered.

Applications that will be considered will include storing glucose levels for later analysis, warning patients of out of range glucose levels, and using glucose levels to directly control an insulin pump (a closed-loop system). Both current and in-development applications will be addressed.

Each of these applications has different requirements regarding reliability, accuracy, durability and design limitations. Safety-critical applications, for example, whose failure could result in loss of life, will face more stringent reliability requirements. This study evaluates the consequences of failure, inaccuracy etc. for each application and subsequently determine the necessary requirements.

2. PROBLEM STATEMENT
Because of the possible medical consequences of the disruption of these smart implant systems, it is necessary that the optimal components are chosen. There have been various studies that have compared components such as sensors [1], MAC protocols [24], glucose monitors [1] and insulin pumps [16]. However, none of these studies have looked at the implications from the application level.

Not all of the considered applications are currently used in practice. Specifically, the components needed in a closed-loop system do not yet fulfill the necessary requirements. Therefore, after the requirements have been determined, several new developments in these components will be considered.
The following questions will be addressed in this study:

1. Which applications of smart implants for supporting diabetes type 1 patients currently exist or are being developed?
2. Which requirements do systems that make these applications possible need to fulfill?
3. Which components are being developed that may fulfill the requirements of a closed-loop system, and in what way?

3. USE CASES

In this section, five different use cases of smart implant systems for patients with diabetes type 1 are covered. These use cases (or applications) have been determined by both identifying applications of devices that are currently in common use, and by considering a promising future use case, the Artificial Pancreas Device System. Their workings are described and their components are listed. In the first three applications, the system only measures the glucose levels. In the latter two, the system uses these measurements to directly influence the amount of insulin that is administered to the patient.

3.1 Informing the Patient Of Glucose Levels

Currently, most patients measure their glucose levels by extracting blood via a fingerstick and applying it to a glucose strip on a hand-held device. This is called self-monitoring of blood glucose (SMBG). Patients are recommended to perform this at least four times a day, although this is less frequently done due to pain and convenience [14]. Alternatively, glucose levels can be measured automatically and repeatedly over a long period of time by making use of a sensor; this is called continuous glucose monitoring (CGM). CGM systems have been shown to lower time patients spend with too low glucose levels (called hypoglycemia), and also to reduce their longer term glucose levels (the HbA1c level) [33].

Current commercially available and FDA approved CGM systems use a small sensor that is inserted about 5 millimeters under the skin. Here, it measures the glucose concentration in the fluid between the cells (interstitial fluid) under the skin. A transmitter that is attached to the sensor sends the glucose data through wireless communication to a receiver each 1 to 5 minutes. The subcutaneous interstitial glucose levels are not necessarily the same as the actual blood glucose levels, and should be calibrated by regular SMBG values. At least four of these calibrations per day are recommended [17].

CGM systems typically consist of the following components: a sensor to measure the glucose concentrations, a transmitter to send the sensor data, and a receiver for this data. For this particular application, the receiver is connected to a device that informs the patient of their glucose levels in a particular way. An example would be a hand-held device that displays the level visually. Another possibility would be to use sound to inform the user, for example by using a text-to-speech engine. The sensor is typically a small disposable enzyme-coated glucose sensor electrode. The sensor measures interstitial glucose through a glucose oxidase reaction. The sensor electrodes can remain in the body for 3 to 7 days before they should be replaced [31]. The relation between these components is displayed in figure 1. This figure is also used in the following two use cases.

3.2 Informing the Patient In Case Of Out Of Range Glucose Levels

An application closely related to the one in the previous section, is warning the patient when their glucose level is, or is about to become too low (hypoglycemia) or too high (hyperglycemia). This could be accomplished by using the CGM systems defined in the application described in the previous section, and performing a simple check, comparing the measured glucose level against a preconfigured range. The patient could be warned by sounding an alarm, or by vibrating a device that the patient carries with him. This application is especially useful for patients that have frequent episodes of hypoglycemia or hyperglycemia, and for monitoring overnight blood glucose levels, when patients are asleep.

