Remote Accessibility to Diabetes Management and Therapy in Operational Healthcare Networks

REACTION (FP7 248590)

D3-10

Survey on commercially available CGM devices and insulin pumps

Survey Report Document

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Table of Contents

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Abstract	This deliverable is a report describing the glucose meters and insulin pumps on the market, with special emphasis on suitability for CGM.
Comments and modifications	
Status	☐ Draft ☒ Task leader accepted ☒ WP leader accepted ☐ Technical supervisor accepted ☐ Medical Engineering supervisor accepted ☐ Medical supervisor accepted ☒ Quality manager checked ☐ Project Coordinator accepted
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0.0	T. Klotzbuecher	2011-01-20	
1.0	L. Ben Mohammadi	2011-02-14	Accuracy studies of CGM sensors added
2.0	T. Klotzbuecher	2011-02-17	Comments from quality manager L. Schaupp implemented
3.0	T. Klotzbuecher	2011-03-04	Comments from quality manager F. Giarugi implemented

1. Executive Summary

Since part of the REACTION project is the investigation of automatic glucose control AGC, two different surveys were made: on the one hand a survey on currently available continuous glucose meters that might be used for REACTION and on the other hand a survey on insulin pumps (note that pumps are not going to be developed within REACTION itself). 5 main insulin pump suppliers have been identified that will be contacted by the REACTION consortium to find out whether they are willing to cooperate.
Non-continuous glucose sensors have been included in this survey, since the first REACTION demonstrator platform will be operated with a non-continuous sensor (Accu Check Inform). The continuously operating sensors are listed with their corresponding specifications. The information about the accuracy of the continuous sensors given in corresponding studies seems to indicate that they do not fulfil the ISO 15197 standard (which is however limited to spot measuring devices), although all listed sensors are FDA approved. None of the CGM systems are approved to replace the spot measurement but they are approved as an adjunctive device – which means therapeutic decisions must not be based on data from the CGM device. Therefore, the state of the art sensors are not suitable for automatic glucose control.

2. Introduction

2.1 Purpose, context and scope of this deliverable

The following document gives an overview on the glucose meters and insulin pumps currently available on the market. Technical specifications of the sensors and pumps are listed and compared, allowing for a decision on suitability for the REACTION project. Especially the list of insulin pump suppliers gives a first indication of whom to contact to make insulin pumps available for the REACTION project.

2.2 Outline

Section 1 gives an executive summary of the current deliverable.

Section 2 describes the purpose, context and scope of this document and gives an outline.

Section 3 gives an overview on the continuous glucose meters currently available on the market. Non-continuous meters are included as well. This includes all technical specifications, as given by the suppliers.

Section 4 gives an overview on the insulin pumps currently available on the market, including technical specifications, as given by the suppliers. A comparison of all pumps is made, serving as a basis for candidate selection of pumps to be included in the REACTION project.

Section 5 gives a list of the tables and figures.

3. Blood glucose meters

3.1 Comparison of Non Continuous Blood Glucose Meters

In this chapter all non continuous blood glucose monitors available on the market are listed and the main properties of the devices are described. The non-continuous blood glucose monitors are usually based on blood glucose test strips to control diabetes. Important links are given as hyperlinks to access information quickly. An overview on the most important suppliers of non-continuous glucose meters is given in Table 1.

Meter Companies - Abbott Diabetes | Bayer | Diabetic Supply of Suncoast | Diagnostic Devices | Entra Health Systems | Hypoguard | HealthPia | Home Diagnostics | Lifescan |Nova Biomedical | Relion | Roche | Nova | U.S. Diagnostics | WaveSense

Table 1: Overview on important suppliers of non-continuous glucose meters, based on test strips.

In the following Table 2 the main properties of the non-continuous glucose meters are given, further information can be found in [1]. The listed sensors are not suitable for automatic glucose control (AGC), since they can not be operated as online sensors. However, since in the first system demonstrator of the REACTION project non continuous glucose sensors are likely to be applied, the list might be useful for the project. These devices will especially be important for the outpatient approach. For the in-hospital glucose management approach the **Accu Chek Inform** will be used because this is a system for hospital care (inc. quality control system).

Abbott Diabetes Care

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Freedom 	2.0x3.3x0.63	1.5 oz	Yes	0.3 microliters	5 secs	250 test	Freestyles	Yes
Lite 	1.57x2.9x0.65	1.5 oz	Yes	0.3 microliters	5 secs	400 test	Freestyle Lite	Yes
Precision Xtra (glucose & ketone) 	2.94x2.1x0.64	1.48 oz	Yes	0.6 microliters	5 secs	450 events	Precision Xtra	Yes

Bayer Diagnostics

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Breeze2 	4.5x2.7x1.1	3.8 oz	Yes	1.0 microliters	5 secs	420 test	Breeze2	Yes

Bayer Diagnostics

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Contour 	3.8x1.2x0.6	3.8 oz	Yes	0.6 microliters	5 secs	480 test	Contour	Yes
Contour USB Meter 	3.75x1.25		Yes	0.6 microliters	5 secs	480 test	Contour	Yes

Diabetic Supply of Suncoast

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Advocate 	3.42x1.77x0.75	2.56 oz	Yes	0.7 microliters	7 secs	450 test	Advocate Strips	Yes
Advocate Duo 	2.95x2.48x1.6	5.57 oz	Yes	0.7 microliters	7 secs	450 test	Advocate Strips	Yes
Advocate RediCode 	3.5	2.0 oz	Yes	0.7 microliters	7 secs	450 test	Advocate Strips	Yes

Diagnostic Devices

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Prodigy® Autocode Meter 	3.79x1.79x1.0	1.86 oz	No	0.6 microliters	6 secs	450 test	Autocode Strips	Yes
Prodigy® Pocket 	3.54x1.38x0.83	1.2 oz	Yes	0.7 microliters	7 secs	120 test	Prodigy Pocket Test Strips	
Prodigy® Voice Meter 	3.78x2.05x0.91	2.76 oz	Yes	0.6 microliters	6 secs	450 test	Prodigy® Personal Strips	Yes

Entra Health Systems

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
MyGlucoHealth Meter 			Yes	0.3 microliters	3 secs	250 test	MyGlucoHealth Test Strips	Yes

Arkray USA (formerly Hypoguard)

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Glucocard 01 	2.0x3.9x0.5	1.6 oz	Yes	0.3 microliters	7 secs	360 test	X-SENSOR Test Strips	Yes
Glucocard 01 Mini 	3.6x1.2x0.5	1.1 oz	Yes	0.3 microliters	7 secs	50 test	Glucocard 01-Mini	Yes
Glucocard X-Meter 	2.0x3.9x0.5	1.6 oz	Yes	0.3 microliters	5	360 test	X-SENSOR Test Strips	Yes
Glucocard Vital 			Yes	0.5 microliters	7 secs	250 test	Glucocard Vital	No

HealthPia America

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
GlucoPack 			No	3 microliters	9 secs	uploaded	GlucoPack Blood Test Strips	Yes

Home Diagnostics

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Prestige IQ			No	4.0 microliters	10 - 50 secs	365 test	Prestige Smart System	Yes

Home Diagnostics

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Sidekick 	1.7x1.5x2.5	1.6 oz	Yes	1.0 microliters	10 secs	50 test	Sidekick Test Strips	No
TRUE2go 	1.7x1.46x0.89	0.6 oz	Yes	.5 microliters	4 secs	99 test	TRUEtest Strips	No
TRUEread 			Yes	1.0 microliters	10 secs	200 test	TRUEread Test Strips	Yes
TRUEresult 	3.44x2.16x0.69	1.66 oz	Yes	0.5 microliters	4 secs	500 test	TRUEtest Strips	No
TrueTrack 	3.52x2.15x0.67	1.66 oz	Yes	1.0 microliters	10 secs	365 test	TrueTrack Smart System	Yes

Lifescan

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
OneTouch Basic 			No	10.0 microliters	45 secs	75 test	Basics	Yes
OneTouch FastTake 			No	1.5 microliters	15 secs	150 test	FastTakes	Yes
OneTouch SureStep 			No	10.0 microliters	15 secs	150 test	SureSteps	Yes
OneTouch Ultra			Yes	1.0 microliters	5 secs	150 test	Ultras	Yes

Lifescan

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
 OneTouch Ultra2	3.8x2.25x0.9	1.5	Yes	1.0 microliters	5 secs	500 test	Ultras	Yes
 OneTouch UltraMini	4.25x1.26x0 .67	1.2	Yes	1.0 microliters	5 secs	50 test	Ultras	No
 OneTouch UltraSmart	3.8x2.3x0.9	2.8	Yes	1.0 microliters	5 secs	3000 test	Ultras	Yes

Nova Biomedical

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Nova Max 	3.6x2.3x0.9	2.65	Yes	0.3 microliters	5 secs	400 test	NovaMax	
Nova Max Link 	3.6x2.3x0.9	2.65	Yes	0.3 microliters	5 secs	400 test	NovaMax	

Relion

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Confirm 			Yes	0.3 microliters	7 secs	360 test	Confirm Strips	
Micro 				0.3 microliters	7 secs	50 test	Micro Strips	

Relion

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Ultima 	2.9x2.1x0.6	1.48 oz	Yes	0.6 microliters	5 secs		Ultima Strips	

Roche Diagnostics

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Accu Check Active 	4.6x1.7x0.9	2.0 oz	Yes	1.0 microliters	5 secs	200 test	Active	Yes
Accu Check Advantage 	3.3x2.2x0.8	1.8 oz	No	4.0 microliters	26 secs	480 test	Comfort Curve	Yes
Accu Check Aviva 	3.7x2.1x0.9	2.12 oz	Yes	0.6 microliters	5 secs	500 test	Aviva	Yes
Accu Check Compact Plus 	4.9 x 2.5 x 1.3 (w/ lancing device) 4.8 x 2.2 x 1.3 (w/o lancing device)	5.2 oz	Yes	1.5 microliters	5 secs	300 test	Compact Drum	Yes
Accu Check Inform 	Meter 1.6 x 3.7 x 7.7 Base Unit 4.1 x 4.4 x 4.4	Meter 325 g (inl. Bat.) Base Unit 385 g	Yes	3.5 microliters	5 secs	> 40000 test (bar code)	Comfort Pro	Yes

U.S. Diagnostics

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Acura 	3.5x1.9x0.5	1.8 oz	Yes	0.5 microliters	5 secs	250 test	Acura Test Strips	Yes

U.S. Diagnostics

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Control AST 	3.6x2.1x0.9	1.9 oz	Yes	1.0 microliters	5 secs	250 test	Control Test Strips	Yes
EasyGluco 	3.6x2.1x0.9	1.9 oz	Yes	1.0 microliters	9 secs	200 test	EasyGluco Test Strips	Yes
Infinity 	3.6x2.1x0.7	1.8 oz	Yes	1.0 microliters	5 secs	365 test	Infinity Test Strips	Yes

WaveSense

Meter	Size (inches)	Weight	Multisite	Sample Size	Test Time	Memory	Strips	Software
Keynote 	1.6x2.8x0.6	1.55 oz	Yes	0.5 microliters	4 secs	300 test	Keynote Test Strips	Yes
Presto 	1.7x3.0x0.6	1.65 oz	Yes	0.5 microliters	4 secs	300 test	Presto Test Strips	Yes
Jazz 	1.81x3.27x0.79	1.69 oz	Yes	0.5 microliters	6 secs	1865 test	Jazz Test Strips	Yes

Table 2: Overview on current non-continuous glucose meters currently available on the market (based on test strips), sorted by supplier companies.

