The artificial pancreas

Inreda Diabetic

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Inreda Diabetic is an innovative and fast growing company that focuses on the development of an artificial pancreas, a medical device for people with diabetes.

The artificial pancreas of Inreda controls the glucose regulation completely, which may lead to a significant improvement of the quality of life. While using the artificial pancreas, you do no longer have to worry about managing insulin, counting carbohydrates or risking a hypoglycaemia. You will get your freedom back!

We aim to optimize the treatment of diabetes and to improve the quality of life of people with diabetes. It is Inreda's mission to develop an artificial pancreas and to make the device available for everyone who needs it. We hope to achieve this in a few stages. First, we make the artificial pancreas available for adults with type 1 diabetes, at a later stage we will also produce a device that is suitable for children.

We strive to publish our information as clear as possible, mainly through our website Inredadiabetic.nl and Facebook.

Answers to your questions

If you are curious about the artificial pancreas of Inreda, we kindly invite you to read this brochure in which we inform you about the course of our developments, our company and our plans for the future.

We describe the start of the Inreda artificial pancreas, how it differs from other devices, its uniqueness, working and usage, and the development from the first prototype to the actual system, and the availability of the artificial pancreas.

If you are interested to know more after reading this brochure, please do not hesitate to contact us.

For general questions, please send an e-mail to:
info@inredadiabetic.nl

For business and PR questions, please send an e-mail to:
business@inredadiabetic.nl

Diabetes

What is diabetes

Diabetes type 1 is an auto-immune disease that anyone can get. Type 1 diabetes is caused by the immune system. Normally, the immune system only cleans up harmful cells that invade the body. When you have diabetes type 1, the immune system attacks the cells that make insulin. Therefore, the body cannot make insulin to keep blood glucose levels in range.

Effects of diabetes

For the treatment of diabetes type 1 it is essential to avoid low (< 4mmol/L) and high (>10mmol/L) blood glucose values as much as possible and to keep the blood glucose values as much as possible in range. Otherwise, acute and chronicle complications may occur.
Acute complications, for example, are hypoglycaemia or hyperglycaemia. Chronicle complications include kidney and eye illnesses. Moreover, diabetes may affect the psychological wellbeing and daily life by the multiple aspects that diabetes entails. For instance, following diet and exercise rules, attaining accurate blood glucose values, abiding by severe treatment regimes and learning to deal with unpleasant symptoms.

Diabetes in The Netherlands / worldwide

In 2017, approximately 425 million people worldwide have diabetes. It is expected that this number will rise to 693 million people in 2045[1]. More than 1.2 million Dutch people have diabetes[2] of which about 10 percent have diabetes type 1. People with diabetes type 1 contribute substantially to the social costs of diabetes. These costs are expected to grow further in the future, caused by an expected increase of diabetes type 1 and a foreseeable augmentation of diabetes related complications.

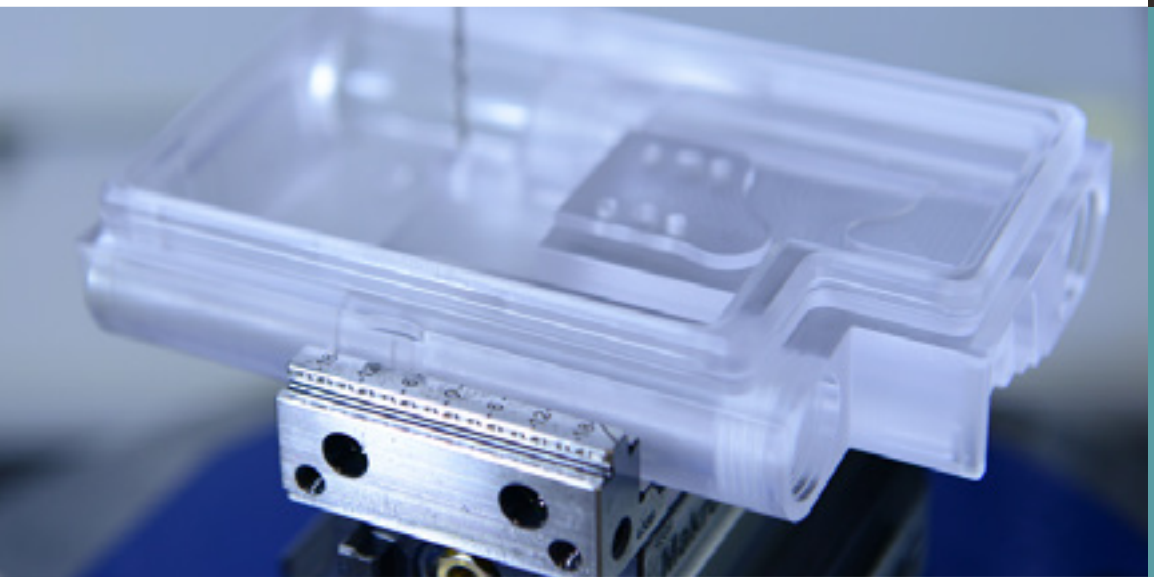
[1] IDF Diabetes Atlas - 8th Edition 2017
[2] Diabetes Fonds Nederland (Fund for Diabetes in the Netherlands)