For this application, the same components as in the first application are required, with exception of the device that informs the user. This device should be able to produce sounds loud enough to alarm the patient, and should be able of producing vibrations. A device that is already in common use that could fulfill this application would be a smart phone.

One commercially available system that implements this application, the Guardian REAL-Time System [27], can (according to the manufacturer) alert patients up to 30 minutes before reaching their thresholds. This system has been shown to improve hypoglycemia detection [19].

3.3 Storing and Making Available Longer Term Data

The data collected by CGM systems can not only be used for immediate use, like in the first two applications. It can also be stored and extracted later in aggregate, for analysis and diabetes management. Both patient and doctor can use this information to identify trends and modify the patient’s treatment. For example, in combination with information about the patient’s lifestyle, the trends could show how the blood glucose level reacts to insulin, physical exercise, intake of food, and other factors. This information could be applied to determine the correct insulin dosing for a certain amount of carbohydrates intake and the amount of insulin necessary for correction of hypo- and hyperglycemia.

There are many different software kits commercially available for patients to manage their diabetes, such as the CareLink Personal Software [26] and SiDiary [37]. Both of these software kits offer the patient tools to track their glucose values and...
manage their own treatment. They also offer the patient the option to share the data with their doctors.

This application makes use of the components of the CGM system, and also consists of a storage element (such as a flash drive) and a communication component to make the data available outside the system, such as a USB port. There are various software kits that make further use of the generated data, but these fall outside the scope of this paper.

### 3.4 Threshold Suspend Device Systems and Control To Range Systems

In this application, the data collected from the CGM system is used to directly influence the administration of insulin via an insulin pump. Low glucose suspend (LGS) systems (also called Threshold Suspend Device Systems [13]) shut off the insulin pump when the measured glucose level reaches or approaches a preconfigured lower threshold, thereby trying to prevent and reduce the severity of hypoglycemic episodes. Control to Range (CTR) systems attempt the same, but also use a higher threshold to prevent hyperglycemia. LGS and CTR are the first two of three systems covered in this paper that attempt to mimic the function of an actual pancreas to some degree, and are considered to be Artificial Pancreas Device Systems (APDS) by the FDA [13].

Insulin pumps are commonly used as stand-alone units; they administer insulin to patients from a reservoir. The insulin is administered via a soft tube called an infusion set, which is inserted directly under the skin in the subcutaneous tissue. This infusion set is replaced every 2 to 3 days. The administration happens continuously, at rate known as the basal rate, which is set by a controller. Furthermore, the patient can let the pump (via a display) administer an extra dose, known as a bolus, in anticipation of an increase of blood glucose (such as before eating a meal). In LGS and CTR systems, the patient still has to set the basal rate and administer bolus doses [13]. Over 200,000 patients use external insulin pumps [34].

Besides the components of a CGM system (a glucose sensor, transmitter, and receiver), any closed-loop insulin delivery system consists of the following components: an insulin infusion pump to store and administer the insulin, a controller to interpret the glucose level measurements and determine how much insulin to administer, and a transmitter and receiver for the communication between the controller and insulin pump.

The relation between these components is depicted in figure 2, which is also used for the next use case.

The first commercially available system that implements an LGS system is the Paradigm Veo from MiniMed [28]. This system is available in Europe, but still pending FDA approval in the USA. It has been shown to reduce nocturnal hypoglycemia in patients at greatest risk [6]. No CTR has yet been approved in either Europe or the USA as of this date.

### 3.5 Control To Target Systems

Although LGS and CTR are considered to be APDS systems, they do not act as long as the measured or predicted glucose value is above the threshold or in a particular range. They also still require patient interaction with the insulin pump to set the basal and bolus rates. Control to Target (CTT) systems, however, attempt to maintain the glucose level at a predetermined point and require no user interaction besides calibration of the CGM, making them fully automated.

CTT systems consist of the same components as LGS and CTR systems. However, CTR and CTT systems are being research that use bi-hormonal pumps instead of an insulin pump. Bi-hormonal pumps use both insulin, which lowers glucose levels, and glucagon, which increases them.

