Official Title

Home Use of MD-Logic Automated Insulin Delivery System: Safety and Efficacy

Brief Title: Fuzzy Logic Automated Insulin Regulation (FLAIR)

NCT 03040414

Date: July 17, 2019

STUDY TITLE: FLAIR. A Crossover Study Comparing Two Automated Insulin Delivery System Algorithms (PID vs. PID + Fuzzy Logic) in Individuals with Type 1 Diabetes

CONSENT TO TAKE PART IN A RESEARCH STUDY

STUDY DOCTOR'S INFORMATION

Doctor's Name: _____
Doctor's Contact Number: _____
Emergency (24-hour) Number: _____
Study Coordinator Name and Contact Number: _____
Site Name: _____
Site Address: _____

SUMMARY

In this form, when it says "you" it is referring to you as the participant if you are an adult, or to the person under your care that would be in the study if you are a legally authorized representative (LAR). Please see the next section called "Legally Authorized Representatives (LAR)" for more information about who can be a LAR. This would be like a parent reviewing the information for their child to be in the study. In this case, "you" would mean "your child."

This consent form will give you important information about this study. It will help you decide if you would like to take part in the study. You do not have to be in this study. You can stop the study at any time. You should read and discuss all the information in this consent form with the study doctor.

- **The study is being done to find out if a new investigational device helps you manage your glucose levels better than a device that is currently available.**
- **The insulin pump used in this study is approved by the Food and Drug Administration (FDA) for type 1 diabetes only for use in this study. For this reason, it is called experimental.**
- **You will be asked to be in the study for about 7-9 months. The study will involve using the insulin pump every day and completing questionnaires about your experience. It will also involve multiple office visits and phone contacts. At the visits you will have physical exams, blood draws, and device training.**
- **The most likely risks to you are getting high or low blood glucose levels. You may also get redness, itching, or discomfort from the continuous glucose monitoring system or pump adhesive (tape). You may also feel pain or bruising from fingersticks and blood draws.**
- **The possible benefits are that you may not get as many high and low glucose values as before, but that is what the study is trying to find out. This research may help people control their glucose levels better in the future.**
- **If you do not participate, you may continue your current diabetes treatment, or talk with your doctor about other forms of diabetes management.**

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LEGALLY AUTHORIZED REPRESENTATIVE (LAR)

A "minor" is a person under the age of 18 years. A LAR for a minor is a natural or adoptive parent, a legal custodian, or a legal guardian. A LAR for an adult that lacks capacity to consent can be an attorney in fact, a court appointed guardian, a participant's spouse, a participant's adult child, or a participant's parent (in that order). This means that if the adult that lacks capacity to consent and has a court appointed guardian, then the spouse would not be permitted to serve as the LAR.

WHAT IS INFORMED CONSENT?

You are being asked to take part in this research study because you have type 1 diabetes. Type 1 diabetes is a condition in which your body does not produce enough insulin to help control your blood glucose (sugar) levels. The goal of this study is to learn things that may help people with type 1 diabetes.

Your study doctor will be talking with you about this study and this form. You can take as much time as you need to think about whether or not you want to be in this study. You can also take a copy of this form with you to discuss with friends, family, or other doctors to help you decide. Please read this document carefully. Do not agree to be in this study unless all of your questions have been answered.

You do not have to be in this study. If you decide not to be in this study, you will not be treated differently as a person just because you didn't want to be in this study. Also, your regular care will not be impacted.

WHO IS DOING THE STUDY?

This study is being coordinated by the Jaeb Center for Health Research in Tampa, Florida and HealthPartners/International Diabetes Center (IDC) in Minneapolis, Minnesota. It is being paid for by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) which is part of the United States National Institutes of Health (NIH). The Jaeb Center for Health Research will use the funding to organize the study. Your study doctor and clinic staff will use the funding to carry out this study. The name of the study doctor and the doctor's contact information is listed on the first page of this form. If one of the study doctors gets money or benefits from a company that makes the devices in this study, then they have to tell the Jaeb Center.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to compare a hybrid closed loop (HCL) system to an advanced hybrid closed loop (AHCL) system. These are also known as automated insulin delivery (AID) systems. AID systems are designed to help people with type 1 diabetes control their blood sugar (glucose) levels. We expect about 112 people will take part in this study at about seven sites in the United States and other countries for about 7-9 months.

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WHAT IS BEING STUDIED?

Two different, but very similar AID systems, are being studied. An AID system is made up of three parts: (1) a continuous glucose monitor (CGM) that measures glucose levels; (2) an insulin pump that delivers insulin; and (3) a computer program on the insulin pump that can tell the pump how much insulin to give you.

This is how the AID system works. The CGM measures the glucose level and sends this to the pump. The computer program on the pump reads this information and automatically increases or decrease insulin delivery. You will need to tell the system when you are going to eat a meal.

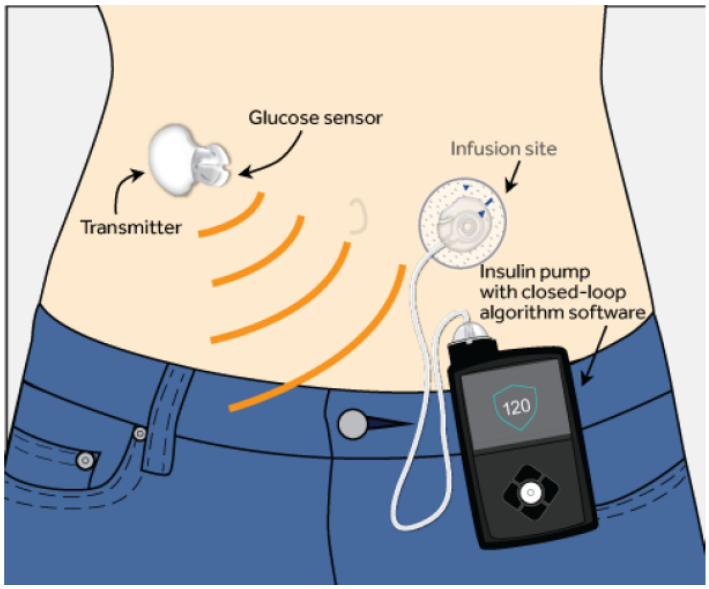
The two AID systems are:

- 670G 3.0 HCL (Hybrid Closed Loop) insulin pump + Guardian 3 CGM
- 670G 4.0 AHCL (Advanced Hybrid Closed Loop) insulin pump + Guardian 3 CGM

One AID system uses the 670G 3.0 HCL pump. It uses software developed by Medtronic MiniMed, Inc. and has been approved for use in the United States by the Food and Drug Administration (FDA) and in Europe.