3.2 Comparison of Current Continuous Blood Glucose Monitors

A continuous monitor reveals short-term trends in the blood sugar as they happen. One can see the direction of the blood sugar is taking in the last 1, 3, 6, 9, 12, or 24 hours, depending on the sample frequencies the monitor offers [2]. Various companies have already released continuous monitors, with more companies developing theirs every day. Significant differences in accuracy can be seen in one individual when two different continuous monitors are worn at the same time. An overview on the suppliers and their continuous glucose sensors is given in Table 3 (in some cases also including the insulin pump).

Companies	Guardian REAL-Time Continuous Glucose Monitoring System	Dexcom SEVEN Plus	MiniMed Paradigm® REAL-Time System	Abbott FreeStyle Navigator®	GlucoDay	OrSense
Availability	FDA approved in June 2006 (monitor) and February 2007 (MiniLink Transmitter) and available for purchase	STS system FDA approved in March, 2006. Upgraded since and available for purchase	FDA approved in March of 2006 and available by prescription for purchase in the U.S.	FDA approved in March of 2008 and available by prescription for purchase in the U.S. in the 2nd Quarter	GlucoDay® S is classified as a Medical Device, Class IIA.	OrSense's NBM-200G is a CE approved non-invasive continuous blood glucose monitor
Picture						
Price	$1339 for monitor, transmitter, charger, and 4 sensors $35 per sensor	$1248 for receiver, case, charger, transmitter $399 per 4 sensors	$999 in addition to initial pump cost, $35 per 3 day sensor			Not yet available as a product!
Weight	2.8 oz	2.9 oz	4 oz			
Screen Size	approx 1.8" x 0.75"	1.875" x 1.5"	522/722 screen			
Monitor Size (L x W)	3" x 2"	3" x 2.5"	No Monitor, displays on pump	3" x 2.5"	Size of a walkman	
Transmitter/ Sensor Size (LxWxH)	1.64" x 1.4" x 0.37"	1" x 0.75"	2" x 1.5" / 0.75" diameter	2" x 1" (combined)		
Sensor Life	3 days	7 days	3 days	5 days	2 days	
Sensor Canula size	14 mm	13 mm	14 mm	5 mm	100 µm diameter	
Angle of Sensor Insertion	45º	45º	45º	90º		
Insertion Device	Sens-serter, manual insertion possible	DexCom SEVEN Applicator	Sens-serter, manual insertion possible	Automatic, comes with sensor		
Start-Up Initialization Time	2 hours	2 hours	2 hours	10 hours		
Calibration	2 hours after insertion, within next 6 hours after first, then every 12 hours. Will alarm if calibration value not entered.	every 12 hours with OneTouch Ultra	2 hours after insertion, within next 6 hours after first, then every 12 hours. Will alarm if calibration value not entered.	Calibrate at 10, 12, 24 and 72 hours after insertion, no calibration for the final 2 days of the 5 day wear	One cali-bration in 48 hours; two points recom-mended in real time mode	
User set alarms on low/high	Yes, 8 different thresholds users can set for different times throughout day and night, different sounds for each alarms, loud backup alarm	Yes, one high, two low (user set limit + 55mg/dl alarm)	Yes, different sounds for each alarm, loud back up alarm	Yes		
Predictive alarms for low/high	Yes, can be set to warn 5-30 minutes before glucose limit has been reached	0	10, 20, 30 minutes	10, 20 or 30 minutes		
Alarms for rate of	Yes, can be set to warn at rates of change from 1.1	one each for high and low (either 2 or 3 mg/dl per				

change	mg/dL per minute to 5 mg/dL per minute	minute)			
Displays glucose numbers	Every 5 minutes	Every 5 minutes	Every 5 minutes	Every 1-2 minutes	Glucose (3 min average) value on the display
Displays Directional Trends	Yes, 3, 6, 12, and 24 hour graphs	Yes, displays a 1, 3, 6, or 12 hour glucose graph	Yes, 3 and 24 hour graphs	5 TRU™ Directional Glucose Arrows indicating rate and direction of change	
Displays Rate of Change	Yes	Yes, arrows indicate steady, slow/medium/fast rise or fall	Yes		Yes
Review glucose data?	Yes, last 24 hours	Yes, last 24 hours	Yes, last 24 hours	Yes, last 24 hours	Accessible Data Base in Network System
Capture events	Yes, user can enter insulin, carbs, BGs, and exercise events	Yes, user can enter insulin, carbs, BGs, exercise, and health events			
Alarms, vibrates, or both	Vibrate, escalating alarm, or both	Alarm or Vibrate, vibrate for low first, then alarm	Vibrate, escalating alarm, or both	Alarm or vibrate	
Waterproof Transmitter	Yes, hot water not suggested	Yes, up to 3 ft for 30 min	Yes, hot water not suggested	Yes, up to 3 ft for 30 min	
Transmitter Batteries	Rechargeable, 14 days or more use per change, 1 year expected life, additional transmitter and charger $649	life uknown, non-replaceable, additional transmitter $250	9 months, additional transmitter $500	watch battery, replace monthly	
Monitor Batteries	1 AAA	rechargeable, every 5 days for 3 hours	1 AAA	2 AAA Alkaline Batteries	
Range	6 feet	5 feet	6 feet	10 feet	
Snooze Alarm	Yes, High snooze can be set from 5 min to 3 hrs, Low snooze between 5 minutes and 1 hour	Yes	Yes, both high and low alarms settings differ	Yes, 1 hour silence	
BG Monitor	Any	Any	Any	Built in Freestyle Monitor	
Computer Software	Medtronic CareLink Personal	DexCom DM Data Manager 3	Medtronic CareLink Online	Precision Link Diabetes Data Management Software	
Upgrade program	Yes, call 1-800-Minimed for info http://www.cozmore.com/	Yes, $150 upgrade price	Medtronic Path way Program		
Warranty	1 year on monitor, 6 months on transmitter	12 months for receiver and transmitter	6 months on transmitter, 4 years on pump		
Money-back guarantee	30 day, not for sensors	30 day, not for sensors			

Table 3: Overview on current continuous glucose meters currently available on the market, sorted by supplier companies.

- **Accuracy of the Guardian CGM readings [3]**

The performance of the Guardian RT in adults was evaluated in a clinical study. Three Guardian RT results were compared to plasma glucose values from a reference method, the YSI[1] 2300 STAT Plus™ glucose analyzer (referred to as YSI). Sixteen subjects with Type I diabetes participated in a single-site in-clinic study. Subjects ranged in age from 18 to 65 years old. Each subject wore two Guardian RT systems simultaneously. One Guardian system was calibrated an average of 3.5 times per day, and the other was calibrated approximately five times per day using the Paradigm Link blood glucose meter. YSI measurements were taken every 30 minutes. In this study, YSI measurements (taken every half hour) were paired with the corresponding Guardian RT reading (taken every five minutes). Pairing was done by selecting the Guardian RT value closest in time to the YSI test result. Agreement was analyzed by comparing paired glucose measurements. The accuracy of the Guardian RT was also evaluated by calculating the percentage of Guardian RT readings within 20 percent and within 30 percent of the YSI reading (or within 1.1 mmol/L (20 mg/dL) in the low glucose range). Results are shown in Table 4.

Plasma Glucose Range (mg/dL)	Plasma Glucose Range (mmol/L)	Number of Paired Readings	Percent Within 20%	Percent Within 30%
Overall		3941	62%	79%
40-80*	2.2-4.4	356	68%	68%
>80-120	>4.4-6.7	769	60%	77%
>120-240	>6.7-13.3	2362	62%	81%
>240	>13.3	454	61%	82%
(*)a. For the Low glucose range, 2.2-4.4 mmol/L (40-80 mg/dL), the value shown is the percent within 1.1 mmol/L (20 mg/dL).				

Table 4: Percentage of Guardian RT Results Falling Within 20 and 30 Percent of the Paired YSI Results, at Various Glucose Concentrations.

A correlation plot of Guardian RT readings versus readings from the reference method, the YSI 2300 Glucose Analyzer is shown in the plot of Figure 1. It is overlaid with the Clarke Error Grid.

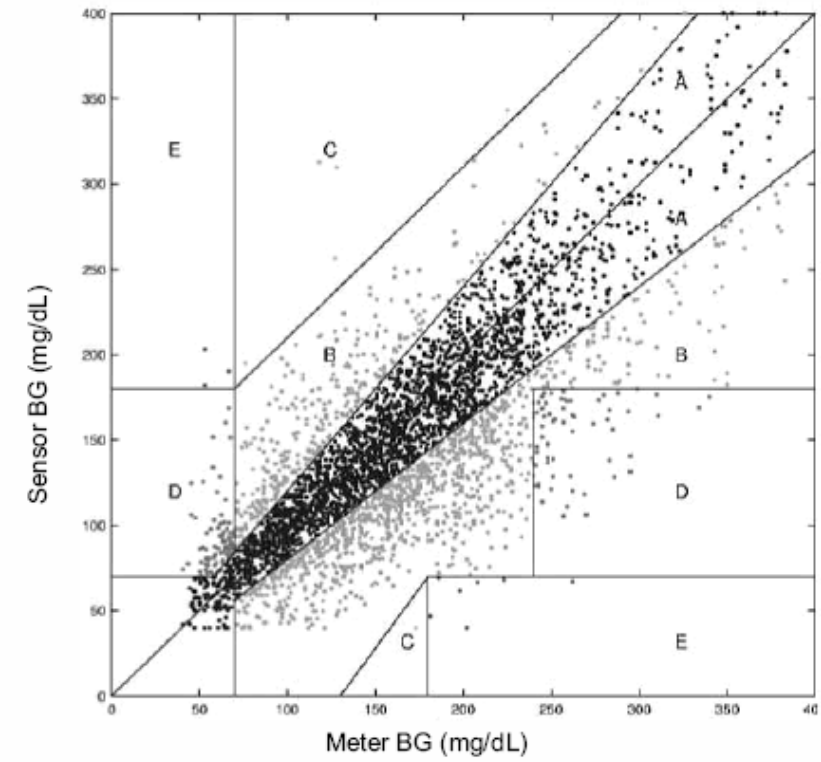

Figure 1: Clarke Error Grid, Guardian RT Results Compared to YSI Results

[1] Yellow Springs Instrument STAT Plus™ Glucose Analyzer

The percent of Guardian RT readings in the previous graph are presented in Table 5 according to the percentage of points falling within each zone (A-E). Results are further broken down (stratified) according to the range of glucose concentrations.

