Final publishable summary report

The aim of PCDIAB was to bring a portable bihormonal artificial pancreas to the patients' home to improve diabetes care and quality of life, eventually diminishing societal costs. To this end, the consortium built a bi-hormonal (insulin and glucagon) artificial pancreas with automated closed loop glycaemic control for insulin treated patients with diabetes and through this.

Since the start of the PCDIAB project a wearable artificial pancreas (AP) suitable for home use has been developed and preparations for the CE-mark application have been made (**Objective 1**). These preparations include the identification, implementation and review of all applicable requirements for CE-marking, composing the technical documentation, and setting up a quality management system. On 14 September 2015, the official certificate for the European patent of our artificial pancreas was granted by the European Patent Office. A first study with a prototype developed in the project showed positive results, as published in a major diabetes journal (**Objective 2**).

The partner that would develop a stable glucagon left the project halfway (**Objective 3**). However, a clinical study with a stable glucagon developed by another company and using our device will start early 2017. The in vitro exposure of continuous glucose sensors to glucagon solutions has been completed (**Objective 4**). It was observed that all glucose sensors maintained stability, sensitivity and linearity when exposed to a specific glucagon solution. The in vivo studies on the effect of glucagon solutions on glucose metabolism at the infusion site indicate that glucose measurement, insulin delivery and glucagon delivery can be combined and performed at a single tissue site, thereby providing firm support for the development of a bi-hormonal single-port artificial pancreas. Two clinical studies were conducted in type 1 diabetes patients in order to evaluate glucagon's possible waning effect on hepatic glucose production during intermittent hyperglucagonaemia produced by repeated subcutaneous glucagon administration. The results suggest that glucagon's potency to increase hepatic glucose production is comparable under fed and fasted conditions, and that the waning of glucagon's effect on the hepatic glucose production may not be influenced by the length of the time interval between two successive glucagon administrations.

A clinical study was performed in diabetes patients to assess the feasibility of combining glucose sensing, insulin delivery and glucagon delivery at a single subcutaneous tissue site. For this purpose, a recently developed treatment device that allows glucose sensing and insulin delivery to be performed at a single subcutaneous tissue site (single-port device) was adapted to also allow the delivery of glucagon to be performed in parallel to glucose sensing and insulin delivery. The results suggest that glucose sensing, insulin delivery and glucagon delivery may be combined and simultaneously performed at a single adipose tissue site. Also, we found that the delivery of glucagon can induce side-effects, like nausea and vomiting and that the potency of glucagon to raise the blood glucose concentration was significantly reduced following the second administration.

Regarding Dissemination, PCDIAB organized an open PCDIAB conference, that focused on disseminating the results of PCDIAB, determining the state of the art, setting the research agenda for the future and the further development of the bihormonal pancreas for monitoring and treating diabetes. This conference was organized with invited speakers from within and outside the consortium, including young scientists, with all major groups working on the bihormonal pancreas around the globe represented.

The PCDIAB consortium built and evaluated a bi-hormonal (insulin and glucagon) artificial pancreas with automated closed loop glycaemic control for insulin treated patients with diabetes and through this, realize a breakthrough in diabetes management.

First Objective of this project was to create a small portable artificial pancreas prototype based on commercially available continuous glucose monitoring devices, insulin pumps and existing technologies such as wireless internet connection and/or blue tooth connection. Compared to the previous prototype, the new prototype will be miniaturized, the housing will be redesigned, the algorithm will be improved and a continuous glucose monitoring performance alert will be developed. The software for the control algorithm will be embedded into the device. The development of this prototype enables wearing the artificial pancreas in daily life.

Second Objective: To test the portable artificial pancreas at home. For the validation of the artificial pancreas prototypes under real life circumstances the clinical trials comprise several safety and effectiveness studies to prepare the artificial pancreas devices for the use at home.

Third Objective: To optimize subcutaneous glucagon administration. To prevent and/or treat episodes of hypoglycaemia in a closed loop setting, administration of subcutaneous glucagon is desirable. The current commercially available glucagon is a freeze-dried powder that has to be re-constituted before use. Long-time use of a bi-hormonal artificial pancreas requires an improved glucagon formulation. The glucagon dynamics and the dose-response relationship will be investigated in clamp studies in patients with diabetes type 1.