An important part of CTT systems is the algorithm that controls the insulin infusion rate (IIR). Two main categories of algorithms have been determined: proportional-integral-derivative (PID) algorithms, and model predictive control (MPC) algorithms [17].

PID algorithms use three variables derived from the glucose measurement curve to determine the IIR. These variables are, as the name implies: the difference between the current and target level, the area under the curve between measurement and target levels, and the rate of change of the measurement level. These variables are then weighted by predetermined (by off-line analysis) constant factors to arrive at the IIR.

MPC algorithms use a model that links insulin infusion and meal ingestion to determine glucose levels. This model can be either based on actual physiological processes [18], or by making use of pattern recognition [38].

As of this date, no CTT systems have been approved in Europe or the United States.

![Figure 2. Depiction of the different possible components of an APDS](image)
4. REQUIREMENTS

In this section, various requirements for different components of the system are listed. Furthermore, the applicability of each requirement for each application is considered. Special regard is given toward problems caused by the component for APDS systems, as no CTR or CTT systems have currently been approved in either Europe or the USA. The requirements are summarized in Table 1.

4.1 Glucose Sensors

It is necessary for all applications that the CGM sensor has a reasonable accuracy. That is, the measured value should never deviate too much from the actual value, as measured by lab tests. This requirement is currently problematic, as CGM sensors that are currently used can deviate as much as 20% [16].

As per ISO 15197, a glucose sensor is considered accurate if its error is within 0.83 mM (15 mg/dL) when measuring a hypoglycemic event of less than 4.2 mM (75 mg/dL) glucose. Error values of 20% or lower are acceptable when testing in the range above 4.2 mM (75 mg/dL). [41] Although this standard is for glucose meters for traditional fingerstick measurement, it may be assumed that the same standards are applicable for CGM devices.

A requirement related to accuracy is response time. If an interstitial glucose sensor is used (the most common option), there is a delay between actual glucose level change and measured change of 12 to 20 minutes [41]. This lag time can increase due to biofouling. There is another delay because CGM sensors do not measure continuously (despite the name), but update between each 1 and 5 minutes. This total delay could distort the actual glucose level, especially when there are rapid changes, like after the patient eats a meal or participates in physical activity. This delay should be minimized as much as possible in applications that depend on timely information, such as glucose level warning systems and closed-loop systems. However, this is not a requirement for systems that depend on longer term data.

Another requirement related to sensors is reliability. The CGM sensor should have a high expected uptime; this is especially important for closed-loop systems and applications that warn patients in case of out of range glucose levels. If the sensor to go offline for an extended time, patient’s health could be impacted directly.

Finally, the durability should be considered. Most sensors are recommended to be used between 3 and 7 days. Regardless of the application, increased durability could result in lower costs (ceteris paribus) and higher comfort for the patient.

Currently, CGM sensors are not yet suitable for CTR and CTT systems. The following issues must be solved before continuous glucose sensors meet the high standards for these applications [16, 22]:

- Accuracy and time lag problems. Due to the fact that CGM sensors are measuring interstitial glucose, there is a time lag between the sensor data and the true blood glucose concentrations. This may result in accuracy problems particularly when glucose levels are changing rapidly.
- Calibration drift. As the relation between CGM values and blood glucose levels is continuously changing, frequent recalibration is necessary, a few times a day, by performing a manual blood glucose test with a fingerstick measurement.
- Risk of interrupted data delivery. Two limitations of currently marketed sensors, include early termination (often due to sensor failures or when the sensor is disconnected from the body) and gaps in data (due to noise and unexplained drop outs).

Given the inaccuracy of current glucose sensors, a Control to Target system is more difficult to achieve than a Control to Range system, and a Control to Range system is more difficult to achieve than a Threshold Suspend Device (LGS) system.

4.2 Communication within the System

In each of the applications considered in this paper, the CGM sensor is connected to a transmitter that communicates with a receiver that is connected to a display device and/or a controller (in case of the closed-loop systems). This controller, in turn, is connected to a transceiver that communicates with a transceiver that is connected to an insulin pump. There are several requirements that can be imposed on the hardware components and communication protocols.