Glucose Range (mg/dL)	Number and (%) of Data Points Evaluated	A + B	A	B	C	D	E
40-80	356 (9)	271 (76.1)	214 (60.1)	57 (16.0)	2 (0.6)	80 (22.5)	3 (0.8)
81-120	769 (20)	768 (99.9)	463 (60.2)	305 (39.7)	1 (0.1)	N/A*	N/A
121-240	2362 (60)	2352 (99.6)	1476 (62.5)	876 (37.1)	4 (0.2)	N/A	6 (0.2)
>240	454 (11)	394 (86.8)	277 (61.0)	117 (25.8)	N/A	59 (13.0)	1 (0.2)
Overall	3941 (100)	3785 (96.0)	2430 (61.7)	1355 (34.4)	7 (0.2)	139 (3.5)	10 (0.2)
(*)a. N/A means that the Clarke Error Grid does not consider the possibility of these zones in that concentration range.							

Table 5: Clarke Error Grid Analysis, Stratified by YSI Glucose Concentrations.

- **Accuracy of the Dexcom SEVEN Plus CGM [4]**

Agreement between the SEVEN PLUS and glucose levels is characterized using paired SEVEN PLUS and YSI results. The SEVEN PLUS and YSI readings were compared by pairing the YSI blood glucose reading to a SEVEN PLUS glucose reading that occurred approximately 5 minutes after the YSI reading was collected. The agreement of the SEVEN PLUS to blood glucose levels was assessed by calculating the percentage of SEVEN PLUS readings that were within 20%, 30%, and greater than 40% of the YSI readings. For readings less than or equal to 80 mg/dL the difference in mg/dL between the two glucose readings was calculated. For readings greater than 80 mg/dL the percent difference (%) from the YSI reading was calculated. The percentages of total readings within 20 mg/dL or 20%, 30 mg/dL or 30%, or greater than 40 mg/dL or 40% were then calculated. The total number of data pairs considered in this analysis was 1,827. Results are shown in Table 6.

YSI Readings (mg/dL)	Number of Paired Readings	% of SEVEN PLUS Readings Within 20%*	% of SEVEN PLUS Readings Within 30%*	% of SEVEN PLUS Readings Greater than 40%* of YSI
40-400	1827	76%	90%	5%
40-80	277	73%	87%	6%
81-180	801	74%	89%	5%
181-300	563	81%	93%	3%
301-400	186	75%	95%	2%
(*) For the 40-80 mg/dL range the absolute difference is presented as the difference in mg/dL between the SEVEN PLUS and YSI, rather than the percent.				

Table 6: Percentage of SEVEN PLUS Results Falling Within 20, 30, and Greater Than 40 Percent of the Paired YSI Results, at Various Glucose Concentrations.

Accuracy between matched pairs was also estimated by calculating the percent difference between the SEVEN PLUS reading and the YSI reading. The SEVEN PLUS and YSI readings were compared by pairing the SEVEN PLUS reading that fell approximately 5 minutes after the YSI reading was collected. For example, if the YSI reading is 100 mg/dL and the SEVEN PLUS reading is 90 mg/dL, a 10% difference between the SEVEN PLUS and the YSI Laboratory machine is reported. The mean

percent difference is the average of all of the positive and negative percent differences between the two devices compared and, therefore, tells you if the SEVEN PLUS on average reads higher or lower than the YSI at each glucose range. Another estimate used to tell you the accuracy of the SEVEN PLUS is the absolute percent difference. The absolute percent difference tells you the overall percent difference or "distance" between the SEVEN PLUS and YSI readings, but does not tell you if the SEVEN PLUS is reading on average higher or lower than the YSI laboratory standard. The mean absolute percent difference is the average "distance" (regardless if positive or negative) between SEVEN PLUS readings and YSI readings. These accuracy measures are summarized in Table 7 below and are based on 1,827 paired glucose measurements.

Glucose Range (mg/dL)	Number of Paired Readings	Mean Percent Difference	Median Percent Difference	Mean Absolute Percent Difference	Median Absolute Percent Difference
Overall (40-400 mg/dL)	1827	-1%	-3%	16%	13%
40-80	277	13%	12%	25%	20%
81-180	801	-1%	-2%	15%	13%
181-300	563	-6%	-7%	13%	12%
301-400	186	-9%	-9%	13%	10%

Table 7: SEVEN PLUS and YSI Blood Glucose Accuracy by Glucose Concentration.

The SEVEN PLUS, on average, reads 13% higher than the YSI at glucose levels of 40-80 mg/dL and reads 9% lower, on average, than the YSI at glucose concentrations of 301-400 mg/dL (Mean Percent Difference). The SEVEN PLUS reads, on average, 25% different than the YSI at glucose levels of 40-80 mg/dL and, on average, 13% different than the YSI readings at glucose levels of 301-400 mg/dL (Mean Absolute Percent Difference). The Median Percent Difference shows that 50% of the time the SEVEN PLUS reads approximately 3% less than the YSI System and the Median Absolute Difference shows that 50% of the time the SEVEN PLUS reads about 13% different then YSI blood glucose readings taken within 5 minutes.

The Clarke Error Grid was used to determine if SEVEN PLUS results are clinically accurate.

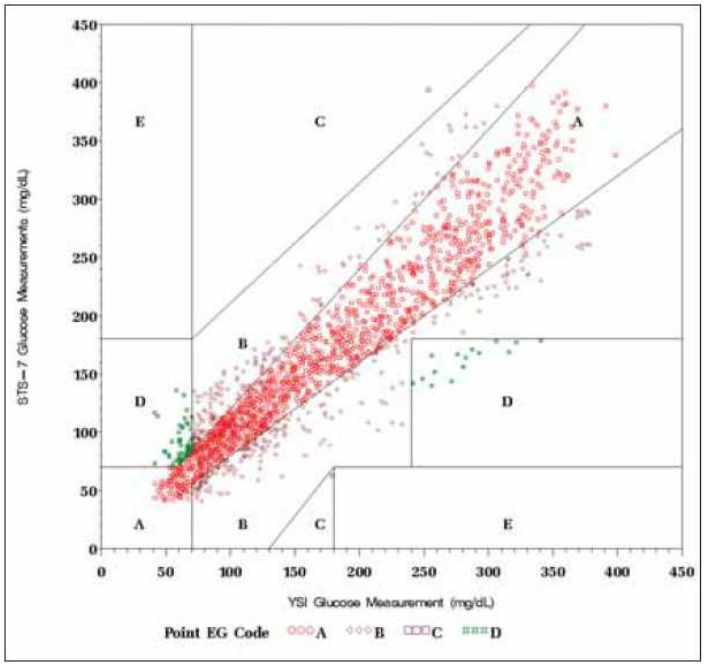

Figure 2: Clarke Error Grid, SEVEN PLUS results compared to YSI results.

The Clarke Error Grid zones are labelled on a correlation plot in Figure 2. Each YSI result (on the horizontal axis) is matched up with its corresponding SEVEN PLUS result (on the vertical axis). A point is recorded where the two readings intersect. These results are based on 1,827 paired data points recorded. The percentages of SEVEN PLUS results in the above graph are presented in Table 8 according to the percentage of points falling within each zone (A-E). Results are further broken down (stratified) according to the range of glucose concentration.

Glucose Range (mg/dL)	Total YSI – SEVEN PLUS Pairs	A %	B %	C %	D %	E %
40-400	**1,827**	**73%**	**23%**	**0%**	**4%**	**0%**
40-80	277	57%	22%	0%	21%	0%
81-180	801	73%	27%	0%	N/A*	N/A*
181-300	563	81%	17%	0%	2%	0%
301-400	186	75%	23%	N/A*	2%	0%
* N/A means that the Clarke Error Grid does not consider the possibility of these zones in that glucose range.						

Table 8: Clarke Error Grid Analysis, stratified by YSI glucose concentrations.

- **Accuracy of the FreeStyle Navigator CGM [5]**

Performance of the FreeStyle Navigator® Continuous Glucose Monitoring System was evaluated in a controlled clinical study. The study was conducted in 3 centers and included a total of 58 subjects with diabetes. Each subject wore two FreeStyle Navigator Sensors over a 5-day period. The subjects wore one sensor on the back of the upper arm and one on their abdomen. The FreeStyle Navigator system was calibrated with capillary fingerstick measurements using the built-in FreeStyle Blood Glucose Meter at approximately 10, 12, 24 and 72 hours after insertion of the sensor.All measurements were performed by a trained clinic study staff or the subject. During the study, subjects came to the clinical center for frequent glucose samples measured once every 15 minutes on the YSI (Yellow Springs Instrument) STAT Plus™ Glucose Analyzer. YSI measurements were performed in duplicate on venous whole blood and the FreeStyle measurements were performed in duplicate on capillary blood from the finger. All YSI whole blood measurements were adjusted by applying a +12% correction factor (based on a normal hematocrit value of 45%).