Origins

Robin Koops

Robin Koops, founder and owner of Inreda, is a mechanic engineer and entrepreneur. At the beginning of his career, he combined these two skills which resulted in the development of machinery for the food and pharmaceutical industry, and in starting his own business.

Since 1995, he has diabetes type 1. Due to daily confrontations with the permanent inconvenience of pricking, measuring and injecting, and because he was not happy with his own treatment, he started looking for a solution.



The idea

He focused on developing a device that could perform the entire glucose regulation autonomously. This would give himself, and many others, more freedom. He worked out his idea which resulted in a concept. In 2004, he started building a first prototype. Together with friends, he combined various ideas, experiences and knowledge and he worked on the development of a bi-hormonal artificial pancreas ever since. Not just for himself, but for all people with diabetes.

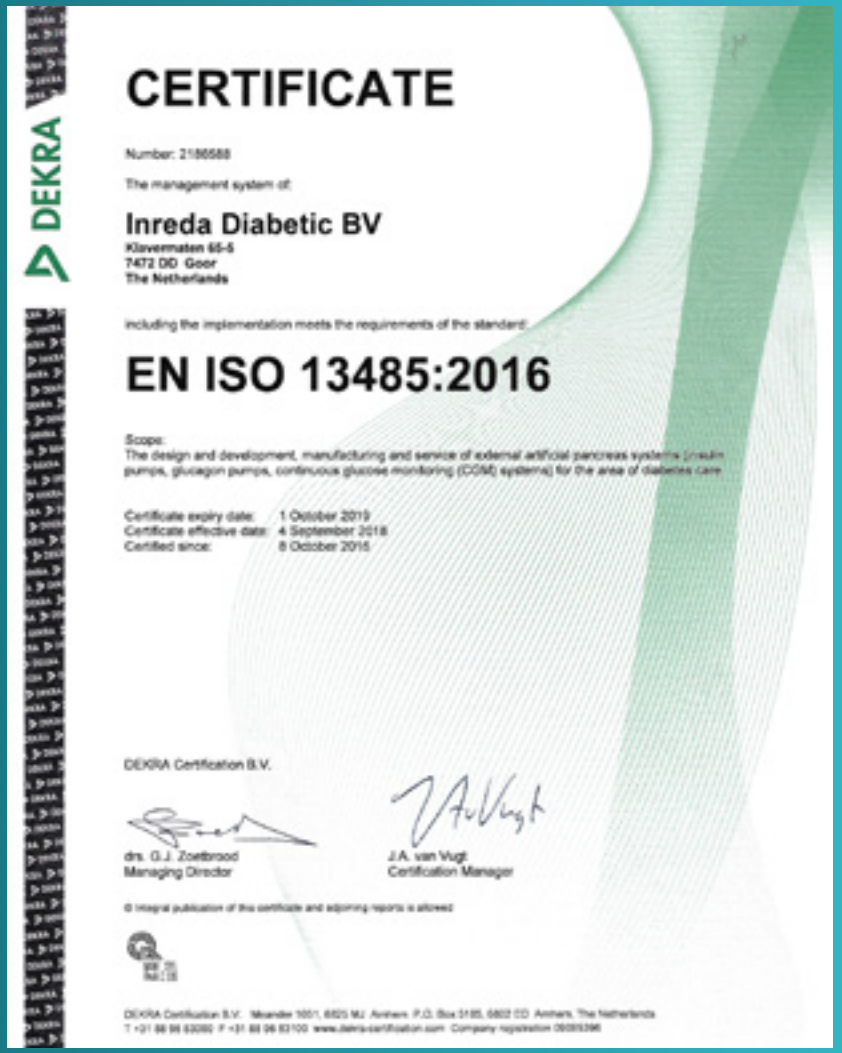
Inreda, a unique company

We develop a bi-hormonal artificial pancreas our way:

People-centered
People are the centre of anything we develop and we are fond of involving you in the development, in order to produce the most intuitive and accessible device.

Reliable
We are professionals developing a high quality device that regulates 24/7 your blood sugar level. So everything we do is tested, tested, and re-tested so that it will be 100% reliable. When there is a choice to be made: we'll always take the route that yields the safest results.