The other AID system uses the 670G 4.0 AHCL pump. It uses software co-developed by Medtronic and DreaMed Diabetes Ltd. This system is considered experimental. This means it can only be used for research. The United States Food and Drug Administration (FDA) has approved its use in this research study. The main difference between the software in the two systems relates to how insulin is delivered after a meal. **One of the experimental features is called Auto Correction or Auto Bolus. When this feature is activated, the system uses sensor glucose values to calculate insulin doses. This automatic bolus feature does not need your acknowledgement to deliver the insulin.**

Both systems use the same CGM. It is made by Medtronic MiniMed, Inc. The CGM is called the Guardian 3. The Guardian 3 has a needle that is used to insert a sensor just under the skin. This sensor then measures the glucose in the fluid beneath the skin. A transmitter takes the measurements from the sensor and sends them to the insulin pump every five minutes. The insulin pump automatically adjusts insulin doses based on your changing glucose levels. The insulin pump gives you insulin through an infusion site.



Both AID systems automatically deliver insulin based on your glucose levels from the

CGM. However, when you are having a meal, you will need to let the system know how many carbohydrates you are eating. The picture shows the parts of an AID system. *Note that "closed-loop" = "auto mode"*

WHO CAN PARTICIPATE IN THIS STUDY?

In general, to take part in this study, you must:

- Have had type 1 diabetes for at least one year using an insulin pump or multiple daily injections of insulin;
- Be at least 14 years old and less than 30 years old;
- Have an HbA1c value of at least 7.0% and no higher than 11.0%;
- If you are female and have the potential of becoming pregnant, you must use a form of contraception;
- Be available to come back to the clinic when needed and be available when the study team reaches out to you;
- Have a computer with internet access for uploading insulin pump data;
- Be willing to discontinue your personal CGM and personal pump (if you use these) while using the study devices (including implantable CGMs);
- Be willing to count carbohydrates;
- Use the study devices every day.

Also, you must not:

- Be using diabetes medications other than insulin;
- Have a disease that could affect HbA1c readings (e.g. anemia, sickle cell disease);
- Have untreated celiac or thyroid disease;
- Have had one or more episodes of severe hypoglycemia within the previous six months;
- Have had one or more episodes of diabetic ketoacidosis (DKA) requiring hospitalization within the previous six months;
- Be on dialysis or have severe kidney disease;
- Be pregnant, breastfeeding, or planning to become pregnant during the study;
- Be working night shifts.

Your study doctor and staff will review more health-related requirements with you.

WHAT WILL HAPPEN IN THIS STUDY?

If you decide to take part in this study, it will take about 7-9 months to complete. There will be about 8-11 clinic visits and 11-14 contacts with study staff. Some participants may need more visits and contacts. The following sections describe the procedures for each period of the study.

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Screening Visit
If you decide to participate in the study and sign this consent form, you will start with the screening visit. The screening visit includes questions and tests that let us know if you qualify for the study.

We will ask you questions about yourself, your diabetes, and your health. A physical exam will be done. There will be a blood draw for HbA1c. A urine pregnancy test will be done for females who have the potential to become pregnant. You will complete questionnaires about your quality of life and your diabetes management.

If you are found to be eligible for the study and you wish to continue, then you will be trained on the study devices. If you do not qualify for the study or if you decide not to continue, that is okay and your doctor's team will discuss your options.

Device Training (also known as the Run-In periods)
There are two device training parts of the study:

1) Pump Run-In (2-4 weeks)
    a. You will be trained on how to use the 670G 3.0 HCL pump;
    b. During the run-in periods, you will need to do a fingerstick to check your blood glucose before each meal and enter the value into the study pump in addition to the amount of carbohydrates you plan to eat;
    c. Then, you will use the pump at home for two weeks to get used to it. If you need more time getting used to the pump, you can use it for two more weeks;
    d. If you currently use an insulin pump, you may be able to skip this period.

2) Pump+CGM Run-In (2-4 weeks)
    a. After you complete the Pump Run-In, you will be trained on how to use the CGM (Guardian 3) along with the study pump;
    b. You will be trained to do a fingerstick when the study pump/CGM requests a calibration and enter the value into the study pump/CGM;
    c. Then, you will use both the pump and the CGM at home for two weeks. If you need more time, you can use both of these devices for two more weeks.

We will give you a study blood glucose meter and test strips to use. You will be trained when to do fingerstick checks such as before meal time, to calibrate the CGM, and to confirm a high or low CGM reading.

While you are using the study pump and CGM, you should stop using your personal pump and CGM (if you use any of these). It is very important that you wear the study devices every day and night during these phases. Each week, the study team will contact you to see how you are doing. They also will ask you to upload your device data. They will show you how to do this using your computer.

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During the Run-In periods, you will not be allowed to use the auto mode feature unless you were already using auto mode on a 670G pump before starting the study. The auto mode feature is the computer program on the pump that automatically adjusts your insulin. Another feature on the pump stops insulin delivery if the system thinks your glucose will be dropping low (predictive low glucose feature). You will be instructed to use this feature during the Run-In periods.
At the end of the Run-In periods, the study team will make sure there is enough information from the study pump and CGM about your glucose levels before you can continue in the study. They will also see if you checked your blood glucose at least three times per day.