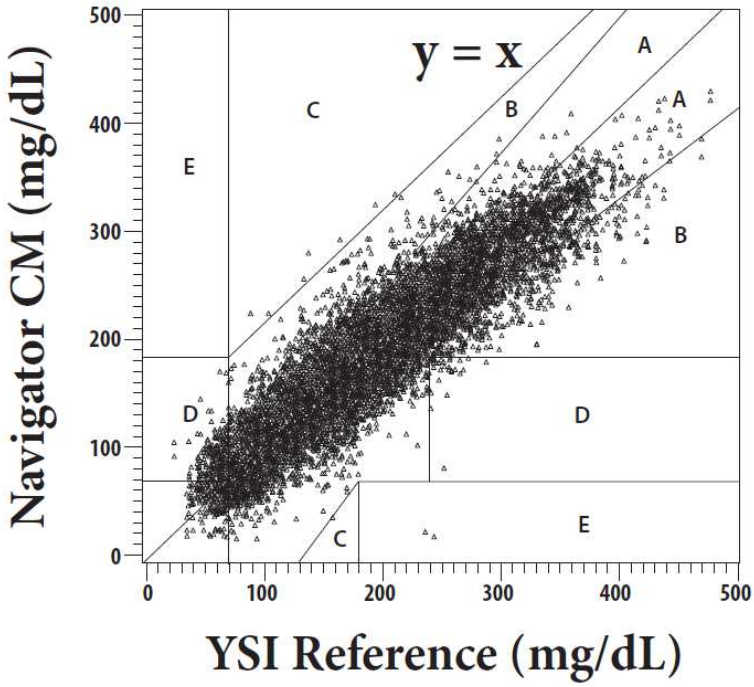

Figure 3: Clarke Error Grid, FreeStyle Navigator results compared to YSI results.

Table 9 below shows the distribution of all the data from the In-Clinic study on the Clarke Error Grid. Accuracy was assessed by comparing the differences between the FreeStyle Navigator system and

the YSI laboratory reference. The Clarke Error Grid Analysis evaluates the clinical relevance of the differences by dividing a correlation plot (Figure 3) into five zones as described in Table 9. The YSI results and the corresponding glucose results from the FreeStyle Navigator system together (called a 'data pair' or 'matched data points') determine what zone of the error grid the results fall into. Table 9 also shows that glucose data measured by FreeStyle Navigator system on the arm and on the abdomen have similar distribution on the error grid. This demonstrates that there is no difference in the performance of the system when worn on the abdomen or on the back of the upper arm.

Zone in the Clarke Error Grid	N (pairs of data)	Percentage in the different zones (%)	Sensor Insertion Site	
			Abdomen %	Arm %
A	16627	81.7	81.5	81.8
B	3398	16.7	16.8	16.6
C	19	0.1	0.1	0.1
D	316	1.6	1.6	1.5
E	2	0.0	0.0	0.0
Total	20362	There is no difference between the performance of the system on the arm and the performance of the system on the abdomen.		

Table 9: Clarke Error Grid Analysis. Continuous glucose results from FreeStyle Navigator system (mg/dL) vs. the YSI (mg/dL).

Table 10 is a summary of the statistics that describe how well data from the FreeStyle Navigator system correlates to the results from the reference method. Glucose results from the FreeStyle Navigator system and the corresponding results from the YSI (a total 20362 pairs of data points) in the In-Clinic study were used to determine the correlation.

Slope	0.92
Intercept	14.3 mg/dL
Correlation Coefficient (r)	0.93
N	20362
Range	25 – 533 mg/dL
Overall mean bias	+0.8 mg/dL

Table 10: Regression Analysis. FreeStyle Navigator System (mg/dL) vs the YSI (mg/dL)

Table 11 displays the distribution of all the data from the In-Clinic study on the Clarke Error Grid. It breaks the data set into smaller groups based on the glucose value reported by the YSI. For each of these smaller groups, the table shows what percentage of data fall into different zones of the grid.

Reference Glucose Level (mg/dL)	Number of Paired Readings	A and B (%)	A (%)	B (%)	C (%)	D (%)	E (%)
20-40	22	54.5	54.5	N/A*	N/A*	45.5	0.0
41-80	1295	77.7	55.2	22.5	0.0	22.3	0.0
81-120	3820	99.9	69.5	30.4	0.1	N/A*	N/A*
121-240	11430	99.9	85.4	14.4	0.1	N/A*	0.0
241+	3795	99.5	91.7	7.8	0.0	0.4	0.1
Overall	20362	98.3	81.7	16.7	0.1	1.6	0.0

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

Table 11: Accuracy performance at different glucose levels using the Clarke Error Grid Analysis.

Table 12 displays the same data as in Table 11 on the Continuous Glucose-Error Grid. This is a modified error grid that is designed to evaluate the clinical accuracy of continuous glucose monitoring systems based on both glucose data points in time and the rate of change of glucose.

Zone	YSI ≤ 70 mg/dL		70 mg/dL < YSI ≤180 mg/dL		YSI > 180 mg/dL		All	
	N	%	N	%	N	%	N	%
Accurate Readings	369	59.5	10407	98.9	8364	98.6	19140	97.5
Benign Errors	5	0.8	99	0.9	74	0.9	178	0.9
Erroneous Readings	246	39.7	22	0.2	41	0.5	309	1.6
ALL	620	100.0	10528	100.0	8479	100.0	19627	100.0

Table 12: Accuracy performance at different glucose levels using the Continuous Glucose Error Grid Analysis.

The state of the art continuous glucose sensors are all based on the glucose oxidase principle with an electrochemical detection. They are applied subcutaneously via a cannula of 5 to 14 mm length in a semi-invasive manner. The sensor unit is separated from the monitor and transmits data via wire or wirelessly, depending on the sensor type. Whether the accuracy of the CGM sensors as specified above will fulfil the ISO 15197 standard is not clear, although the listed sensors all have FDA approval.

The international standards organization (ISO) established a standard for evaluating the accuracy of spot measuring blood glucose meters, called **ISO 15197**. According to this standard it should hold:

- 95% of all measured values should fall within +/- 20% error above or equal to 75 mg/dL
- 95% of all measured values should fall within +/- 15 mg/dL below 75 mg/dL

The standard also allows manufacturers of glucose sensors to report the percentage of the values that fall within 15%, 10% and the American Diabetes Association (ADA)-desirable 5% (expressed in concentration units [mg/dL] for glucose values below 75 mg/dL).

The ADA has suggested that blood glucose meter systems should have an inaccuracy of less than 5% (assumed to be for 95% of values, similar to ISO 15197). According to the data currently available, at 5% inaccuracy, the most accurate meter today has only 63% acceptable values, the average meter has less than 50% [6]. From a thought experiment looking at the effect of inaccuracy of blood glucose measurement on insulin dose and subsequent hypo- and hyperglycemia, it was concluded that systems had to be very accurate, with 99% confidence limits of an inaccuracy of less than 5% [7]. No system today meets that standard. A more detailed overview on the current CGM sensor is also given in [8]. It can therefore be concluded that all approved CGM sensor on the market today are not suitable for automatic glucose control (AGC).

- **Accuracy of the OrSense CGM [9]**

OrSense's CE approved non-invasive glucose monitoring technology was tested to establish accurate performance in multiple settings and over a wide range of patient populations. These trials included over 450 patients, accounting for over 130,000 glucose paired readings. OrSense's devices measured glucose continuously for up to 24 hours. The OrSense system participated in several major studies

covering multiple applications. The first study, a hyperinsulinemic, hypoglycemic blinded study, focused on establishing the system's performance at low glucose levels. The second group of studies included a multi-site study evaluated system performance in hospital intensive care unit and in the operating room.. The third group of studies assessed up to 24 hours of continuous monitoring in a home like setting.

HYPERINSULINEMIC HYPOGLYCEMIC BLINDED STUDY

This trial established product performance in the most challenging condition – hypoglycemia – where accurate performance is essential for ensuring clinically acceptable outcomes. The system displayed high accuracy and an excellent correlation with the reference devices - gold-standard lab measurement systems.

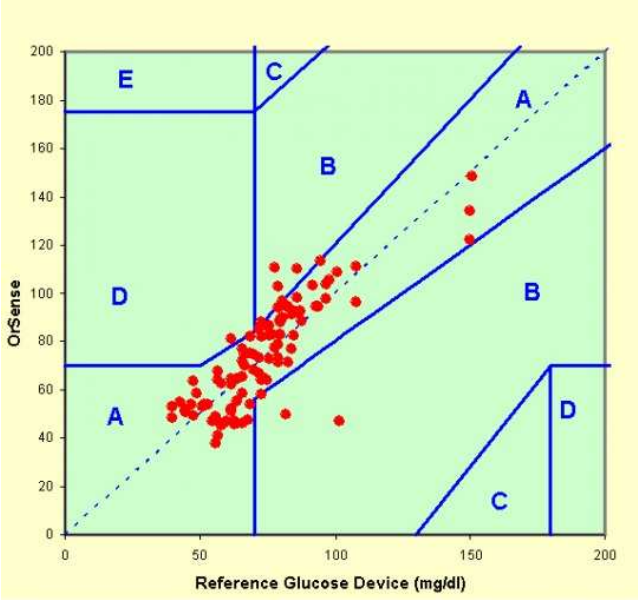

Figure 4: OrSense's NBM100G hypoglycemic blinded study results - Clarke Error Grid Region A:79%, B:20%, C:0%, D:1%, E:0% Median Absolute Error 8mg/Dl (13.2%) Ref: Kononenko et al., 5th Diabetes Technology Meeting, Nov 2005

HOSPITAL INTENSIVE CARE UNIT AND OPERATING ROOM

Tight glycemic control in hospital critical care units has emerged as a key medical need in recent years. OrSense´s non-invasive continuous monitoring solution is optimally suited for this setting. OrSense's NBM systems participated in a multi-site study in both intensive care and operating room units. The system was tested on over 30 diabetic and non diabetic patients for up to 24 hours. In this configuration, OrSense's multi-parameter system reported in parallel continuous, non-invasive hemoglobin and oxygen saturation readings.