Socially responsible
Be sure that we deploy all our knowledge and expertise (from design & engineering to business model) to get a high quality device for the most affordable price. We are for example investigating how our device will fit in the insurance models. We think it is our responsibility to develop a socially realistic solution.



CERTIFICATE

Number: 2186588

The management system of:

Inreda Diabetic BV
Klavermaten 65-5
7472 DD Goor
The Netherlands

including the implementation meets the requirements of the standard:

EN ISO 13485:2016

Scope:
The design and development, manufacturing and service of external artificial pancreas systems (insulin pumps, glucagon pumps, continuous glucose monitoring (CGM) systems) for the area of diabetes care

Certificate expiry date: 1 October 2019
Certificate effective date: 4 September 2018
Certified since: 8 October 2015

DEKRA Certification B.V.

drs. G.J. Zoetbrood
Managing Director

J.A. van Vugt
Certification Manager

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T +31 88 96 83000 F +31 88 96 83100 www.dekra-certification.com Company registration 09091396

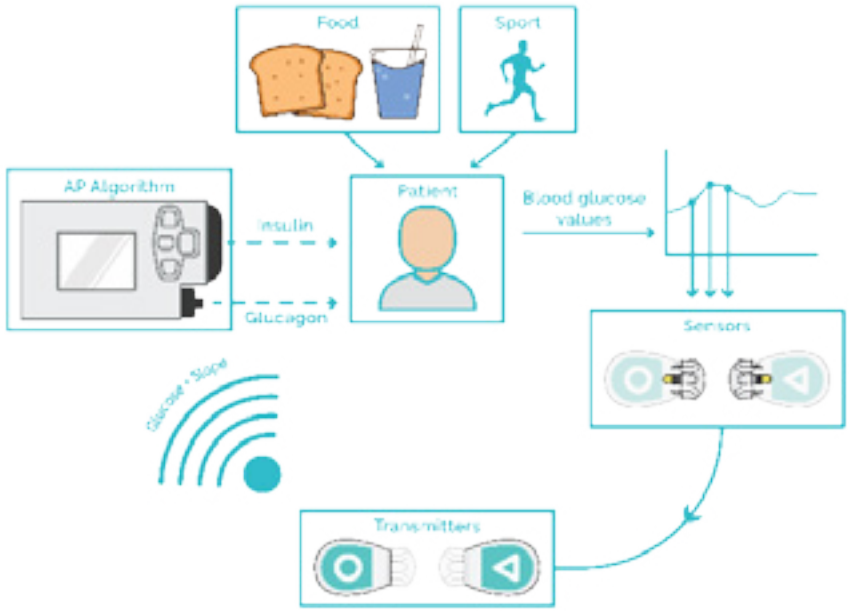
Certified
Inreda, as one of few, is a fully certified (ISO 13485:2016) company and allowed to develop, produce and market artificial pancreas systems.