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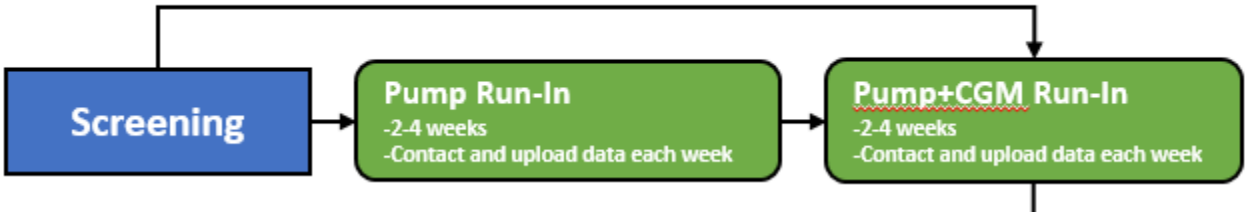
The figure and table below summarize the Screening and Run-In periods.



	Screening/Start of Run-In[5]	Pump Run-In[1.]		Pump+CGM Run-In[1.]	
		1 week after screening.	2 weeks after screening.	1 week after screening[2] or end of pump run-in.	2 weeks after screening[2] or end of pump run-in.
Procedure.	Visit.	Contact.	Visit.	Contact.	Visit.
Provide consent.	**X**				
See if you are eligible.	**X**				
Medical history and physical exam.	**X**				
HbA1c.	**X**				
Study pump training.	**X[2]**				
Study CGM training.	**X[3]**		**X**		
Questionnaires.	**X**				
Check for safety concerns.		**X**	**X**	**X**	**X**
Upload device data from home.		**X**		**X**	
Upload device data at clinic visit.			**X**		**X**
Review blood glucose readings for any insulin adjustments needed.		**X**	**X**	**X**	**X**
Pregnancy test[4.]	**X**				

[1]Run-in periods may be repeated once.
[2]Pump training will occur if you quality for the study.
[3]Current pump users at screening may skip Pump Run-In and proceed directly to Pump+CGM Run-In at investigator's discretion. CGM training will occur if you qualify for the study.
[4]Additional pregnancy tests to be performed any time pregnancy is suspected.
[5]The Screening and start of run-in training visits may occur on the same day or separate days but no more than 14 days apart.

Main Study

After you complete the Run-In periods, the study team will see if you are ready to start the main part of the study.

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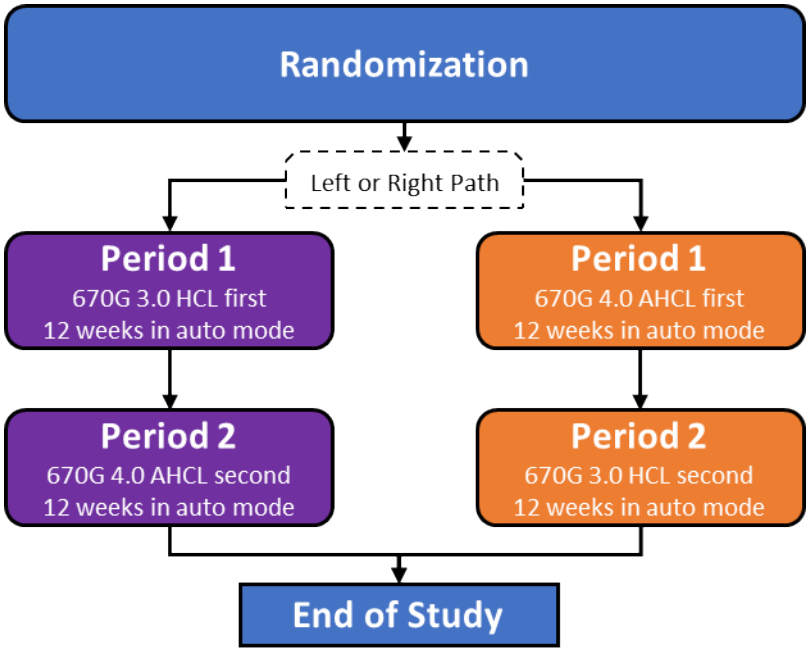
To begin the crossover trial, you will have a blood draw to measure your HbA1c, C-peptide, and glucose. C-peptide is a blood test to find out how much insulin your pancreas is still making. A urine pregnancy test will be done for females who have the potential to become pregnant.

A computer program will be used to select which of the two AID systems you will use first. This is like flipping a coin to decide the order in which you will use the systems. You will be trained on each of the study systems before you start using them.

The figure below shows you which path you will follow depending on which system you are randomly assigned to use first in Period 1 (either the left path or the right path).



Period 1 begins after the computer selects which path you will follow during the study. You will be trained on how to use the auto mode feature on the insulin pump. However, you will not be allowed to use the auto mode feature for the first 6-10 days of Period 1 unless you are using the 670G 3.0 HCL pump and used the auto mode feature on the 670G pump before you entered the study. You will be instructed to use the predictive low glucose suspend feature at all times during the study. After about 6-10 days into Period 1, you will be contacted by your study team who will instruct you on turning auto mode on.

You will then use the first AID system for 12 weeks during Period 1 with the auto mode feature turned on.

During this time, you will be expected to:

- Complete an overnight fingerstick (between 2-3AM) for the first 2-3 nights after auto mode is turned on.
- Use the pump and CGM every day;
- Perform a fingerstick blood glucose check
    - At least twice daily to properly calibrate the CGM;
    - Before meals and enter the blood glucose value into the bolus calculator on the study pump;
    - When you receive a CGM hypoglycemia threshold alarm or the CGM value is below the alarm value;
    - When the CGM reading is >300 mg/dL for more than one hour, or ≥400 mg/dL at any time
        - If the blood glucose is >300 mg/dL, check for blood ketones with the study ketone meter
            - If the ketone level is >0.6 mmol/L, contact study staff for further instructions, which may include replacing the insulin infusion set
- Perform quality control checks on the blood glucose and ketone meters (we will give you instructions);
- Try to keep the same low and high glucose alarms consistent in each study period;
- **Use the pump in auto mode except when you are sick and when you take acetaminophen (Tylenol)*;**
- Be available when the study team contacts you;
- Be available to come back to the clinic several times for check-ups;
- Upload device data before each time the team contacts you and also every two weeks;
- Contact the study staff if:
    - blood ketone readings are greater than 1.5 mmol/L;
    - you are having any problems with the system;
    - you have any symptoms of very high blood sugars, severe low blood sugar, or development of other medical problems;
    - you want to stop participating in the trial for any reason;
    - you think you could be pregnant.