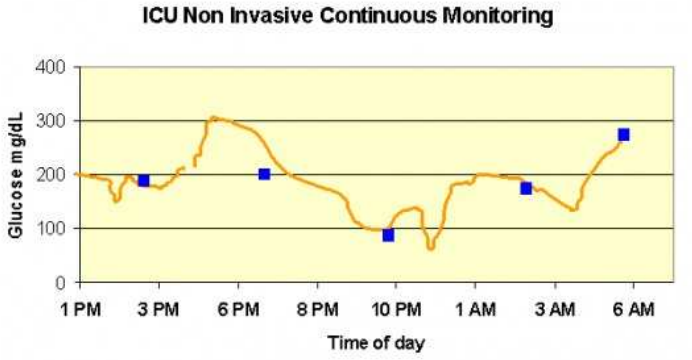

Figure 5: NBM100G continuous monitoring in a hospital's ICU - 18 hours session. Ref: Kononenko et al. Evaluation of a non-invasive blood glucose monitoring device for critically ill patients. Crit Care. 2006; 10:P255

HOME CARE SCENARIO STUDY

This set of trials established accurate product performance in a similar environment to its intended use, i.e. patient's self-monitoring of blood glucose at home. OrSense's device was used continuously, 8-24 hours per day, for up to 10 days per patient, with daily calibration. Trials were performed at the Sansum Medical Center, Santa Barbara, California and at the Sheba Medical Center – Center of Advanced Technology – Ramat Gan, Israel.

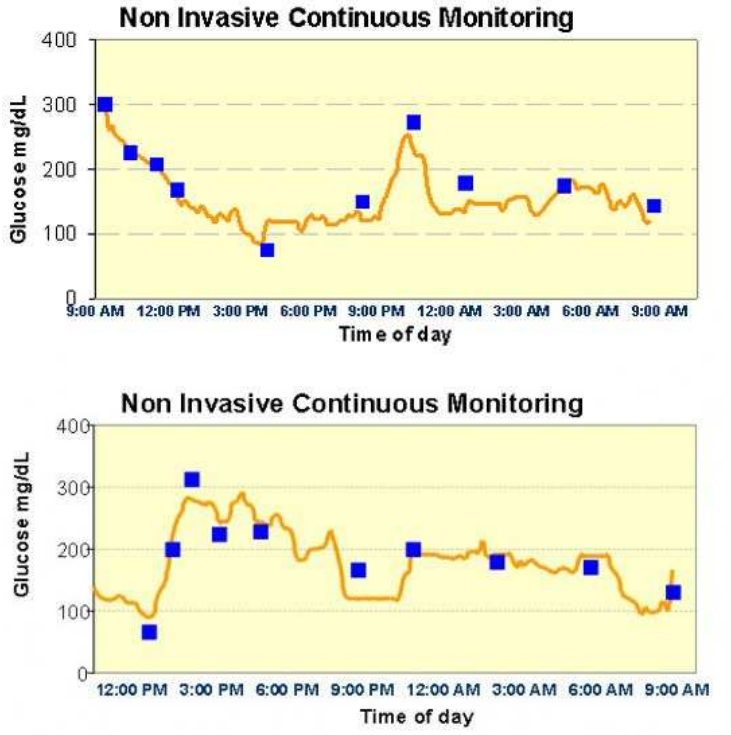

Figure 6: Continuous monitoring (yellow line) and spot reference data (blue squares) plotted against time for DM1 subjects (F, 21) & (F,24). Ref: (1) Amir et al. Continuous Non Invasive Glucose Monitoring Technology Based on "Occlusion Spectroscopy" Journal of Diabetes Science & Technology July 2007 Ref: (2) Zisser et. al. 7th Diabetes Technology Meeting Nov 2007

4. Insulin pumps

The following chapter gives an overview on the approved insulin pumps available on the market. This includes a description of the device and its main features and properties. The below mentioned suppliers are also considered to be the main candidates for being involved within REACTION, concerning automatic glucose control.

4.1 Accu-Chek Spirit by Disetronic (Roche)

Roche Diagnostics launched the Accu-Chek® Spirit insulin pump system in October, 2006. Roche acquired the durable Disetronic pump line in 2003 and then redesigned the pump and added additional features. The new system includes an insulin pump, a blood glucose monitor, and a PDA with bolus calculator software. The Accu-Chek system has everything needed for monitoring, analysis and insulin delivery as well as a choice of features that are important to people considering insulin pump therapy.

Figure 7: Accu-Chek Spirit by Disetronic.

The Accu-Chek® Spirit insulin pump system includes:

- an Accu-Chek® Spirit insulin pump
- the choice of an Accu-Chek® Aviva, Accu-Chek® Compact Plus or Accu-Chek® Active meter
- a free Palm PDA or a Treo smart phone for an additional charge to perform bolus calculations and enable easy carbohydrate counting
- Accu-Chek Pocket Compass software with bolus calculation
- Choice of carrying case

Features such as three operating menus, four bolus options and five basal rate profiles make insulin pump therapy more flexible and convenient. The pump has side-mounted tactile buttons for no-look delivery, together with a bolus calculator on a separate PDA device. This allows the user to calculate a bolus discretely and program their pump for insulin delivery without ever having to remove their insulin pump from their pocket, purse, or bra. The screen can be quickly aligned to a vertical or horizontal display so the user can wear the pump the way they want.

Spirit® features include alternate basals, extended boluses, two easy methods for precise bolus delivery, vibration and audio modes, precise measurement of residual insulin, a continuous clear display, backlighting, lots of additional memory for basals and boluses, waterproof design, etc. A single AA alkaline or rechargeable battery lasts around 4 weeks. Basal insulin delivery occurs every 3 minutes, regardless of basal rate.

The Spirit® sports a 315 unit cartridge. The Spirit® has a bidirectional infrared (IR) port which can communicate directly with IR ports common to today's computers. Data can also be downloaded to a PC, and basal rate profiles can be uploaded from a PC to the pump. The Spirit® also has a child-block feature that is helpful for younger children. When the child lock is activated, the pump can be temporarily reactivated by a parent or school nurse to give a bolus. Afterwards, it will automatically relock itself. For more info, see also [10].

4.2 The OneTouch Ping by Animas

The OneTouch Ping is the newest insulin pump from the Animas Corporation. It is a glucose management system that includes an insulin pump and a glucose meter-remote. The two devices communicate wirelessly with each other. Users can calculate insulin doses and deliver boluses through the glucose meter-remote or manually on the pump.

Figure 8: OneTouch Ping by Animas.

OneTouch Ping is a collaborative effort between two of the companies in Johnson & Johnson's Diabetes Care Group: Animas, which manufactures insulin pumps, and LifeScan, which makes the OneTouch brand of glucose meters and test strips.

Pump's features:

- flat panel, self-illuminating, color screen
- available in 5 colors
- the pump can be clipped to a belt, tucked in a pocket or secured under clothing
- waterproof in up to 12 feet of water for 24 hours
- lowest basal increments (0.025 u/hr) and lowest bolus increments (0.05 u) currently available on an insulin pump
- uses OneTouch Ultra test strips
- works with ezManager® MAX Diabetes Management Software and is compatible with the OneTouch® Diabetes Management Software
- works with Mac OSX and PCs, including Vista
- built-in 500-item CalorieKing® food database
- all pump accessories, except the leather case, for the 2020 will fit the OneTouch Ping

Upgrading

An old Animas pump can be upgraded to a Ping through their ezAccess Program. Different prices have to be paid, depending on the old pump:

Animas 2020 - $299
Animas 1250 - $399
Animas 1200 - $599

Cons

- Extra device compared to Deltec, but Deltec system is larger.
- Pump is larger than small meters

Bottom Line

This is a slick system for pump wearers who want to give boluses remotely and discreetly. It brings pump wearers closer to insuring that all boluses are read into pump data.

Model	OneTouch Ping
Dimensions [mm]	50.8 x 82.55 x 21.59
Volume	5.525 ci 90.54 cc
Weight [oz]	3.9 oz
Reservoir Size	200 plastic
Connection	Luer Lock
Screen Size	992 sq mm color screen
Colors	Blue, Silver, Black, Pink, Green
Basal Increment	0.025u
Total Basals	12/day
Basal Profiles	4
Basal Interval	30 min
Basal Delivery	Varies, 0.2 u/hr every 3 minutes
Temp Basal	90% to +200% in increments of 10% for 0.5 to 24 hours (30 min increments)
Bolus Increments	0.05 Visual or 0.1, 1.0 or 5.0 audio
Carbohydrate and Correction Factors	Yes, carbohydrate and blood glucose values can be entered into the pump or meter-remote
Bolus Type	Units or Carbs: standard, extended or combination
1u bolus duration	1 or 3 sec
Battery	Pump uses 1 AA lithium or AA alkaline
Battery Life	4-6 weeks with lithium, 2-4 weeks with alkaline
Motor	DC
Memory	Non-volatile: • 500 boluses • 270 basals • 120 daily totals • 60 alarms • 60 primes • 900 blood glucose levels
Software Download	ezManager® Max downloads in 3 minutes with dongle and software that are available at Animas
Waterproof	12 ft for 24 hours
Guarantee	4 years

See information for the older Animas pumps. For more info, see also [11].

4.3 Medtronic 522/722

Medtronic MiniMed's current Paradigm 522 and 722 or x22 insulin pumps are nearly identical to the x15 pumps except for the addition of a graphical readout for the Paradigm RT continuous monitor.

Figure 9: Medtronic 522/722.

Continuous Monitor

Medtronic's Paradigm RT system consists of a plastic base with a sensor wire that is inserted using a 25 gauge needle through the skin,a radio transmitter attached to the skin in a separate location and then connected to the sensor base via an external wire, and the pump screen that displays the readings. In the current setup, the sensor is attached to the skin and a radio transmitter that is 1 3/8 inches in diameter is attached nearby. The transmitter is now built by hand until a new and smaller transmitter and automated manufacturing facilities receive FDA approval. The next version of the transmitter will attach directly on top of the sensor and be closer in size to the current small Dexcom sensor/transmitter.

The ability to display readings from a continuous monitor on a pump rather than having to carry a second device is attractive. One disadvantage of combining devices is that the screen size on the current pump is small compared to systems like the Dexcom STS and the Abbott Navigator which have larger and crisper displays. Another disadvantage is that the RT system is reported by clinicians who have patients on all three con mon systems (Paradigm RT, Dexcom STS, and the not yet released Abbott Navigator) to be the least accurate. Readings can be 30, 50, or more mg/dl high or low, so when treatment with insulin or carbs appears to be needed based on the RT readout, the RT's reading must be verified by a fingerstick before any action is taken. Read the study comparing two different continuous monitors with an Ultra fingerstick meter.

Test results are transferred from the sensor/transmitter to the pump by radiowaves. The radio transmission has a short range. This does not create problems on airplane flights, but cell phone and microwave interference may occur on occasion. When infrequent interference occurs, readings will not be visible on the pump, but the Medtronic transmitter remembers the last 40 minutes of readings and the receiver catches up once it is back in range. This may occur in other situations, such as when showering. Insurance coverage for this $1000 device plus $350 a month cost for sensors has been very limited and this has kept demand low to this point.