First of all, the patient’s privacy should be warranted. In the applications considered in this paper, this mainly means preserving the confidentiality of the data generated by the CGM system and commands to the insulin pump. In order to prevent unauthorized devices from intercepting this data, the connection should be encrypted.

The system should also be secure from outside interference. The system should prevent manipulation of blood glucose data, for example. If manipulated glucose values are presented to the patient, like in the first application, the user could self-administer a wrong amount of insulin, which could have medical consequences. The situation is potentially more severe in APDS systems, because here the glucose value directly influences the amount of insulin administered. The system should also prevent manipulation of the communication between controller and insulin pump. A study on the security of implantable devices showed that an expert could tap into the wireless communication between a glucose monitor and an insulin pump, and could wirelessly control the insulin dosage [25]. Since this has a direct medical consequence, and could affect any patient with an insulin pump, this requirement should have a high priority. Data corruption should also be prevented, because this could in theory have the same consequences as intentional manipulation.

4.3 User Interface

The first three use cases inform the user in one way or another. In order to inform the patient of their current glucose level, there has to be a visual or auditory user interface.

If the use case is displaying values, a simple visual interface that displays the latest glucose measurement in a common format (like mmol/liter) is sufficient. This would not require a screen with a high resolution. Although the screen should be bright enough for the user, a higher brightness results in a higher power consumption. A possibility would be to give the patient the option to set the brightness to a level he is comfortable with.
Alternatively, the system could provide a text-to-speech engine, so that users can hear the measurement value. This would be especially useful for users with bad eyesight, which can be caused by diabetes 1, although this is rare [43].

In the case of warning the patient when a hypo- or hyperglycemia occurs, a clear and loud auditory alarm would be sufficient. Alternatively or in addition to this, the system could offer the option of vibrating.

### 4.4 Insulin Pump

Insulin pumps should have a sufficiently large insulin reservoir for common usage. The pump should alarm the user if the reservoir is nearly or completely empty. The patient should also be warned in case of occlusion (blockage) of the infusion set.

Currently commercially available insulin pumps are only FDA approved for continuous subcutaneous infusion of insulin. However, in order for insulin pumps to be suitable for APDS systems, they should be capable or non-continuous (intermittent) use.

The insulin pump should allow for accurate control of the bolus insulin dose, for both large and small doses. The delay between pump actuation, insulin infusion and insulin action should also be minimized as much as possible to allow for better control.

Lastly, for use in a (portable) APDS the pump must be made sufficiently robust to withstand all kinds of external factors like air pressure fluctuations, water ingress, and mechanical shocks.

### 4.5 Control Algorithm

The control algorithm or CTT should be sufficiently robust to determine the correct insulin doses in various situations. The glucose level that results from the insulin doses should not stray too far from the target point (for CTT systems), or cross the predetermined threshold(s) (in LGS and CTR systems). For a successful closed loop control system, the control algorithm must be tunable for individual characteristics and account for glucose fluctuations caused by a person’s physical conditions (like stress and illness) and behavior (like physical exercise and carbohydrate intake) [37].

Control algorithms currently under development for APDS are missing three important features [20]: Firstly, the current algorithms are still not sufficiently robust to predict correct doses of insulin in various situations. Secondly, the current closed loop systems are not able to prevent hypoglycemia effectively in case of rapid falling glucose levels. Therefore, in order to avoid hypoglycemia, glucose levels are kept at safe but too high levels, ultimately resulting in higher HbA1C levels. Finally, the current algorithms are not able to distinguish between noise (random fluctuations in glucose levels) and a true spikes, caused by the user eating a meal.

### 4.6 Ethical Issues

Since the system makes use of sensitive, medical data, ethical issues have to be considered. Privacy and security issues regarding in-system communication have already been discussed. However, it should also be considered how this data is used when it is made available outside the system, e.g. in telemedicine. In this case, security issues are a consideration, just like during in-system communication. This makes end-to-end (from patient to doctor) encryption necessary. This data should be stored securely. Finally, data confidentiality should be assured, so that only users authorized by the patient have access to their data.