Fourth Objective: To test possible interaction between subcutaneous glucagon administration and continuous glucose monitoring, to enable future development of a single-port system. Single-port entails that only one skin perforation is made, and a single catheter is used both for insulin delivery and glucose sensing. By inserting a special catheter into subcutaneous adipose tissue of patients with diabetes simultaneous insulin delivery and glucose sampling can be performed. Previous studies by consortium partners have shown that the glucose concentration observed at the tissue site of insulin delivery correlates well with that seen in plasma. One of the partners is developing a single-port artificial pancreas by modifying an insulin infusion catheter to accommodate a continuous, off the-shelf glucose sensor. To this, glucagon delivery will be added, provided no interaction can be shown between glucagon delivery, insulin delivery and continuous glucose monitoring.

Overview of project objectives:
OB 1 To create a small portable artificial pancreas prototype [M 9]
OB 2 To test and validate the portable artificial pancreas at home, in daily life [M 45]
OB 3 To develop a glucagon formulation [M36]
OB 4 To test possible interaction between subcutaneous glucagon administration and continuous glucose monitoring, to enable future development of a single-port system [M36]

Please provide a description of the main S & T results/foregrounds. The length of this part cannot exceed 25 pages.

Since the start of the PCDIAB project, a wearable artificial pancreas suitable for home use has been developed and preparations for the CE-mark application have been made. These preparations include the identification, implementation and review of all applicable requirements for CE-marking, composing the technical documentation, and setting up and implementing a quality management system. The quality management system will be certified according to ISO 13485 in August 2016. and covers R&D, production and after-sales/service. The results of the pilot study have been used to further improve the artificial pancreas; one important reason was to allow patients to operate the system independently without assistance of the research team. After the upcoming clinical study Inreda can apply for the CE-mark. Furthermore, the AMC and Inreda intensified the collaboration with a pharmaceutical company in order to facilitate the pumpable glucagon coming on the market. In August 2016 a stable glucagon solution with preservatives will become available. On 14 September 2015, the official certificate for the European patent of the artificial pancreas was granted by the European Patent Office.

D2.11 and **D2.13** were uploaded in August and March 2013 and describe the embedding software.
The software for full functioning of the AP was developed and enables the AP to work autonomously and without remote control. The software was extensively tested and validated. Each active artificial pancreas device wirelessly transmits relevant data to the central database. Authorized persons can log in to the web portal and access and visualize the data. This system was used for telemonitoring during the pilot trial. The developed communication protocol ensures unambiguous external communication of the AP. The protocol is based on the FTP standard, includes error checking and facilitates unambiguous processing and exchange of data in the PCDIAB user portal. D2.11 was delivered not after 6 months but after 12 months because the delivery date set in the DoW (M6) was wrong due to an administrative error. To illustrate this, the DoW mentioned in the task description of Task 2.1 “A clear milestone is in month12 when the embedded software should be available for the CRC device”. Indeed D2.11 was delivered by month 12.
D2.2 was uploaded in August 2013 and described the wireless connectivity.
The AP will connect to the central database via the internet. In order to give the AP access to the internet we use a WIFI (Wireless) access point. The AP connects to a mobile access point that is connected to a local available router. The hardware was selected and tested. The wireless WIFI hardware was successfully integrated in the housing of the AP device. In the second half of the project the wireless connectivity was further optimized.
D2.33, **D2.31** and **D2.32** were uploaded in February 2013, August 2013 and February 2014, respectively and describe the miniature hardware.
The design of the housing of the artificial pancreas has been optimized, including several fittings for dedicated components and the used materials. The final model is presented in deliverable 2.34: Design for housing final two port model. This device is ready for CE testing and was used in the pilot trial. In addition, a standardized workflow of the design process has been established. For the one port model (combination of subcutaneous glucose sensor and infusion set) a conceptual design has been created (deliverable 2.35: Design for housing CRC one port model). All dedicated electronics should fit inside the one port model. This design consists of three parts, namely the glucose sensor transmitter, the infusion set cannula and the infusion set tube with adapter. The infusion set cannula and infusion set tube with adapter are disposables, which will have to be changed every three days. The transmitter can be re-used on new infusion sets for at least three years.
D2.4 was uploaded in February and describe the CGM alter performance and validation.
The developed AP includes a closed-loop algorithm that uses two continuous glucose measurements as input and insulin and glucagon administration as output. The sensitivity of the glucose sensors changes during their lifetime and they are likely to fail within one week. Therefore, an algorithm