It is especially important to use an accurate glucose meter to calibrate the RT continuous monitor. Among more accurate meters are the Abbott meters that use Freestyle strips, Lifescan meters using Ultra strips, and less expensive Wave 1 and Wave 2 meters by Agamatrix.

Pump

The 522 and 722 pumps differ from each other only in size of the reservoirs (176 versus 300 units) along with a smaller overall case size for the 522. Power is provided by a single AAA battery. Basal rates can be adjusted in 0.05 unit increments, while bolus increments are still in 0.1 unit steps, compared to 0.05 in the Animas IR1250, the Cozmo, and the OmniPod pumps.

Users can set carb and correction factors with different ratios at different times of day. Backlighting is available as is a lockout feature for children. Reminders can be set for taking boluses at specific times

each day, to alarm a half hour to five hours after boluses or after low or high blood sugars, and to replace the infusion set in three or four days at a particular time of day.

Currently, four infusion sets (Silhouette, Sof-set, Quick-set, and 30 degree bent metal needle) are available from Medtronic for the Paradigm's proprietary connection. In addition a Luer lock connection is available from SpectRX called Simple Choice that will work with the Paradigm. To use standard Luer lock infusion sets on a Paradigm, visit the Applied Diabetes Research site to order their special reservoir for the Paradigm.

The pump screen on the x22 times out quickly when a bolus is interrupted by a phone call or other life event, or when loading and priming the pump. Unlike other pumps where the screen might time out but bring you right back to the part of the load process you were involved in, when the x22 pump's screen goes off, the user has to retrace their steps to where they were.

Users can set the duration of insulin action to values between 2 and 8 hours in one hour increments, compared to 15 or 30 minute increments available in other pumps. The default value of 6 hours is very reasonable on this pump. See setting the duration of insulin action for more detailed information on this important setting.

Figure 10: Logic and Link Meter.

The x22 pumps continue to use the Link meter which allows direct entry of glucose readings into the pump, although the manufacturer, Becton Dickinson chose to discontinue it's Logic and Link meters and strips in September, 2006 due to lack of profitability. Complaints about the lack of accuracy of this meter have been received from users. Pump data can be downloaded from a PC to the Medtronic CareLink® Therapy Management website or to a PC using a new Medtronic cable. A Windows computer with Internet Explorer is required.

Similar to the cost for previous software upgrades, the cost to upgrade from the older x15 pump to a new x22 pump costs $799. A $400 rebate is received once the current insulin pump is returned to Medtronic in the postage-paid envelope that is provided.

Medtronic 522 and 722 Insulin Pumps	
Pros	**Cons**
Oldest pump company Simple operation Good statistics Small remote (additional cost) for discrete boluses Easy clip attachment for wear on belt, etc.	Oldest pump company Slow bolus delivery Bolus Wizard may on occasion recommend excess boluses Proprietary infusion sets Volatile memory may allow basal rates and time to be lost Reservoir fill icon is inexact, hard to tell how many units are left Basal delivery stops when reservoir is empty Upgrades cost $400
Verdict: A solid pump with simple operation. Avoid the continuous monitor until accuracy improves. Before bolusing, monitor Bolus Wizard recommendations by checking active insulin.	

Table 13: Pros and Cons of the Medtronic 522 and 722 Insulin Pumps.

Programming Issues:

Boluses recommended by the pump may occasionally be excessive

Some pumps, such as the Deltec Cozmo, balance any active bolus insulin against both carb and correction boluses. In contrast, the Paradigm series pumps (x11 through x22), as well as the current Omnipod pump, ignore active insulin or Bolus on Board for all carb boluses. In some situations, such as when carb boluses are given within 2 or 3 hours of each other, as occurs in children and adults who like to snack, the Paradigm pump may recommend carb boluses that are too large and cause unnecessary hypoglycemia.

For example, a pumper has given an earlier bolus that was too large and happens to have 5 units of active insulin on board a couple of hours after their last bolus. If their blood sugar is 108 mg/dl (6 mmol) and they eat a snack that requires 3 units to cover it, the Paradigm and Omnipod pumps will recommend giving 3 additional units. In the same situation, the Cozmo pump will recommend that no bolus be given or that some additional free carbs may be needed to offset the remaining bolus insulin. The Animas pump, meanwhile, will discount for active bolus insulin if the person's blood sugar is below their selected target, but give the full calculated carb bolus of 3 units if their blood sugar is above target.

A Paradigm user can double check the recommended bolus if they hit the down arrow three times to scroll down on the screen where the bolus recommendation is given. They will see entries for the meal bolus, correction bolus, and active insulin. They can then decide whether to subtract the active insulin amount from both the carb and correction bolus amounts to reduce the risk of a low blood sugar.

For pumpers who have frequent highs because their basal rates and bolus doses are too low, some excess bolus insulin may not be much of a problem. However, in situations like that discussed above, a pumper might go low if they follow the pump's recommended bolus dose. Some pumpers who have gone low in this situation have mistakenly blamed the lows caused when the Paradigm does not account for all of their active insulin as being caused by excess basal insulin and have unnecessarily lowered their daytime basal rates to solve the problem.

Medtronic administration and engineering personnel are aware of this situation. Whether they will remedy this in software upgrades is unknown. The cost of recalling pumps, the time required to retrain users, and an adamant demand by some pumpers that this approach not be changed may be causing a lack of action. Omnipod administrators discussed the issue prior to release of the Omnipod and decided upon a Medtronic approach to their bolus recommendations. They are aware of the pitfalls and are currently considering whether to change bolus recommendations in their next generation Omnipod.

Saving of Basal Rates

Software and hardware improvements to the 511 pump to prevent loss of basal rates have resulted in the "save settings" feature on the x15 and x22 series. This allows the current pump settings to be saved for recovery if basal rates are inadvertently lost. The battery can now be removed for at least 30 to 40 minutes before the time setting is lost. Pump settings and basal rates can also be saved to the pump or to a PC. Other pumps so rarely experience this problem that they do not require this type of backup, but all pump wearers should keep a written record of current settings in case disaster strikes.

Do Not "Clear Pump"

In the utilities section, one option near the bottom is "clear pump". It means exactly that---all basals and history are erased when this option is selected and agreed to. It was placed into the pump at the request of sales reps and pump trainers who use pumps to show various scenarios which they then clear. But it can create problems for the unaware user.

The risk of this is low, but a teen may decide to clear their pump as a way to erase the size or incompleteness of their boluses. The pump may also be cleared if a user mistakenly thinks it is a good way to silence an alarm, or if someone accidentally presses the wrong sequence of buttons because they are hypoglycemic or distracted. Once the pump has been cleared, an alarm will warn that the clock setting has been lost, but no warning is given that the basal rates have also been erased.

Hardware Concerns with O-ring Leaks

O-ring leaks may rarely occur inside a reservoir. The reservoir above came from a 64 year old woman who arrived at a clinic one morning with a 364 mg/dl blood sugar. Usually in excellent control (70 to 120 mg/dl before meals), her glucose had been normal the night before. She said she had experienced several unexplained high readings in the previous weeks. The week before she had experienced nausea and positive ketones in the urine, with a blood sugar over 450.

Figure 11: Reservoir with O-rings.

The source for her problem turned out to be leaky O-rings. When a single reservoir in a box leaks like this the entire box of reservoirs should be replaced. Reservoirs are manufactured from molds. These molds are routinely replaced due to wear but may occasionally be used too long. If one reservoir leaks, others with the same lot number will also be likely to leak. The woman reports that her unexplained highs disappeared once she started a new lot of reservoirs.

Dislodged Reservoir

One design issue in the Paradigm pump involves the cap on the infusion set that connects it to the reservoir and also holds the reservoir in place. This cap with coarse threading is locked in place with a half turn and is kept in place by only a small indentation in the plastic cap near the end of the threading.

The Paradigm reservoir has nothing to hold it in place, so it floats on top of the advancing driver that normally pushes the plunger inside the reservoir forward. If the cap is noticed to be loose and then retightened with a half turn, most of the insulin that was not delivered during the time the cap was loose will suddenly be delivered. Unlike small amounts of insulin that might be delivered if a Luer lock connection is retightened, this half turn can deliver doses as large as 15 to 20 units, depending on how long the loose cap went unnoticed. Not realizing that this large bolus has already been delivered, the user may proceed to give an additional correction bolus for the high blood sugar. The two large overlapping boluses could cause a severe low blood sugar.

If a high blood sugar occurs with a loose reservoir cap on a Paradigm pump, never retighten the cap until the infusion line has been disconnected from the infusion site. Children and active adults should not fiddle with this connection. Medtronic suggests that users keep the Paradigm pump in its protective carrying case to avoid hub detachment. An add-on safety lock was designed to prevent dislodgment, but it cannot be used at the same time as the Paradigm belt clip so most users don't use it.

International Standards for Medical Electrical Equipment (IEC 60601-2-24, section 54.101) warns against floating reservoirs in medical devices, saying "means shall be provided to ensure correct clamping and location of a syringe barrel." Keeping the reservoir locked in place prevents it from floating on top of the driver. This standard was developed by experts in the field to avoid unnecessary over-delivery.

For more info, see [12].

4.4 Dana Diabecare II

Sooil has been making insulin pumps for the world market since 1981. Their newest pump, the DANA Diabecare II, received FDA approval in August, 2000, and about a year later began to be distributed in the U.S. The Korean-assembled DANA II is new to the U.S., but Dana has over 40,000 pump wearers worldwide.

The pump is waterproof and sports a Swiss-built DC motor and full-sized 300 unit reservoir. It is the lightest pump available at only 1.8 ounces, with a size 12% smaller than the Paradigm. The menus are icon-driven with a large display screen, although the screen resolution is not great. Power is derived from a single proprietary 3.6V battery which lasts 2 to 3 months.

Residual insulin is displayed on the screen and an alarm sounds when the reservoir gets down to 20 units. Basal rates can be programmed each hour in tenths of a unit increments. Basal delivery occurs every 4 minutes, compared to every 3 minutes for the Animas and Disetronic pumps, and every 5 to 20 minutes (i.e., basal rates of 1.2 to 0.3 u/hr) for MiniMed users

The DANA II offers some unique features such as preset meal boluses. With this feature, standard boluses can be set for breakfast, lunch, or dinner to allow quick coverage of standard meals, although true carb counters may frown on this simplistic approach. The pump also has a Guided Management approach where a pump lockout can be set for children, or a 30 minute melody reminder can be set following boluses.