<table>
<thead>
<tr>
<th>Table 1. A summary of the different requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Component</strong></td>
</tr>
<tr>
<td>Glucose sensors</td>
</tr>
<tr>
<td>Communication within the system</td>
</tr>
<tr>
<td>User interface</td>
</tr>
<tr>
<td>Insulin pump</td>
</tr>
<tr>
<td>Control algorithm</td>
</tr>
<tr>
<td>Ethical issues</td>
</tr>
</tbody>
</table>

### 5. DIRECTION OF NEW DEVELOPMENTS

In this section, new developments of two components are considered, namely glucose sensors and insulin delivery systems. Improvements in both of these components will be necessary for making an APDS possible.

#### 5.1 Glucose Sensors

For new applications there is a need for a new generation of sensors that have a longer lifetime, are non- or minimally-invasive, or fully implantable for periods of months to years, require only occasional (weekly to monthly) recalibration, be accurate under a variety of conditions without the requirement for calibration by fingerstick, respond more rapidly to changing glucose levels and can easily be implanted and replaced.

New techniques might be used like sensors based optical, ultrasound, and magnetic-impedance-based detection principles [40].

Improved sensor concepts are important for widespread acceptance and use of continuous glucose monitoring systems. For the development of an Artificial Pancreas a new generation of sensors is essential.

A number of interesting and innovative techniques are discussed below.

#### 5.1.1 Microdialysis-based continuous glucose monitoring

Microdialysis-based systems do not use an implanted sensor but a fine, hollow microdialysis fiber placed subcutaneously. The fiber contains isotonic fluid and the glucose in the interstitial fluid diffuses into the isotonic fluid in the fiber, where it is pumped to an electrochemical sensor. The sensor is outside the body and so avoids the problems of fouling. Consequently, it requires only one calibration per day and has less sensor drift than the subcutaneous sensor. Microdialysis systems have however extra lag time as the dialysate has to be pumped to the sensor and use more power. They are also larger. The lifespan of the sensor is 2–4 days [42,32]. The GlucoDay is the only commercially available sensor based on this principle. It is not
approved by the FDA yet so not available in the USA but already approved and available in Europe.

5.1.2 Implantable biosensor
Researchers at the University of California at San Diego and biotech company GlySens have developed a new implantable biosensor that can monitor blood glucose levels on a continuous basis and transmits the information to an external receiver. Tests on animals show that this implantable biosensor can be used for over 500 days without the need to be replaced. After human clinical trials and FDA approval, the device could be available for use by diabetes 1 patients within the next few years [3].

5.1.3 Needle-free Transdermal Continuous Glucose Monitoring
The Symphony tCGM is a non-invasive continuous glucose monitoring system. It is a two-part device that monitors blood glucose levels by taking readings through a user’s skin rather than via finger pricks. The unit’s first component is the skin permeation system, which removes the patient’s outermost layer of dead skin cells where the biosensor is to be attached. The patient then attaches the biosensor, which monitors blood glucose levels every minute, to the prepared skin area. The developers claim a high accuracy of about 95% [8]. The system is currently pending FDA approval [9].

5.1.4 Glucose Monitoring in Tears
Studies have indicated that there is a good correlation between glucose levels in tears and BG levels. The time lag between BG levels and glucose levels in tears has been specified to be about five minutes, which is much better in comparison with interstitial fluids [44]. However a lag time of 20 minutes has also been reported which is about equal to interstitial fluids [2].

Below two techniques are described in which glucose levels in tears are measured. The main advantage to this principle is that measuring in tears is non-invasive.

Researchers of the University of Washington in cooperation with Microsoft are developing a contact lens provided with a chemical that reacts to glucose in tears. The coating causes the lens to change color. This change in color of the contact lens in response to the patient’s blood glucose levels provides input for the glucose measurement. The blood sugar is recorded by the patient using a smartphone to take a picture of his/her own eyes. A smart phone app compares the color difference between the two eyes to produce a blood glucose calculation [39].