capable of detecting glucose sensor performance was developed based on data available from the clinical studies with the AP. Special attention was given to documented special events (calibration, sensor changes, etc.) and an algorithm with a level of confidence between 0 and 100% for sensor performance was designed. The algorithm uses six parameters: the first is the difference between a finger stick measurement and corresponding sensor value; the second is the difference between the two used sensors; the third and fourth are a measure for correlation between the two sensors; the fifth is a measure for noise present in the sensor signal; and the sixth is a measure for the duration of a flat signal. The algorithm was tested on a control dataset. This provided a median level of confidence of both sensor 1 and 2 of 80% during the 30 minutes prior to special events (N=3) and 60% during the 30 minutes prior to calibration (N=2). During the remaining parts of the signal the median level of confidence of sensor one and two was between 90 and 95%. Several periods with low levels of confidence that were not marked as special events in the corresponding documentation were identified. In conclusion, an algorithm to quantify sensor performance has been successfully developed. The weights of the parameters need to be optimized using data of the recently completed clinical study.

D2.5 was uploaded in August 2015 and describes the exercise detection.

Firstly, an exercise detection method using a heart rate belt has been implemented in the artificial pancreas. Heart rate belts with the ANT+ communication protocol can be connected to the artificial pancreas. This method comprises four heart rate categories; the higher the heart rate, the lower the percentage of the initially calculated insulin dose that is administered to the patient. Secondly, to overcome the limitations of a heart rate belt it was investigated whether an accelerometer incorporated in the artificial pancreas could be used for exercise detection. Equivalent to the heart rate categories, accelerometer categories were determined from the data obtained during the control period of the pilot study. The analogy between the heart rate and accelerometer categories was studied using the data from the artificial pancreas period of the pilot study. In 85% of time the same category was assigned by the two measurement methods.

D3.1 was uploaded in August 2015 and describes the feasibility and efficacy of portable system.

A pilot trial with the integrated and wearable artificial pancreas has been performed. Ten adult patients with type 1 diabetes completed this randomized cross-over study. Treatment with the artificial pancreas started with one day and night in the clinical research center, followed by three days at home. The control period consisted of four days of insulin pump therapy at home with blinded continuous glucose monitoring for data collection. Day two till four were included in the analysis. We found that the mean glucose level was comparable for the two treatments, while the time spent in euglycaemia was significantly increased during use of the artificial pancreas. In addition, glycemic variability and time spent in hyperglycemia were reduced. Separate analysis of day time and night time shows that the improvements were mainly achieved during the night. The results of this study suggest that our integrated artificial pancreas provides better glucose control than insulin pump therapy in patients with type 1 diabetes at home and that the treatment is safe. We found a high time spent in euglycaemia (3.9-10 mmol/l) during use of the artificial pancreas: median 84.7% (inter quartile range [IQR] 82.2-87.8%). During the night time only (12 PM-7 AM) the time spent in euglycaemia was very high: median 97.7% (IQR 94.7-100.0%). The median time spent in hypoglycemia (<3.9 mmol/l) was only 1.3% (IQR 0.2-3.2%) during use of the artificial pancreas. An abstract of this study is submitted to the 9th International Conference on Advanced Technologies & Treatments for Diabetes (Milan, Italy, February 3-6 2016). The manuscript of this study has been published in Diabetes Obes Metab. 2016;18:34-9. To evaluate the patient acceptance of an artificial pancreas system, the consortium consulted over 300 patients divided amongst 3 countries with an online survey on patient acceptance of the AP which showed that acceptance of the AP is high.

D3.2 (Prospective randomized trial) was not reported to the EC.

Delay in earlier deliverables resulted in delay of task 3.2 (D3.2), which was approved by the project

officer. Unfortunately, this task could not been performed during the extension of 9 months due to the delay in earlier deliverables, as already communicated to the project officer.
D3.3 was uploaded in February 2014 and describes the user questionnaire.
Together with INR, PRO and GRZ, AMS managed to assemble data from over 300 online surveys from diabetes patients of 3 countries (Germany, Austria and the Netherlands). Overall, the patient acceptance of the AP was high, with higher acceptance in the Netherlands than in Austria and Germany. The survey also allowed patients to make remarks about the AP and having to wear the two glucose sensors and two infusion sets and on the size of the AP. Based on these remarks, further development of the AP to reduce the size and the number of needles as well as patient education seems indicated.