A unique system

Other than other systems
Inreda is not the only company that works on the development of a system which may simplify the lives of people with diabetes. However, there are some important differences between Inreda's system and the development of other medical devices.

Closed loop systeem
Inreda is making a fully 'Closed Loop' system. This means that this device is able to regulate the blood glucose autonomously, without the intervention of the user. This is the opposite of an 'Open Loop' system where the user himself has to administer insulin. Also, there are 'Hybrid Closed Loop' systems. Here, the delivery of insulin is stopped when the blood glucose values are low, and the insulin is delivered automatically when the blood glucose values are high. Still, the user needs to bolus manually when the blood glucose values are high. Only a fully 'Closed Loop' system, such as the artificial pancreas of Inreda, really liberates you. Because you do not have to think about your glucose regulation anymore.

Bi-hormonal
The team of Inreda believes that you can only achieve a full 'Closed Loop' if you use both insulin and glucagon. Administrating glucagon leads to an increasing blood glucose value when being low. Together, insulin and glucagon regulate the blood glucose. This is what makes Inreda's artificial pancreas unique.

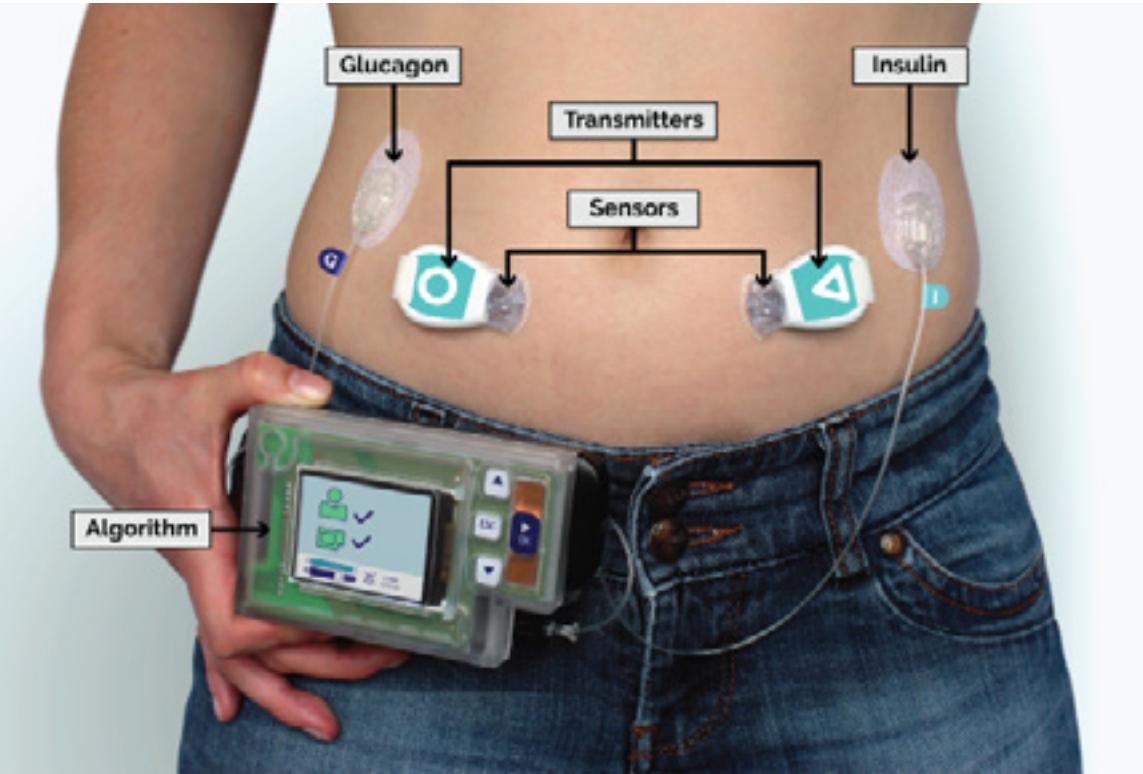


Self-learning
The artificial pancreas comprises self-learning software. The software calculates the amount of insulin or glucagon that needs to be delivered at all times. The software adapts even better to your situation as you use the system longer, and the regulation is getting better. This makes the system self-learning.