5.1.5 Glucose monitoring by a combination of ultrasonic, electromagnetic and thermal techniques
GlucOTrack is a device to check BG’s via a non-invasive sensor in an ear clip. The principle is based on detection of ultrasound, conductivity, and heat capacity. The three measurements are fed into an algorithm which determines the BG. Monthly calibration is required. Accuracy is about 75%–80%, which is still not good enough for APDS. The device is not available for sale yet [35].

5.2 Insulin Delivery
5.2.1 New delivery routes
When insulin is injected directly into a vein, the effect on the blood glucose level occurs rapidly. However due to blood clotting problems with catheters, the development of this route of insulin delivery is problematic.

Today the usual mode for delivery of insulin with an insulin pump is by subcutaneous infusion. The absorption of subcutaneously infused insulin takes extra time resulting in insulin peaks up to 120 min after injection of a subcutaneous bolus. This makes effective control for an APDS in case of fast changing glucose levels practically impossible. Therefore alternative routes are being investigated.

Intraperitoneal delivery could be an interesting alternative. Advantages of this route are reproducibility and fastness of the absorption process (about 15 minutes), resulting in better blood glucose control [7]. Disadvantages are that this route is more invasive and more expensive. Intraperitoneal delivery requires surgery and is associated with risk of infection and catheter occlusion due to insulin aggregation [23].

The only device available today that delivers insulin intraperitoneally is the Diaport system by Roche. It has been approved in Europe, but not in the United States.

5.2.2 Implantable pumps
Development of fully implantable devices will minimize inconvenience and viability. However implantable pumps are only feasible as long as these devices can reliably operate for a long time without maintenance. In addition, fully implantable systems potentially offer alternative insulin delivery routes, such as the vasculature or the abdominal cavity [40].

Debiotech has developed different types of very small implantable delivery pumps based on chip technology. The pumps are using a piezoelectric actuator that moves the membrane in a reciprocating movement to compress and decompress the fluid in the pumping chamber [5]. Implantable pumps, however, are still under development and are not approved yet.

5.2.3 Dual hormone pumps
Dual hormone pumps that infuse either insulin or glucagon could be interesting for application in an APDS. Normally the dual hormone pump delivers insulin. However in case of hypoglycemia, glucagon is delivered to increase the blood glucose. Studies using this technique in a closed loop system show improved glucose control and reduced risk of hypoglycemia compared with conventional insulin pump therapy [35,15].
6. CONCLUSION
This study sought to define the requirements of the main applications of smart implant systems supporting patients with diabetes. It also sought to determine how components are being developed for future applications.

The first sub question asked which applications, current or future, can be identified. The main three current applications were found to be: informing the patient of their current glucose level, warning the patient in case of out of range glucose levels, and storing and making available longer term data. As for future applications, two types of Artificial Pancreas Device Systems were identified. The first one, LGS and CTR systems, aim to maintain the glucose level in a certain range. The first devices implementing LGS systems are just becoming commercially available. The second type of APDS is the CTT system, which tries to keep the glucose level at a specified value. This type of system is not yet available commercially.

The second sub question asked which requirements of the applications from the first sub question can be identified. These are numerous and can be found in table 1. The requirements span the following components: the glucose sensor, communication within the system, the user interface of the display device, the insulin pump and the APDS control algorithm. Finally, the ethical issues of the system were considered, and were found to mainly concern data use outside the system. APD systems are currently not yet commercially available (with the exception of an LGS system); the reasons for this were also considered when answering this sub question. The main problems were found to be caused by the glucose sensor and insulin pump.

The third and final sub question asks which new developments of components of APDS systems can be identified, so that a closed-loop system may become available. In order to answer this question, new developments of glucose sensors and insulin delivery mechanisms were considered. Regarding glucose sensors, devices have been developed that offer higher accuracy, lower response time and higher durability. As for insulin delivery, new methods offer faster insulin action, higher patient convenience, and improved glucose control. In the future, a combination of these new components and techniques may offer a way to create an APDS.

7. REFERENCES