Additionally, the in vitro exposure of continuous glucose sensors to glucagon solutions was completed. It was observed that all glucose sensors maintained stability, sensitivity and linearity when exposed to a specific glucagon solution. The pH value of the glucagon solution is pivotal for the stability and sensitivity of the measurements by the glucose sensors. The in vivo studies on the effect of glucagon solutions on glucose metabolism at the infusion site were also completed. Ethical approval for performing the study on 'single-port technique for glucose sensing and delivery of insulin and glucagon' was obtained in July/August 2015. The study was started in the last week of August 2015 and completed in the beginning of October 2015.

D4.1 was uploaded in august 2013 and describes the in vitro exposure of continuous glucose sensors to glucagon.
It was observed that all glucose sensors maintained stability, sensitivity and linearity when exposed to the glucagon solution from Novo Nordisk (NOV). However, when the glucose sensors were exposed to the glucagon solution from Eli Lilly, they all suffered instability and a major loss of sensitivity. The different pH values of the solutions are suspected to be the reason for the different behavior of the sensors when operated in the NOV versus Lilly glucagon solutions.
D4.2 was uploaded in September 2014 and describes in vivo studies on the effect of glucagon solutions on glucose. The human study was performed in 10 diabetic subjects. The observed attainment of a stable interstitial-to-plasma glucose ratio during the delivery of the hormones and the reattainment of pre-administration values following termination of the hormone delivery suggest that glucose measurement, insulin delivery and glucagon delivery can be combined and performed at a single tissue site.
D4.3 was uploaded in October 2015 and describes the single-port technique for glucose sensing and delivery of insulin and glucagon. This task was started in month 26. First, using the results of Task 1 and 2 (D4.1 and D4.2), a glucagon delivery unit was integrated into our previously developed single-port treatment device (https://ec.europa.eu/digital-agenda/en/news/artificial-pancreas-whats-status). Then, a study protocol was designed to test in diabetic patients the feasibility of combined glucose sensing and delivery of glucagon and insulin at a single adipose tissue site using the constructed bi-hormonal single-port prototype. Ethical approval for performing this study was obtained in July/August 2015. The outcome of this study suggest that glucose sensing, insulin delivery and glucagon delivery may be combined and simultaneously performed at a single adipose tissue site. Such a combining of glucose sensing and infusion of insulin and glucagon at a single tissue site (single-port treatment approach), would allow a drastic reduction in the size of a bi-hormonal artificial pancreas system, which in turn could increase patient convenience and enhance acceptance of diabetes treatment with such a system.

Due to the terminated participation of Novo Nordisk in November 2014, TA 5.1 could not been completed. However, collaboration with another pharmaceutical company, regarding a glucagon analogue, was established.

D5.1 could not been submitted to the EC to the fact that Novo Nordisk terminated participation in November 2014. The main reason for this decision is that the use of current reconstituted glucagon solution in the planned multicenter trial at the end of the project would requite extensive physical and chemical stability testing by Novo Nordisk. Recently, collaboration between a pharmaceutical company specializing in the development of protein drugs, Inreda and the AMC was established. A stable glucagon analogue will be used in a clinical trial to be performed outside the consortium. Following expected positive results, this glucagon analogue is likely to become available for the final PCDIAB clinical trial.

D5.2 was uploaded in august 2015 and describes the glucagon dynamics (repeated dosing).

Two clinical studies were conducted in type 1 diabetes patients in order to evaluate glucagon's waning effect on the hepatic glucose production during intermittent hyperglucagonaemia produced by repeated
subcutaneous glucagon administration. The goal of the first clinical study was to assess glucagon's waning effect on the hepatic glucose production under fed and fasted conditions. Unfortunately, the study was performed only on four instead of, as originally planned, seven type 1 diabetes subjects owing to the frequent occurrence of undesirable effects (nausea and vomiting) related to the administered dose of glucagon. The results from the four studied subjects suggest that glucagon's potency to increase the hepatic glucose production is comparable under fed and fasted conditions.