***Avoid taking medications with acetaminophen (Tylenol is one brand) while in auto mode, if possible. If you take acetaminophen, the CGM may read your glucose levels as being higher than they really are. With these high CGM readings, your pump could give you more insulin than you need and cause you to have low blood sugars.**

Medications containing acetaminophen are often used for colds, pain, fever, and cough. If acetaminophen is taken, you should turn off auto mode and use blood glucose meter readings to follow your glucose levels. *Do not use these additional blood glucose meter readings to calibrate the sensor.* Auto Mode use can resume 12 hours after the last dose of Acetaminophen.

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After 12 weeks of using the pump in auto mode, you will complete Period 1. An HbA1c test will be performed and you will answer questionnaires about your experience.

You will then begin Period 2 and will use the other AID system. You will be trained on this system. If you are female and have the potential to become pregnant, you will have a urine pregnancy test done before starting Period 2. You will repeat all the same procedures in Period 2 as you did in Period 1.

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The table below shows you what will happen during the Main Study.

Schedule and Procedures during the Main Study

	Randomization.	Period 1 (P1).								Period 2 (P2).							
		Start Auto Mode.	Time from Starting Auto Mode.							Start Auto Mode.	Time from Starting Auto Mode.						
		6-10 days[1]	24[3] hours.	5[3] days.	2 wk.	4 wk.	6 wk.	9 wk.	12 wk.	6-10 days[1]	24[3] hours.	5[3] days.	2 wk.	4 wk.	6 wk.	9 wk.	12 wk.
Visit (V) or Contact (C).	V	C	C	C	V	C	V	C	V	C	C	C	V	C	V	C	V
Re-review of eligibility.	X																
Follow-up visit.	X				X		X		X				X		X		X
Height, weight, blood pressure.	X								X								X
HbA1c.	X								X								X
C-peptide and glucose.	X																
Auto mode training.	X																
Turn auto mode on.		X								X							
Questionnaires.									X								X
Check for safety concerns.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Upload device data from home.		X	X	X		X		X		X	X	X		X		X	
Upload device data at clinic visit.	X				X		X		X				X		X		X
Review glucose patterns.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test[2].	X																

[1]Auto mode will begin 6-10 days after Randomization and after the end of Study Period 1. Participants who used a 670G in auto mode before screening and will be using the 670G 3.0 HCL pump during the study period may turn auto mode on at the start of the period. All follow-up visits are relative to the day auto mode is started.
[2]Additional pregnancy tests to be performed any time pregnancy is suspected.
[3]Contact must be completed by phone. You will be reminded to complete an overnight fingerstick (between 2-3AM) for 2-3 nights after starting auto mode for AHCL. This will be repeated if your setpoint is lowered to 100 mg/dL.

Medtronic CareLink® System
This system allows your device to send information over the internet using a telecommunication network (such as a cellular network, wireless network, etc.). The information available from the Medtronic CareLink system is the same information the study team would collect from your device during an in-person office visit. Separate instructions with more information about how to use the CareLink system will be provided to you.

Medtronic takes steps to protect the privacy of the health information sent to the Medtronic CareLink Network over the internet. However, Medtronic cannot guarantee the health information is protected against unauthorized interception.

WHAT ARE THE RISKS OF THIS STUDY?

If you choose to take part in this study, you need to know that there are some risks of being in this study.

If a treatment or procedure has increased risks because it was not done according to study procedures due to error, you will be informed, and the necessary steps will be taken to care for you.

Hypoglycemia (Low Blood Glucose)
As with any person who uses insulin, there is always a risk of having low blood glucose, or hypoglycemia. Symptoms of low blood glucose can include:

- sweating;
- shaking;
- not feeling well;
- fainting;
- seizures.

In very rare cases low blood glucose can lead to coma, brain damage, or death. Even if low blood glucose does occur, it almost always goes away quickly with treatment to raise the blood glucose.

Hyperglycemia (High Blood Glucose)
Hyperglycemia usually does not cause many obvious symptoms, but you may be thirsty, or have a higher level of glucose in your urine. In severe cases of hyperglycemia, diabetic ketoacidosis (DKA) or coma may occur. When there is not enough insulin present, the body cannot use sugar (glucose) as a fuel source. Therefore, fat is used for fuel instead. When fat breaks down, it produces ketones which can build up in the body. DKA can lead to kidney failure, irregular heartbeat, heart attack, muscle breakdown, and even death. DKA can occur quickly in someone using a pump if the infusion set gets twisted or disconnected for example, or some other problem occurs so that insulin is not being delivered. You will be given a blood ketone meter to check for ketones as directed by your study team.

Fingerstick Risks

It may hurt when the lancet goes into your finger but not for long. In about one in ten cases, a small amount of bleeding under the skin will cause bruising. The risk of an infection is less than one in 1,000.

Blood Draw Risks

Anytime you have your blood drawn you may have bruising, discomfort, bleeding, infection, or fainting. These risks are possible but unlikely, and are usually mild. All of the blood tests for the study will take about 5-6 teaspoons in total. Possible risks from blood draws include:

- Bruising (common);
- Temporary arm discomfort from the needle stick (common);
- Clotting (unlikely);
- Excessive bleeding (unlikely);
- Lightheadedness (rare);
- Infection (rare);
- Fainting (rare).

Insulin Pump Risks

The risks of using an insulin pump may include:

- Slight discomfort during insertion of the infusion set (common);
- Slight bruising at the site of infusion set insertion (common);
- Infusion set occlusions (common);
- Hyperglycemia secondary to occlusion or infusion site failure (common);
- Pump malfunction and mechanical problems (common);
- Lipodystrophy/lipoatrophy (hard lumps in fatty issue) (common);
- Bleeding at insertion site (rare);
- Infection at insertion site (rare);
- Allergy to the infusion set or adhesive (rare);
- Allergy to insulin (very rare).