Working principle

All components in one

All components for the treatment are integrated in one device and they communicate mutually. This is very smart and it advances its usability.



The system

The artificial pancreas measures the blood glucose values with two continuous glucose sensors. Two small transmitters send these values continuously to the artificial pancreas. Also, physical activities are monitored. The system uses the information of these measurements to calculate how much insulin or glucagon should be delivered. This is done by the unique and self-learning software, called algorithm. With this information, the pumps deliver the correct amount of insulin and/or glucagon, the blood glucose value of the user is adapted and the glucose sensors perform a new measurement: this is the so-called 'Closed Loop' system.

Previous experiences in studies

The results of the studies and the clinical tests that Inreda has performed are very promising.

Safe treatment

Study results show that the treatment with our artificial pancreas are at least as safe as current treatments.

Better glucose values

The study results also demonstrate that the blood glucose values of people with diabetes type 1, by using the artificial pancreas, are better regulated compared to current treatments. These results were obtained in a home situation. Treatment with our bi-hormonal artificial pancreas even assures that 85% of the time the blood glucose values remain within the range of normal values against 69% in case of the current treatment. Moreover, an analysis of the day and night values shows that especially at night significant better results are reached.

More freedom

Being a fully automated system, the main advantage of the artificial pancreas is that the glucose regulation and the quality of life can be ameliorated considerably. Using the artificial pancreas means that people with diabetes are freed from their meal and exercise regimes. At the same time, the artificial pancreas assures a good glucose regulation. Also, less finger pricks are needed compared to conventional treatments. Finger pricks are only needed to calibrate the sensors. Using this system, people with diabetes get their (quality) of life back!

Choose the artificial pancreas

Self management

To make the change from self management to a fully automated treatment is a big step for people with diabetes. They know from their own experience the impact of diabetes on their daily lives. And now they have to hand over control to a device and learn to trust that their glucose regulation is taken over effectively.

Program for Training and Coaching

This is a huge step. Inreda now knows from experience that trust can be gained with the right guidance. The user can then quickly experience the advantages of automated glucose regulation.
Therefore, Inreda offers a unique program for training and coaching. During this program that comprises two days, people will get to learn all the details about the artificial pancreas together with a small group of other users. Also, the user can talk with other users about the psychological aspects that possibly will occur when taking the step towards automated treatment. Further, items such as healthy lifestyle and healthy food will be discussed.

Diminish or prevent complications

While using the artificial pancreas of Inreda, people with diabetes are better capable of keeping the blood glucose values in range. We expect that this will diminish or prevent part of the acute ánd long term complications. Hence, the artificial pancreas will possibly decrease significantly the social costs related to diabetes.

Milestones

Origins
The invention and development of the first artificial pancreas started in 2003.

Prototype 1
Working principle
In 2004, a system with the size of a file cabinet was produced. This system comprised two laptops and an extensive amount of electronics. The patent that Inreda registrered in 2007 is founded on the working principle of this prototype.

Prototype 2
Successful
After successful tests with the device at the hospital in Almelo, the second prototype was ready in 2008. The size of this prototype had been reduced by half. In two pilot studies at the Academic Medical Center in Amsterdam prosperous results were reached with this prototype.

Prototype 3
Home situation
In 2011, the third prototype was developed. This prototype had the dimensions of a laptop. This size enabled people to actually wear the device. At the beginning of 2012, the first study in a home situation had been performed.

2003

Studies
Inreda has performed several clinical studies with the already existing prototypes. These studies are connoted as APPEL: **A**lgorithm to control **P**ostprandial, **P**ost exercise and night glucose **E**xcursion in a portable closed **L**oop format.

2004-2007

The first tests
Prototype 1 has been tested in cooperation with the hospital in Almelo in the Netherlands.