As no difference in glucagon action between the two metabolic states was seen in the four subjects, a new study protocol was designed to determine in diabetic patients the duration of glucagon's waning effect on the hepatic glucose production. To avoid the occurrence of nausea and vomiting, the administered glucagon dose per injection was reduced to one half of the dose administered in our first study. This time the study was completed as planned in 5 subjects. The results of the study suggest that the waning of glucagon's effect on the hepatic glucose production may not be influenced by carbohydrate ingestion and/or the length of the time interval between two successive glucagon administrations.

D5.3 was uploaded in august 2015 and describes the dose response.

The study was conducted as an open, randomised 3-period cross-over experiment in six otherwise healthy patients with type 1 diabetes. At each of the 3 periods, different blood glucose levels were established in 4 steps (8, 6, 4, and 2.8 mmol/L), and a predetermined glucagon dose was given at each glucose level. The sequence of glucagon dosage schedules for the three periods was randomized (A: 0.11 mg at first 3 blood glucose levels and 1.00 mg at the fourth, B: 3 x 0.22 mg and 0.66 mg, C: 3 x 0.44 mg and 0.33 mg). In summary, subcutaneous administered glucagon produces a predictable pharmacodynamic response at lower doses than the usual rescue dose and across a range of hypo- to hyperglycaemic blood glucose levels. This information can be used to further optimize the control algorithms of bihormonal closed-loop systems. The results were presented at the scientific sessions of the American Diabetes Association Meeting in June 2014 and the European Association for the Study of Diabetes in September 2014, both as a poster. A manuscript was published: Blauw H, Wendl I, DeVries JH, Heise T, Jax T, PCDIAB consortium. Pharmacokinetics and pharmacodynamics of various glucagon dosages at different blood glucose levels. Diabetes Obes Metab. 2016;18:34-9, PMID: 26343550.

The potential impact of the PCDIAB project lies in simplified and improved diabetes care, the enhancement of the quality of life for patients with diabetes, diminished occurrence of diabetes related complications and diminished health costs in the long run. Also, the project will strengthen competitiveness of European industry across a complete value chain involving large, mid-sized and small companies, enabling Europe to lead progress in artificial pancreas systems. Finally, the project will put European research and clinical organizations in leading positions with an increased number of high-skilled jobs in the medical device industry.

Expected final results:
We expect to optimize the current artificial pancreas system which will be:
-portable
-including small pumps for continuous subcutaneous insulin and glucagon infusion
-including a continuous glucose monitoring performance alert
-responsive to the meal intake and activities of the patient
-CE marked

In addition we developed another single port prototype, which will be developed in parallel, for use in a research setting only.

Through the development of the artificial pancreas, patients with insulin treated diabetes will be in control to achieve near-normal glucose levels while avoiding hypoglycaemia within their home. We investigated user-acceptance in different countries and the results will be implemented into our market strategy. The final market product will be CE marked and ready for production, leaving some room for final changes to improve usability or adjustments to specific disposables.

Potential impact/expected use:
The developed bihormonal portable artificial pancreas system with automated closed–loop glycaemic control will monitor glucose and treat diabetes patients wherever they go and take into account their meal intake and activities. In addition, the AP will stimulate patients to participate more actively in their care process. Both factors will improve the quality of life of the artificial pancreas users.

The incorporation of a continuous glucose monitoring performance alert in the artificial pancreas in combination with the subcutaneous needle obstruction alert for insulin and glucagon administration, low battery alert, hypo-, and hyperglycaemia alert will improve the management of the glucose levels. Moreover it will enable diabetes patients to achieve tight glycemic control and will increase their willingness to do so. This is expected to result in a decrease of clinical complications and hospital admissions due to hyper- or hypoglycaemia.

All these expected outcomes will lead to a breakthrough in the field of diabetes health systems. The outcomes will
a) improve disease management through more precise measurement of health status and involvement of the patients in their care process, increase the worldwide access of patients to better, secure and safe personalized health systems and reduce hospitalization and its costs without compromising the health care quality and
b) reinforce the leadership and innovation of the industrial partners and contribute to the knowledge-based society and accelerate the establishment of standards on personal health systems for diabetes.