Continuous Glucose Monitoring (CGM) Risks

Potential risks from using a CGM include:

- Discomfort when the sensor is inserted into the skin (common);
- Slight bruising at the insertion site (unlikely);
- Bleeding at the insertion site (common);
- Infection at the insertion site (rare);
- Allergy to CGM sensor adhesive material (common);
- Sensor breakage or damage (rare).

AID System Risks

Even though the study systems have been tested extensively prior to this study, there is still a risk that parts of the system may not work right. As a result, more or less insulin than what you need could be delivered and could lead to hypoglycemia or hyperglycemia. The following are possible reasons the system may deliver too much insulin or incorrectly stop insulin delivery:

- CGM sensor reads higher or lower than your actual glucose level;
- Acetaminophen interference causing the CGM sensor to read higher than your actual glucose level. With these high CGM readings, your pump could give you more insulin than you need and cause you to have low blood sugars. **If acetaminophen is taken, you should turn off auto mode and use blood glucose meter readings to follow your glucose levels. *Do not use these additional blood glucose meter readings to calibrate the sensor.* Auto Mode use can resume 12 hours after the last dose of Acetaminophen**;
- Part of the insulin infusion system doesn't work correctly.

Risk if sensor glucose is inaccurate when auto correction (auto bolus) is active:

- If a sensor glucose is much higher than a blood glucose at that time, there is a risk of hypoglycemia, because the amount of insulin delivered could be larger than if blood glucose was used.
- If you feel low (but sensor glucose value is not low), you should do a blood glucose check with the meter.

Risk if sensor glucose is inaccurate in calculating a meal bolus:

- If a sensor value is much lower than a blood glucose would be at that time, there is a risk of hyperglycemia, because the amount of insulin delivered could be smaller than if blood glucose was used.
- If a sensor glucose is much higher than a blood glucose at that time, there is a risk of hypoglycemia, because the amount of insulin delivered could be larger than if blood glucose was used.
- If you feel low (but sensor glucose value is not low), you should do a blood glucose check with the meter.

Unknown Risks

It is always possible that anyone using a device for the first time may have an allergic reaction to the adhesive used to attach the system to the body. Also, there may be additional risks from the device or the study procedures that are not known. If we find out that there are any new risks, you will be told about them. You will be able to decide if you want to continue in the study based on this new information.

Risks to Confidentiality

This study will be capturing some information about you that includes identifiable, personal information, like your date of birth. The study has procedures in place to protect that information. There is a chance that a loss of that protection could occur. This would be a loss of confidentiality. Please see the "How will my information be protected and kept confidential" section below for more information.

Risks for Unborn Babies

The risks of the devices in this study on an unborn baby are unknown. For this reason, anyone who is pregnant cannot be in this study. Anyone who becomes pregnant during the study will have to stop being in the study. Urine pregnancy tests are done as part of this study for anyone that is considered to be able to get pregnant. For example, anyone that has started having menstrual periods, or is still having menstrual periods, will have pregnancy tests no matter how young or old they are. They will also be asked about how they plan to make sure that they do not become pregnant while in the study (like if they use birth control). The study doctors are required to do this even if someone thinks there is no possibility of pregnancy.

For minors, the results of a pregnancy test will only be told to the LAR if the minor has given permission by signing an Assent form. Minors will be told about the pregnancy tests in an Assent form. If you are not comfortable with any of the following, then you should not allow the minor to participate:

- The minor getting information about pregnancy;
- The minor discussing pregnancy with you and the study doctor;
- The minor having pregnancy tests;
- The minor giving permission to share results of pregnancy tests.

Women who are breastfeeding are not eligible to participate in this study.

Questionnaires

You will be asked about your personal attitudes, feelings, and behaviors related to diabetes. The risk of these questions is that you may feel uncomfortable or upset. If any questions make you uncomfortable, you can refuse to answer. You can decide to take a break or stop taking part in the study at any time. If your response to questions regarding your mental state or well-being raises concerns, we may reach out to talk to you about this. Similar questionnaires and interviews have been used in other studies and this reaction is uncommon.

Please discuss the risks with your study doctor or any other health care provider.

WHAT ARE THE BENEFITS OF TAKING PART IN THIS STUDY?

The possible benefit is that you may not get as many high and low glucose values (hyperglycemia and hypoglycemia) as before, but that is what the study is trying to find out. It could also be that you may not receive any direct benefit from being in the study. People who take part in this research study will add to new knowledge that may help other people with type 1 diabetes.

ARE THERE OTHER OPTIONS THAN BEING IN THIS STUDY?

If you do not take part in this study, your options include standard treatment like continuing to use your current diabetes treatment (either insulin injections or insulin pump), talking with your doctor about other forms of diabetes management, participating in other research studies, or you may choose not to do anything. Your study doctor will discuss these choices with you.

CAN I STOP BEING IN THE STUDY?

You can stop being in the study at any time. If you decide to stop being in this study, you will not be treated differently as a person. Also, your regular care will not be impacted. Please talk to your study doctor or staff so they know why you are stopping the study and can help you do so safely.

If we find out that there are any new risks, you will be told about them. You will be able to decide if you want to continue in the study based on this new information.

The study may stop or the study doctor may decide to take you out of the study at any time. You do not have to give permission for the study to stop or for the study doctor to remove you from the study. You will be told if this happens.

Some reasons why you may be removed from the study include:

- The doctors feel that it is in your best interest;
- The doctors think that being in the study may cause you harm;
- If you experience an injury related to the study;
- If you need additional or different medication;
- If you do not follow the study instructions.

If you withdraw, are removed from the study, or the study is stopped, you may continue to receive care like you normally would if you were not in this study. Also, you will no longer be able to use the study device and must return it. You may be asked to complete a final visit to see how you are doing and to collect final questionnaires and an HbA1c test.