2008 - 2011

APPEL 1 & APPEL 2
Prototype 2 has been tested in two pilot studies together with the Academic Medical Center (AMC) in Amsterdam: APPEL 1 (2010) and APPEL 2 (2011). The purpose of the first study (APPEL 1) was to test this prototype against the conventional insulin pump therapy. In the APPEL 2 study, the prototype was compared to a conventional insulin pump, comprising two meals and physical activities.

2011-2012

APPEL 3
With prototype 3, we had successfully developed a somewhat wearable device. With this model, Inreda, as one of the first companies worldwide, could perform a test in the home situation. In this test (APPEL 3), the artificial pancreas was used by 11 people in their home situation for 48 hours. This test showed that on the first day the artificial pancreas was just as effective as the conventional treatment. On the second day, the artificial pancreas was even more effective in regulating the blood glucose values, especially during the night.

Prototype 4
Integrated system
Next, we focused on combining all components in one system. This resulted in a prototype that has a size comparable to that of a normal insulin pump.

Market model
CE marking
With this prototype, we will request for CE marking. Hence, this will be the first generation artificial pancreas produced by Inreda which is officially released.

Developments
In the future, we will focus on the development of next generations of the artificial pancreas. Dimensions, weight and overall wearable comfort are most important in this process.

2013-2015

APPEL 4
The APPEL 4 study took place in the spring of 2015: 10 people tested the artificial pancreas during 4 days (1 day at the hospital and 3 days in their home situation). The results of this study – performed in cooperation with the AMC in Amsterdam and Rijnstate hospital in Arnhem – are promising. Finalizing these studies means that we are moving towards the last stage of the development of our product.

2016-2018

APPEL 5
Mid 2019, we will start the APPEL 5 study: a large group of people with type 1 diabetes will use the artificial pancreas in a home situation during two weeks.

2019>

APPEL 6
Next, more large studies will follow, where the artificial pancreas will be used in a home situation during several months. We aim to show the results of treatment with this device during a longer period of time. Also, we need to perform studies with a new glucagon. The results of each of these studies define the scope of the next study. Therefore, the exact course of the future developments is hard to determine behorehand.

Future

Availability

A safe system

We use all our knowledge and experience to make a high tech system against a low price. In addition, we strive to make the artificial pancreas available for everyone who needs it. This means that the artificial pancreas will be produced against as low as possible costs, both for the user and the reimbursement authorities.
We investigate, for example, how the artificial pancreas could fit in the current insurance models in a different way. A model in which we, as manufacturer, are also willing and daring to take the risk in order to achieve the goals of the treatment.

CE certification

It is essential that the artificial pancreas is safe and effective. European law stipulates that only safe systems that comply with the regulations, are allowed on the market. When all the conditions are gratified, an independent notified body will disseminate the CE certification. We expect to obtain CE certification for the artificial pancreas in the spring of 2020.

Launch on the market

After we have obtained CE certification, we will launch the artificial pancreas on the market in a controlled way. We do this in order to collect a lot of data about how effective the artificial pancreas is when used by a large group of people and during a longer period of time. Other than collecting data, we strive to realize reimbursement for the artificial pancreas. A first study shows that the artificial pancreas as a treatment for diabetes is a cost efficient solution. However, more studies are necessary in order to determine the costs long-term and the possibility of reimbursement for the artificial pancreas.

Frequently asked questions

Is the artificial pancreas available for everyone as from mid 2020?

Unfortunately not. Once the artificial pancreas has obtained CE certification, there needs to be done a lot of other studies, especially to test the glucagon. Also, we need to perform studies to get the system reimbursed.

Can I apply to participate in a study?