The DANA II pump and supplies are priced competitively at 20% less than other pumps and supplies in the US market. This is especially helpful for those who pay out of pocket for their pump. One disadvantage is that the pump has a proprietary reverse luer lock connection between infusion sets and the hub, so only Dana infusion sets will work with this pump, and procrastinators may want to think twice about this pump if they order supplies at the last minute. Only metal needles are currently available, but Teflon sets are expected to arrive sometime in the summer of 2002.

The small size and lower retail price bring Dana pumps to the attention of many, especially the cost conscious and HMOs who are trying to limit costs. For more info, visit [13].

4.5 Nipro Diabetes Systems

With offices in Miramar, Fla., Nipro Diabetes Systems manufactures the Amigo Insulin Pump in the U.S. Its parent company, Nipro Corporation, is a multi-billion dollar company headquartered in Osaka, Japan that has been a leader in the healthcare field since 1954. Nipro Diabetes Systems provides extensive insulin pump training and education through Certified Diabetes Educators, 24 hours a day. The company is committed to supporting people with diabetes by developing and marketing high-quality, safe and effective products that enhance its customers' lives.

Figure 12: Amigo® Insulin Pump.

Nipro Diabetes Systems introduces its Amigo® Insulin Pump to help keep blood glucose in control for children and adults with types 1 and 2 diabetes. Built for safety, reliability, accuracy and durability, the Amigo Insulin Pump features computerlike help screens for easy programming. Dedicated to supporting the ever-changing treatment of diabetes, the Amigo was designed by people who live with diabetes along with a group of healthcare professionals who specialize in the chronic disease.

Similar to a computer, the Amigo features wizards to walk the wearer through pump programming sequences and on-screen help messages. Other benefits include:

- Offers four basal profiles with up to 48 basal rates in a 24-hour period and a temporary profile that can be set in either units per hour or a percentage of the current basal profile.
- Delivers insulin every three or 15 minutes in as little as five hundredths of a unit.

- Bolus delivery options of Normal, Extended and Layered; and a Direct Bolus for delivering insulin through clothing without looking at the pump.
- Bolus Estimator – Wearers enter information about their current blood glucose and the food they are eating and the Amigo calculates the bolus for food and high blood glucose correction so no manual calculation is needed.
- Housed in a shatter, resistant, waterproof case.
- Syringe cap with 90% infusion-set connector so it lies flatter and has no point stickingout to catch on skin or clothing.
- Safety features – Offers several user-programmed settings that notify users when insulin is low, reminding them when to test blood glucose and when they have exceeded hourly insulin delivery quotas.
- Six fashionable colors.

For more info, visit [14].

4.6 Insulet Omnipod

Figure 13: Insulet Omnipod pump.

Insulet Corporation is a privately-held company that has been in business for since 2000. With the advice of diabetes patients, educators, and physicians, Insulet Corporation has developed a new solution to assist in diabetics efforts to live a healthier life. The OmniPod™ Insulin Management System has been specifically designed to make living with diabetes easier than ever by bringing together the proven healthcare benefits of continuous subcutaneous insulin delivery with FreeStyle® blood glucose monitoring technology in a safe, convenient, and discreet two-part system. This innovative two-part system eliminates the need for daily insulin injections, does not require you to be tethered to a conventional insulin pump via tubing, and makes intensive insulin therapy easier than ever. It also enables you to check your blood glucose level with FreeStyle blood glucose test strips, but without carrying a separate blood glucose meter.

The OmniPod is a small lightweight device that is worn on the skin like an infusion set. It delivers insulin according to pre-programmed instructions transmitted wirelessly from the Personal Diabetes Manager(PDM). The PDM is a wireless, hand-held device that is used to program the OmniPod with customized insulin delivery instructions, monitor the operation of the OmniPod, and check blood glucose levels using FreeStyle blood glucose test strips. There is no tubing connecting the OmniPod to the PDM. The OmniPod is worn comfortably and discreetly beneath the clothing, and the PDM can be carried separately in a backpack, briefcase, or purse. Similar to currently available insulin pumps, the OmniPod Insulin Management System features fully programmable continuous subcutaneous insulin delivery with multiple basal rates and bolus options, suggested bolus calculations, safety checks and alarm features.

The OmniPod Insulin Management System received 510(k) clearance from the FDA on January 3, 2005.

Technical Specifications

Size	OmniPod: 1.6 in. x 2.4 in. x 0.7 in. PDM: 2.5 in. x 4.5 in. x 1.0 in.
Weight	OmniPod: 1.2 oz. (with full reservoir) PDM: 4.4 oz. (with batteries)
Screen Size	PDM: 1.75 in. x 1.75 in.
Integrated Reservoir Size	OmniPod: 200 units (delivers U-100 rapid-acting insulin)
Memory	PDM: 5400 records or 90 days of data
Watertight	Yes, IPX8 rating (8 feet for 30 minutes)
Basal Programs and Segments	7 programs with up to 24 segments each. Programmable in 30 minute increments
Basal Increments and Maximum	0.05 U/hr. increments, up to 30 U/hr.
Temporary Basal Type	Percentage or U/hr.
Temporary Basal Duration	1 to 12 hours, in 30 minute increments
Bolus Increments	0.05, 0.1, 0.5, 1.0 units
Integrated Infusion Set	Each OmniPod features an integrated angled infusion set with automated cannula insertion and no tubing.
Power Source	PDM: 2 Alkaline AAA Batteries (approximately 4 weeks)
Infusion Set	Automated cannula insertion
Other Features	• No tubing • Integrated angled infusion set, inserter and insulin reservoir • Integrated FreeStyle® blood glucose monitoring technology • Test strip port light • Integrated food database with over 1000 common food items • Setup wizard • Suggested bolus calculator • Insulin on board calculation • Adjustable duration of insulin action • Programmable reminders and alerts • Personalized ratios/factors/targets/presets • Adjustable auto off • LCD backlight • Child lock-out feature • 4 year PDM warranty

Table 14: Technical specifications of the OmniPod insulin management system.

For more info, visit [15].

4.7 Solo (Roche)

The SOLO micropump insulin delivery system combines key features of traditional insulin pumps like on-pump bolus buttons and detachability, with a small, slim, tube-free size, thus providing flexibility, discreetness and freedom, all in one little package. The system is made of two key parts that work together wirelessly - the micropump and the remote. The micropump delivers insulin in a personalized way based on your personalized insulin program and keeps your remote updated on its status [16].

Figure 14: Solo insulin pump.

The micropump is worn on your body to deliver the insulin you have programmed and is composed of two parts. The 90-day reusable pump base stores all your pump settings for precise 24-hour basal and bolus delivery, so you can bolus with or without your remote when needed. The SOLO pump base holds the electronics, memory, pump motor, bolus buttons and a buzzer that will let you know if there is a safety issue, so it has the key functions of a traditional insulin pump – just in a smaller package!

The disposable 200 unit insulin reservoir should be replaced every 2 or 3 days. The reservoir is transparent so you can see the integrity of your insulin, if there are any bubbles and how much is left. The reservoir is more sophisticated than the standard insulin cartridge, because it also holds the precision dispensing screw, plunger and a zinc-air mercury-free battery to power your pump base. With our easy filling device, filling the reservoir is a breeze – and you don't have to use an insulin syringe.

SOLO micropump	
Dimensions	2.4 x 1.5 x 0.5 inches (6.1 x 3.8 x 1.3 cm)
Weight with full reservoir	0.85 oz (24 gr)
Pump base	3 month life after initial pairing
Occlusion & other safety alarms	Audible on micropump
On-pump bolus buttons	Can be customized and disabled
Detachable/reattachable	Yes, by disconnecting from cradle
Reservoir	
Reservoir Capacity	200 units of U100 insulin (Min. 70 units)
Reservoir Description	Transparent with volume fill lines
Reservoir Filling Device	No syringe needed
Use Rapid Acting Insulins	Humalog®, NovoLog®/ NovoRapid®, Apidra®
Reservoir Change Frequency	3 days NovoLog®/ NovoRapid® 2 days Humalog®, Apidra® (based on insulin manufacturer labeling)
Cannula cradle infusion set	

Cannula	9 mm, 90°insertion; soft Teflon®
Insertion needle	27 gauge; hidden from view
Automated inserter	Virtually painless, auto-needle retraction
Adhesive	Hypafix®- hypoallergenic, latex-free
Change frequency	2-3 days
Site change reminder	Yes
Allows disconnection	Yes
Remote	
Dimensions	4.2 x 2.2 x 1.0 inches (10.6 x 5.6 x 2.5 cm)
Weight with batteries	5.2 oz (148 gr)
Batteries	2 AA alkaline
Guided procedures	Start-up; reservoir replacement, micropump replacement, priming, Bolus Guide
Safety lock-out	Auto keypad lock
Flexible programming	Reminders and alerts
Remote screen	Large, backlit, color graphics
Status bar and screen	Current updates from micropump
Color panels	Multiple (7) color choices
Remote notifications	User selected –audible, vibrate or both
Communication distance	5 feet (1.5 meters)
Soft keys	User selectable based on frequent use
Basal delivery options	
Basal programs	7 programs; 30 minute segments Unique graphic 24 hour format
Basal increment	0.05 unit per hour
Minimum basal rate	0.10 unit per hour
Maximum basal rate	30 units per hour
Temporary basal options	Percentage or U/hr adjustment up to 24 hours
Bolus delivery options	
Bolus types	Normal, Long, Duo, Correction
2-way bolus	Remote or micropump buttons
Bolus increment	0.05 unit
Minimum bolus	0.10 unit
Maximum bolus	30 units
Bolus on Board (BOB)	Helps prevent insulin stacking; BOB includes carb and correction boluses as long as BG is entered; programmable 2-8 hours
Bolus Guide	Suggests bolus based on carbs, current blood sugar, target blood sugar, boluses on board and personalized settings
Bolus Guide settings ranges	
Insulin Sensitivity Factor (ISF)	10-400 mg/dL per unit of insulin

(also called Correction Factor)	Settings can be done in 30 min segments
Insulin to Carbohydrate Ratio (ITC) (also called Carb Factor)	3-150 grams of carb per unit of insulin Settings can be done in 30 min segments
Blood glucose targets	70-200 mg/dL Settings can be done in 30 min segments

Table 15: Specification of the Solo insulin pump system.