ARE THERE COSTS RELATED TO TAKING PART IN THE STUDY?

The costs of routine treatment, office visits, and tests that are part of your regular care will be billed to you or your insurance company like they normally would if you were not in a study.

The study will provide all of the devices and supplies needed for the study to you at no cost (except for insulin). At the end of the study, or if you decide to withdraw from the study, you must return the insulin pump, CGM system, and potentially other study supplies you were given to the study staff at the clinic. You will be able to keep the blood glucose meter and blood ketone meter at the end of the study.

Any additional tests and procedures needed for your regular medical care will be billed to you or your insurance company like they normally would. Since you will need to use your own insulin in the study, you or your insurance company are responsible for the cost of your insulin.

STUDY TITLE: FLAIR. A Crossover Study Comparing Two Automated Insulin Delivery System Algorithms (PID vs. PID + Fuzzy Logic) in Individuals with Type 1 Diabetes

IS THERE PAYMENT FOR TAKING PART IN THIS STUDY?

For your time and inconvenience related to your participation in this study, you will be compensated for each study clinic visit and contact that you complete. If you take part in the study, you will receive $50 for each required clinic visit that is completed and $10 for each required contact that is completed. You may be compensated if there are additional expenses related to travel. If you withdraw from the study, you will still be paid for the visits that you have completed. You will not receive extra payments for visits that are required as part of your normal care or for visits that are for treating an illness or injury.

The use of your samples may result in commercial profit. You will not be compensated for the use of your samples other than what is described in this consent form.

Because payments made to you for participating in this study may be reported to the Internal Revenue Service (IRS) as income, you may need to provide your social security number or a Form W-9 to your study doctor's office. These will not be shared outside of your doctor's office, other than as required to the IRS.

WHAT HAPPENS IF I HAVE AN ILLNESS OR INJURY FROM BEING IN THE STUDY?

If you have an illness or injury that is related to your participation in the study, then you can get care like you normally would. If you have an emergency, please seek emergency care as soon as possible. Please tell the emergency doctor that you are in a research study. Please also tell your study doctor about the emergency as soon as you can. The study does not plan to provide costs for care or other expenses relating to illnesses or injuries. The costs of care for illnesses or injuries will be billed to you or your insurance company like they normally would. Your study doctor, the study doctor's office, the Jaeb Center, and HealthPartners/IDC, and NIDDK are not planning to cover payment for lost wages, direct losses, or indirect losses. More information can be obtained by contacting the doctor's office using the information on the first page of this consent.

CONTACT INFORMATION FOR QUESTIONS OR PROBLEMS

If you have questions about this study; a research illness or injury; or have concerns, suggestions or questions about the study, then contact your study doctor using the contact information on the first page of this form.

Contact the Jaeb Center for Health Research Institutional Review Board (IRB) Office at 813-975-8690 or irb@jaeb.org if you:

- Have questions about your rights as a research participant;
- Wish to talk about your concerns or suggestions about the research;
- Want additional information about the research; or
- Want to provide comments about the research.

STUDY TITLE: FLAIR. A Crossover Study Comparing Two Automated Insulin Delivery System Algorithms (PID vs. PID + Fuzzy Logic) in Individuals with Type 1 Diabetes

HOW WILL MY INFORMATION BE PROTECTED AND KEPT CONFIDENTIAL?

As required by law, study-related records with identifying information will be kept confidential. Safety measures for the access, security, and privacy of your information have been put in place by law. Your date of birth and initials may be used in the study to help the researchers keep the right information together. This information will be protected as described below. Unless the law requires it, your name, address, social security number, telephone number, or any other direct identifying information will not be used to identify you.

Certificate of Confidentiality

NIDDK has given the study a Certificate of Confidentiality. This adds special protection for study information that identifies you and allows us, in some cases, to refuse to give out information that could identify you without your consent. This could be done when the information is requested by a federal, state, local court or public agency. If you need medical help, we may still share your identifiable information. As described in this form or in other cases, we may share identifiable information. For example, if the government inspects us, they may see your identifiable information. Your study doctor and research team will follow local laws and will tell the local or state authorities:

- if certain diseases are present;
- if they suspect neglect, abandonment, or abuse of you; and
- if your study doctor or research team learn that you plan to harm yourself or someone else

Purpose of Authorization

We have rules to protect information about you. Federal and state laws also protect your information. By signing this form you are giving your permission, called your "authorization," for the use and disclosure of information protected by the law.

You must sign the Protected Health Information Authorization at the end of this form if you want to be in the study. When you sign the form, you give permission for the use and sharing of your Protected Health Information (PHI) for the study. PHI is health information that identifies you. Your authorization is beneficial and important for the study. Without your authorization, you will not be able to be in this study.

Using and Sharing Your PHI

Your study doctor will collect information about you. This information includes things learned from study procedures as well as your name, address, date of birth, and information from your medical records. These are examples of identifiable information. A code number with your initials will replace your name, address, telephone number, or social security number in the results given to the Jaeb Center for Health Research in Tampa, Florida.

The following people or companies involved in this study may see your study results with things like your date of birth, initials, and date of procedures:

- Your study doctor's office;

- Jaeb Center for Health Research;
- Laboratories;
- Pump manufacturer;

The study doctor's office ***will not*** share study results that can identify you except as explained in this form or when required by law. The Jaeb Center and your study doctor's office will guard the privacy of your study PHI. Study results without the identifiable information may be shared for educational purposes and in medical journals and at scientific meetings. Your records will be confidential. No one will share your identity in educational purposes or in a medical journal or at a scientific meeting.

Results from the study ***will not*** be sent to you. They will be made available on www.clinicaltrials.gov after the study is completed.

Who Can Receive and Use Your Study Information?
It is possible that people outside of this doctor's office and the Jaeb Center may need to see or receive your information from this study. Some examples include government agencies (such as the Food and Drug Administration), committees that monitor safety, other sites in the study, and companies that are providing either funding or supplies for the study, laboratories, and centers that may receive images. In most cases the information will have a code number with it instead of your name, address, telephone number, or social security number.