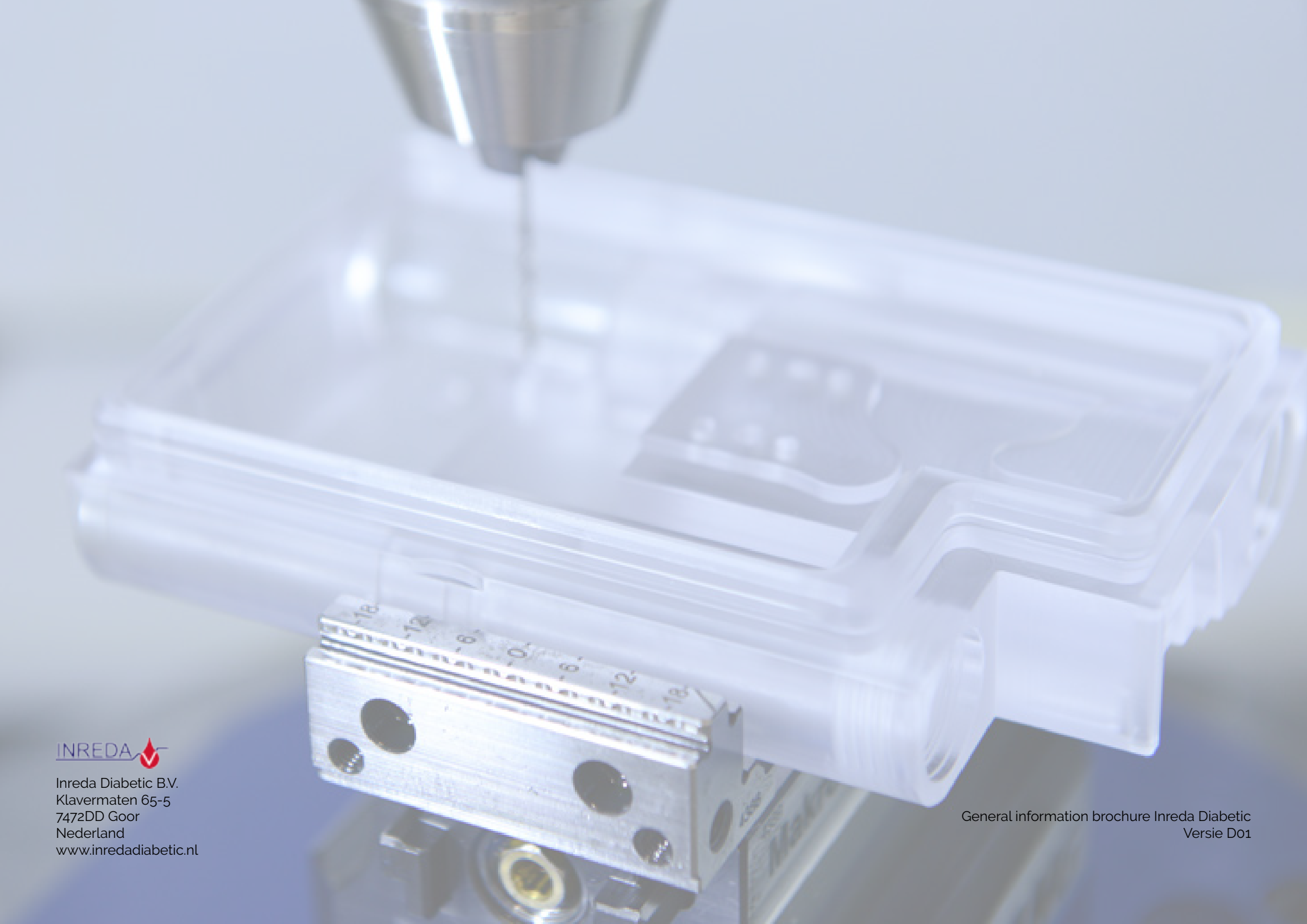
Absolutely. To do so, please fill in the form on our website: inredadiabetic.nl/en/get-involved/.
However, participation in a study depends on many factors. At the moment, we do not know yet which hospitals and doctors will be involved. Eventually, your doctor and you will decide together whether it is possible to participate in a study. Naturally, we will keep you informed of the next steps once you have applied.

Is the artificial pancreas also suitable for children?

The first model that will be available on the market is not suitable for children. However, we are working on a second generation that can be used by children. We expect that this model will be available in a few years time.

Is it possible to buy the artificial pancreas, even if I do not participate in a study?

No, for the time being it is not possible to buy the artificial pancreas. As indicated before, we will perform several studies with a large group of people during a longer period of time after obtaining CE certification. It is important to collect these data too, before the artificial pancreas will be available for everyone who needs it.



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