4.8 CeQur

CeQur is dedicated to helping people with type 2 diabetes stay on track and in control of their disease by developing and commercializing advanced insulin delivery systems that can be easily integrated into daily life. CeQur's lead product candidate is a small, wearable insulin delivery device that delivers both basal and bolus doses subcutaneously. Its simple and discrete design enables patients to more easily comply with insulin regimens and experience the benefits of intensive insulin therapy, all while remaining free from the discomfort and inconvenience of multiple daily injections. CeQur, Ltd. was established in January 2008 as a spin-out from Danfoss A/S, a large, global Danish industrial products group that developed the initial concept and early prototypes of the CeQur technology. Once this novel technology was validated in clinical testing, Danfoss recognized the need for new, specialized skills to successfully develop, manufacture and market the product, and established CeQur Ltd. Along with a group of other committed investors, Danfoss remains a significant stakeholder in CeQur. CeQur is headquartered in Montreux, Switzerland, with operations in Nordborg, Denmark and near Boston, Massachusetts.

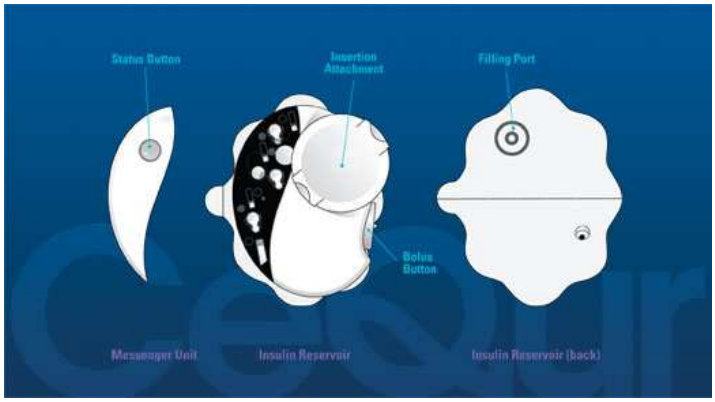

Figure 15: CeQur insulin pump.

The CeQur device, a small discreet, wearable insulin patch infuser, is for the continuous subcutaneous delivery of rapid acting insulin for the management of type 2 Diabetes mellitus. The CeQur insulin delivery device is designed to meet the specific needs of people with type 2 diabetes who could benefit from intensive insulin therapy. Its simple and discrete design may enable patients to more readily experience the benefits of intensive insulin therapy, all while remaining free from multiple daily injections. The CeQur insulin infuser includes a disposable insulin reservoir that attaches to a reusable electronic messenger. The device easily attaches to the patient's abdominal area with a safe and secure adhesive backing. Once in place, insulin is delivered subcutaneously through a fine, soft tube or cannula from the reservoir that is changed by the patient every few days. The CeQur insulin delivery device is designed to use just one type of insulin for both basal and bolus dosing, and will be available in multiple basal rates.

REACTION partners IN-JET and MUG have been in contact with CeQur and they might be a potential candidate for cooperation within REACTION.

4.9 Comparison of pumps

Table 16 gives an overview on the technical data of currently available insulin pumps for comparison [17].

Manufacturer	Animas	Disetronic (Roche)	MiniMed	Insulet	Sooil USA
Model	Ping 	Spirit® 	Paradigm Revel 	OmniPod 	DiabecareIIS 
Dim. [mm]	51 x 77 x 18	80 x 47 x 24	523: 50.8x76.2x20.3 723: 50.8x91.4x20.3	pod: 41x61x18 pda: 66x110x26	46 x 77 x 19
Volume	5.525 ci 90.54 cc			Pod: 2.7 ci PDA: 11.5 ci	4.3 ci 67 cc
Weight [oz]	3.9	2.8, 4.8 with batt full cartridge inf set	523: 3.53 oz 723: 3.81 oz	OP: 1.2 oz (full res.) PDM: 4.0 oz (w/ batteries)	1.9 oz
Reservoir Size	200u plastic	315u	523: 176 u 723: 300 u	200u	300u plastic
Connection	Luer lock	Luer lock	Proprietary	Built-in	Proprietary
Screen Size	992 sq mm			1,848 sq mm on PDA controller	595 sq mm
Colors	blue, silver, black, pink, green	Blue, with 30 pump skins in colors and styles	blue, clear, pink, purple, smoke or customize	white	Black, Gray, Pink, Green, White
Basal Increment	0.025u	0.1u from 0.1 to 25.0 u/hr	0.025 u	0.05 u u/hr, up to 30 u/hr	0.1 u/hr or 0.01 u/hr
Total Basals	12/day	24/day	48/day	48/day	24/day
Basal Profiles	4	5	3	7	1
Basal Interval	30 min	60 min	30 min	3 min	60 min
Basal Delivery	varies, 0.2 u/hr every 3 min	every 3 min	varies, 0.6 u/hr = every 10 min		Every 4 min
Temp Basal	-90% to +200% in increments of 10% for 0.5 to 24 hours (30 min increments)	in 10% increments from 0% to 200%, and 15 min to 24 hr	+/- 0.1 u increment as single basal rate for 0.5 to 24 hrs or as % of current basal	% or u/hr (1-12 hrs, in 30 min increments)	10% increments from 0% to 200% and up to 12 hours
Bolus Increments	0.05 visual or audio, 0.1, 1.0, 5.0 audio	0.1, 0.2, 0.5, 1.0, 2.0	0.1 visual, 0.5 or 1.0 visual or audio, remote	0.05, 0.1, 0.5, 1.0u	0.1, .05, 1.0u

			extra		
Carb and Correction Factors	yes, carb and bg values can be entered into the pump or meter-remote	yes, manual carb, BG from Accu-Chek BG monitor	yes, manual carb, BG direct from BD meter or manual entry	yes	Yes, manual carb
Bolus Type	units or carbs: standard, extended, combination	quick, scroll, extended, multiwave	units or carbs: standard, extended, combination	Meal, correction, meal & correction; normal, extended, combination	Normal, extended, combination
1 u Bolus Duration	1 or 3 sec	5 sec	30 sec.	40 sec.	12 sec
Battery	AA lithium or alkaline x 1	AA x 1 Alkaline or Rechargeable	AAA for pump, A23 for remote	AAA x 2 (PDA)	1/2 AA 3.6v lithium
Battery Life	4-6 with lithium, 2-4 with alkaline	4 week	3 weeks	4 weeks	8-10 weeks
Motor	DC	DC	DC	stepper	DC
Memory	non-volatile: 500 boluses, 270 basals, 120 daily totals, 60 alarms, 60 primes, 900 bg levels	non-volatile: 90 days (4,500 events); history recall of last 30 boluses, alerts, daily insulin totals, and temporary basal rate increases	4000 events, volatile (basal & history loss can occur): 24 boluses, 7 day totals	90 days of data (up to 5400 records)	Last 500 boluses, primes and daily totals. Last 100 alarms (all time and date stamped)
Software Download	ezManager Max, downloads in 3 minutes with dongle and software that is available at Animas	Pocket Compass with Bolus Calculator , insulin pump configuration software, IR Communication Port	Medtronic CareLink® Therapy Management System and ParadigmPAL™ 3.0 Software at Medtronic	Omnipod Extension for the CoPilot Health Management System	none
Water	12 ft for 24 hrs	IPX 8, 60 minutes at 2.5 meters	splash resistant	watertight	Watertight
Extra Features	Meter-remote offers wireless bolus calculation and delivery within 10 ft. ezCarb software stores up to 500 food items from CalorieKing database on the meter-remote. Calculator features for carbohydrates, blood glucose	choice of standard, advanced or custom selectable user menus, icon- and menu-driven programming, backlit display, reversible display screen, 12 languages, audible or vibrating bolus confirmation and	Enhanced CGM Feature, Predictive Alerts, Low and High Alerts, Rate of Change Alerts, REAL-Time Trend Graphs	backlight, reminders & alerts, child lock, integrated Freestyle meter, 1000 common foods in PDA, Tubeless	Carb Counting Program, Auto Dose capability, Bolus frequency restrictions, preset meal and default bolus. PIN# programming and access to functions including daily maximums and

	corrections and insulin; reminders for time of day and when to perform blood glucose checks. Pump and meter-remote are available in Spanish. PC and Mac downloads are available with ezManager Max software	alerts.			mode settings for healthcare professions / caregivers. Backlight, icon menu. Auto display of remaining insulin and remaining battery life. Lock-out feature with PIN unlock. Twelve languages
Guarantee	4 years	4 years	4 years	4 years	4 years

Table 16: Comparison of the main insulin pumps currently on the market.

5. Figures and Tables

5.1 List of tables

5.2 List of figures

References

[1] http://www.diabetesnet.com/diabetes_technology/blood_glucose_meters.php#ixzz14890MbuN
[2] http://www.diabetesnet.com/diabetes_technology/continuous_monitoring.php#axzz1485odXHL
[3] User guide Guardian real time glucose monitoring system
[4] User guide SEVENPLUS continuous glucose monitoring system
[5] User guide FreestyleNavigator continuous glucose monitoring system
[6] B.H. Ginsberg, Factors affecting blood glucose monitoring: sources of errors in measurement, J. of Diabetes Sci. Technol. 3 (2009) 903
[7] J.C. Boyd, D.E. Bruns, Quality specifications for glucose meters: assessment by simulation modelling of errors in insulin dose, Clin. Chem. 47 (2001) 209
[8] J.S. Skyler, Continuous glucose monitoring: an overview of its development, Diabetes Technology & Therapeutics 11 (2009) 5
[9] http://www.orsense.com/?id=815
[10] http://www.diabetesnet.com/diabetes_technology/insulinpumps_disetronic.php#ixzz14Of2i7Jd
[11] http://www.diabetesnet.com/diabetes_technology/insulinpumps_animas.php#ixzz14OgpRoa8
[12] http://www.diabetesnet.com/diabetes_technology/insulinpumps_minimed.php#ixzz14OioY5PU
[13] http://www.diabetesnet.com/diabetes_technology/insulinpumps_danadiabecare.php#ixzz14P1ARJBv
[14] http://www.diabetesnet.com/diabetes_technology/insulinpumps_nipro.php#ixzz14P1fO1ML
[15] http://www.diabetesnet.com/diabetes_technology/insulinpumps_insulet.php#ixzz14P4UUMkC
[16] http://www.solo4you.com/?page=AboutSolo&ID=9&pageType=0
[17] http://www.diabetesnet.com/diabetes_technology/insulin_pump_models.php#axzz1Ctfcdkdd