There are some situations where the information will not have a code number but may include your name, address, telephone number, or social security number (PHI). Once PHI is disclosed by your study doctor and the clinic staff, it may no longer be covered by the privacy laws. Everyone who needs to see your information will be told it is confidential, but we cannot guarantee full confidentiality once it leaves the doctor's office.

Other Considerations
The information collected in the study may be used in future studies without additional permission from you. This may include research done by other researchers. The information that may be shared will not contain any information that could identify you. There may still be a chance that someone could identify you, but this is not likely. A copy of the information collected as part of the study will be made public in a dataset. This will be done after the study ends. This dataset will not contain any PHI. The study results will also be made public. These results will not have any information that could identify you.

A limited dataset that contains some PHI may be provided to certain researchers. This PHI will not include things like your name, address, identifying pictures, or medical record numbers. Any researcher would need to sign an agreement to protect your PHI before getting this dataset as required by law.

Contact from the Jaeb Center
You may also have communication with the study doctor's office by phone, text, or by video (like FaceTime or Skype). There is a chance that someone could see or hear the conversation like they could if you were speaking or texting with anyone.

Clinical Trial Reporting
A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time. A copy of one of the study consent form templates will also have to be posted on a federal Web site.

Can You Cancel Your Authorization?
You may cancel your permission for the collection of your study PHI at any time. You will need to contact your study doctors and give them a written notice of cancellation, or you may contact the JCHR IRB Office at 813-975-8690 or irb@jaeb.org. When you cancel your permission or when you withdraw from the study directly, you are no longer part of the study. No new information about you will be gathered for the study, except when there is a safety concern related to the study. If there is a safety concern, your entire medical record may need to be reviewed.

The Jaeb Center will receive all the information that was collected for the study up to the time that you cancel or withdraw from the study. The Jaeb Center will receive any new information about any safety concerns that may be related to the study.

When Will the Use and Sharing of Your PHI Stop?
Some of your study PHI does not have a code number with it. Your permission for the use and sharing of your PHI lasts 50 years from the date that you sign this form or until the end of the study, whichever comes first.

The rest of your study information that is not PHI does have a code number with it. When it is collected, it becomes part of a research report. Your permission for the use and sharing of this coded information will never end. This coded data does not have your name, address, telephone number, or social security number.

STUDY TITLE: FLAIR. A Crossover Study Comparing Two Automated Insulin Delivery System Algorithms (PID vs. PID + Fuzzy Logic) in Individuals with Type 1 Diabetes

When the participant is a minor, check "N/A" here and skip this page. N/A ☐

Adult Participant's Full Name (printed) _____

When the Participant Lacks Capacity to Consent Participation in the Study N/A ☐

I, _____ (print name of legally authorized representative ("LAR")) attest that I am authorized to provide consent and authorize the use and disclosure of the participant's protected health information on behalf of the participant named above as I am one of the following LARs (checkbox), and there is not a LAR that has higher authority (see following order):

☐ Attorney in Fact;
☐ Judicially Appointed Guardian;
☐ Participant's Spouse;
☐ Participant's Adult Child; than
☐ Participant's Parent

_____ _____
LAR Signature Date

I certify that the participant lacks capacity to consent and that the LAR named above is in fact the person authorized to consent on behalf of the participant.

_____ _____ _____
Investigator's Printed Name **Investigator's Signature** **Date**

Adult Study Participation

By signing below, you/the participant agree to take part in this study. Your signature means that:

- you have read this informed consent form;
- you have been given the chance to discuss the study and to ask questions to your satisfaction;
- you freely choose (or you freely choose to allow the participant) to participate and you/the participant can withdraw at any time and you will receive a copy of this consent form;
- you authorize the use and disclosure of your protected health information. This information is collected as part of participation in this study. You/the participant cannot be in this study if you do not provide this permission.

_____ _____
Participant's Signature Date

STUDY TITLE: FLAIR. A Crossover Study Comparing Two Automated Insulin Delivery System Algorithms (PID vs. PID + Fuzzy Logic) in Individuals with Type 1 Diabetes

When the Participant is Not a Minor, check "N/A" and skip this page. N/A ☐

Minor's Full Name (printed) _____

Minor's Legally Authorized Representatives (LARs) Permission

I, _____ (print name of LAR) attest that I am one of the following individuals authorized to provide consent for the child named above as I am one of the following LARs (checkbox):
☐ Natural or Adoptive Parent; ☐ Legal Custodian; or ☐ Legal Guardian

By signing below, you agree to allow your child to take part in this study. Your signature means that:

- you have read this informed consent form;
- you have been given the chance to discuss the study and to ask questions to satisfaction;
- you authorize the use and sharing of your child's protected health information that is collected as part of the study;
- you freely choose to allow your child to participate, you and your child can withdraw your child at any time, and you will receive a copy of this consent form.

_____ _____
LAR Signature Date

Investigator's Certification

I certify that to the best of my knowledge the participant or LAR(s) understand(s) the nature, demands, risks, and benefits involved in the participation of this study.

_____ _____ _____
Investigator's Printed Name **Investigator's Signature** **Date**

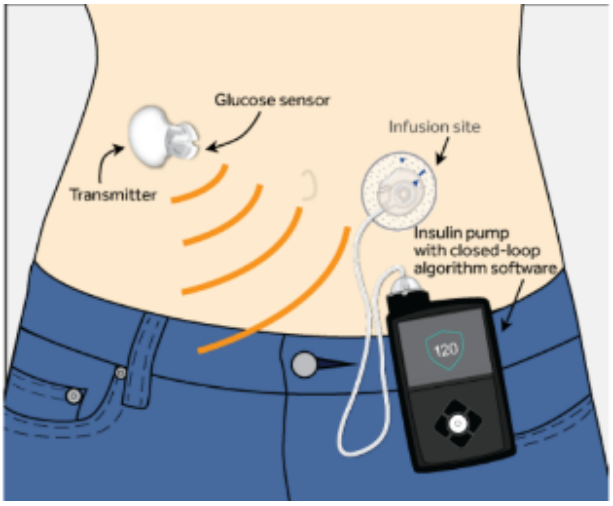
STUDY: FLAIR. A Crossover Study Comparing Two Automated Insulin Delivery System Algorithms (PID vs. PID + Fuzzy Logic) in Individuals with Type 1 Diabetes

ASSENT FORM

For Children 14 – 17 years old

STUDY DOCTOR'S INFORMATION
Doctor's Name: _____
Doctor's Contact Number: _____
Emergency (24-hour) Number: _____
Study Coordinator Name and Contact Number: _____
Site Name: _____
Site Address: _____

A research study is like a science project at school and it is a way to learn new things. We are doing a study to find out more about two different, but very similar, insulin pump systems that can automatically give you insulin. These systems are called Automated Insulin Delivery (AID) systems (see picture).



An AID system is made up of:

1. A continuous glucose monitor (CGM) that measures glucose (sugar) levels using a sensor;
2. An insulin pump that delivers insulin;
3. A computer program on the insulin pump that can tells it how much insulin to give you through an infusion site. This computer program is called the auto mode feature (or closed-loop as shown in the picture).

This is how the AID system works. The CGM measures the sugar level and sends it to the pump using a transmitter. The computer program on the pump reads these sugar levels. The pump then uses this information to increase or decrease insulin delivery. You need to tell the system when you are going to eat a meal. You will need to do a fingerstick to check your blood sugar at each meal. You also may need to do a fingerstick at other times for the system to work.

The two different AID systems being studied are:

- 670G 3.0 HCL (Hybrid Closed-Loop) insulin pump + Guardian 3 CGM
- 670G 4.0 AHCL (Advanced Hybrid Closed-Loop) insulin pump + Guardian 3 CGM

The AHCL system is not approved by the government to be used for type 1 diabetes, but doctors can still use it if they think it will help people. We are asking you to be in the study because you have type 1 diabetes. You do not have to be in this study if you do not want. It is up to you. You can even say okay now and you can change your mind later. All you have to do is tell us. No one will be mad at you if you change your mind. You can still get help with your type 1 diabetes if you are not in the study.

If you agree to be in this study, here is what will happen and what you will need to do.
The study team will first check to see if you qualify. Then you will be trained on how to use the study devices. You will get to use each AID system for about three months. The training period will last from two to eight weeks. Unless you currently use an insulin pump, you will use the 670G 3.0 HCL pump for at least two weeks to get used to it. Then you will use the 670G 3.0 HCL pump along with the study CGM (Guardian (3)) for at least two weeks. When the study team believes you are ready, you will start the main study. During the main study, you will first use one of the AID systems for three months. Then you will start using the other system for three months.

During the study, you will be contacted by the study team to check on you. You will also need to come back to the clinic several different times for follow up. There will be a needle poke to test your blood at some of these visits. You will need to poke your finger to check your blood sugar 3-4 times a day or more. You will answer some questions about your diabetes and the AID systems at three of these visits.

During the study, you might have high or low blood sugar levels. It is possible the AID system might not work the way it is supposed to. You might get redness, itching, discomfort, or bruising from the CGM sensors or from the insulin pump sets. You might also get pain or bruising from fingersticks and blood tests. Some of the questions on the questionnaires might make you feel uncomfortable. You do not have to answer any question you do not want to answer.

If you are female and you are pregnant right now, you cannot be in this study. If you become pregnant, you will not be able to stay in the study. If you think you could be pregnant, please tell the study team that you do not want to be in this study. The study team is not allowed to tell your parents. You may be asked to have pregnancy tests for this study. If you are asked, then you have to have these tests in order to be in the study. The study doctor will talk to you and your parents about the results. If you do not want to have the tests, or you do not want the study doctor to talk to you and your parents about the test results, then you do not have to be in the study. If you are not okay with being in this study, then do not sign this form. If you sign this form, then you are saying that it is okay to do the pregnancy tests and to talk to you and your parents about the test results. You do not have to be in the study if you don't want to.

We do not know if you will be helped by being in this study. We may learn something that will help other children with type 1 diabetes. This study was explained to your parents and they said that you could be in it. You can talk about this with them before you decide. Before you say yes to be in this study, we will answer any questions about the study that you may have. If you have other questions after you sign this form, you can ask us and we will answer them or get an answer for you. You can stop being in the study at any time. If you turn 18 years old while you are in this study, then we will keep getting information about you until your next visit to the study doctor's office. At that visit, you will be given the adult consent form to read and sign if you want to stay in the study. If you do not want to stay in the study you do not have to.

STUDY: FLAIR. A Crossover Study Comparing Two Automated Insulin Delivery System Algorithms (PID vs. PID + Fuzzy Logic) in Individuals with Type 1 Diabetes

Child's Name (print) _____

Child's Permission

Signing below means:

- You have read this form and that you choose to be in this study.
- If you are a female, signing this form means that you are okay with having pregnancy tests and with the study doctor talking to you and your parents about the test results

If you don't want to be in this study you do not have to sign. Being in this study is up to you, and no one will be mad at you if you don't sign, or even if you change your mind later. If you want to be in this study, please sign your name. You will get a copy of this form in case you want to read it again.

_____ _____
Sign Your Name Date

Parental/LAR Attestation

Where we say "parent" in this form, we mean a natural or adoptive parent, a legal custodian, or a legal guardian (collectively known as "Legally Authorized Representatives" or "LARs" for short)

I, _____ (print name of LAR) attest that I am one of the following individuals authorized to provide consent for the child named above as I am one of the following LARs (checkbox)

☐ Natural or Adoptive Parent; ☐ Legal Custodian; or ☐ Legal Guardian.

I am signing below to confirm that the study has been explained to the child in my presence in a language that the child could understand. The child was told to ask questions and the questions were answered so the child could understand.

_____ _____
Sign Your Name Date

Investigator's Certification

I certify that to the best of my knowledge the child understands the nature, demands, risks, and benefits involved in the participation of this study

_____ _____ _____
Investigator's Printed Name **Investigator's Signature** **Date**