In preparation of the dissemination PCDIAB results, at the TU a group of 14 bachelor and master students have carried out research into the technology acceptance of the artificial pancreas by patients, nurses and physicians, in order to be able to stimulate the dissemination of the artificial pancreas in the market. In addition, it will enable us to train and educate patients, nurses and physicians about the artificial pancreas. The students in collaboration with the PhD student and project leader of the UT constructed a questionnaire based on exiting scales. The main conclusions of their joint research were that characteristics of the individual and the product as well as influence in the social environment have an important effect on the intention to use the artificial pancreas of patients, nurses and physicians. For example, the perceived usefulness of the artificial pancreas was an important predictor of the intended use in all three groups. The results were disseminated through the following online available theses (http://essay.utwente.nl/view/year/):

- Bolks, E.J. (2014). Awareness, Knowledge and Acceptance of the Artificial Pancreas by Patient. Bachelor thesis University of Twente.
- Klabbers, W. J. W. (2014). A physicians' decision-making process in prescribing an artificial pancreas is influenced by their perceived social expectations of patients. Bachelor thesis UT
- Preussner L. B. (2014). Market introduction implications of the artificial pancreas – a comparison between influencing market introduction factors, similarities and differences across the Netherlands, Germany and Austria. Bacelor theis of UT
- Schnarr, J. (2014). The Moderating Effect of Treatment Type on the Relationship Between Diabetes Patients' Treatment Satisfaction and Their Intention to Use an Artificial Pancreas. Bachelor thesis University of Twente.
- Schnarr, R. (2014). Influence of Sex on Product Characteristics' and Subjective Norm's Impact on the Acceptance of the Artificial Pancreas. Bachelor thesis University of Twente.
- Schönbeck, L (2014). Innovations in medical technology – The influence of personal and product characteristics on physicians' acceptance of the Artificial Pancreas. Bachelor thesis University of Twente.
- Albers, M. (2015). The effect of the social influence of a diabetes nurse's working environment on the intention to recommend the artificial pancreas as a treatment method for Diabetes Type 1. Bachelor thesis University of Twente.
- Dirkes, S. (2015). To what extent do product characteristics and age have an impact on patient's intention to use the artificial pancreas? Bachelor thesis University of Twente.
- Muche, L (2015). The Influence of Nurses' Individual Characteristics on Their Intention to Advise an Artificial Pancreas. Bachelor thesis University of Twente.

• Taros, T. (2015). The extent to which product characteristics of new innovations influence nurses' intention to advise them. Bachelor thesis University of Twente.

• Hüer, L (2015). Influence of Technology Readiness and Age on a Physician's Intention to Prescribe the Artificial Pancreas. Bachelor thesis University of Twente.

• Wilhelm, A. (2015). Market segmentation of diabetes type 1 patients as potential consumers of the Artificial Pancreas. Bachelor thesis University of Twente.

• Uncu, C. (2014). The effect of stakeholders' general beliefs of technology on perceived usefulness and eventually intention to use a product in medical innovation management: A review of type 1 diabetes patients and physicians in the Netherlands. Master thesis University of Twente.

Based on the results of this study, among others, the UT is implementing in collaboration with INR a communication plan. This communication plan aims to include 1) what information will be communicated, 2) when it will communicated, 3) how it will be communicated, 4) who will communicate it and 5) how reactions to new information communicated are handled.

An overview of PCDIAB dissemination activities:

Publications:

- Blauw H, Wendl I, DeVries JH, Heise T, Jax T, PCDIAB consortium. Pharmacokinetics and pharmacodynamics of various glucagon dosages at different blood glucose levels. Diabetes Obes Metab. 2016;18:34-9.
- Blauw H, van Bon AC, Koops R, DeVries JH, PCDIAB consortium. Performance and safety of an integrated bihormonal artificial pancreas for fully automated glucose control at home. Diabetes Obes Metab. 2016;18:671-7
- Blauw H, Keith-Hynes P., Koops R., DeVries JH. A Review of Safety and Design Requirements of the Artificial Pancreas. Annals of Biomedical Engineering. In press

- Blauw H, T. Oukes, A.M. von Raesfeld Meijer, J.H. DeVries. (in progress) Acceptance of and user experience with AP for Diabetes Technology and Therapeutics. Target journal: Diabetes Technology & Therapeutics

The technology acceptance studies resulted in an ATTD poster and will be further developed into two scientific publications:

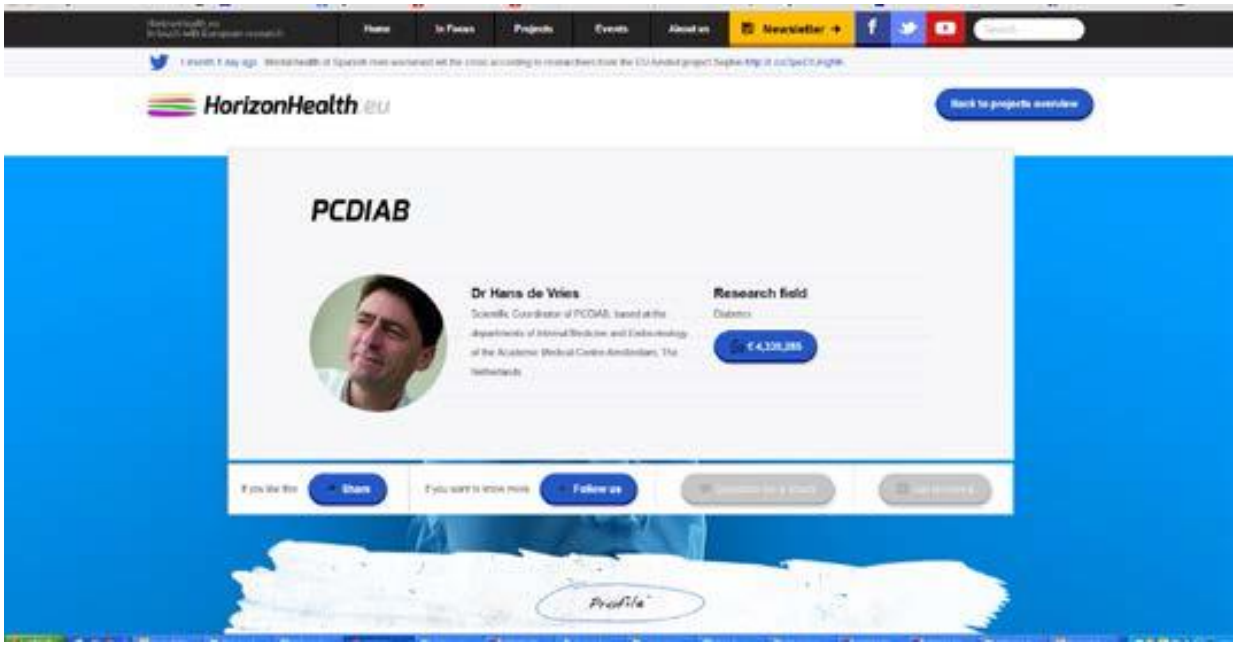
- Oukes, T., Blauw, H., DeVries, JH. and Raesfeld, A. von (in progress) The acceptance of the artificial pancreas by persons with Diabetes Type 1 Diabetes: the difference between invited and self-selected patients. To be submitted in 2016 to: Diabetes Technology & Therapeutics
- Oukes, T., Lebbink, E.., DeVries, JH. and Raesfeld, A. von (in progress) The acceptance of the artificial pancreas by health care professionals: the influence of personal characteristics, product features and the social environment. To be submitted in 2016 to: Diabetes Technology & Therapeutics

The single-port activities are expected to result in the following publications:

- Regittnig W, Urschitz M, Lehki B, Mader JK, Kojzar H, Ellmerer M, Pieber TR. Bolus Delivery with Insulin Pumps in Type 1 Diabetic Patients: Effect of Bolus Delivery Speed on Insulin Absorption from Subcutaneous Tissue. Submitted to Diabetes Technology and Therapeutics, 2016
- Tschaikner M, Jungklaus M, Ajsic A, Tuca A, Pieber TR, DeVries JH, Regittnig W, on behalf of the PCDiab consortium. Combining Glucagon and Insulin Infusion with Glucose Sensing in Subcutaneous Adipose Tissue of Type 1 Diabetes Patients. Prepared for submission to Diabetes Care, 2016
- Tschaikner M, Powell K, Jungklaus M, Fritz M, Ellmerer M, Hovorka R, Lane S, Pieber TR, Regittnig W. Miniaturization of the Artificial Pancreas by Conjoining Glucose Sensing and Insulin Delivery in Subcutaneous Adipose Tissue. Submitted to Biosensors and Bioelectronics, 2016
- Regittnig W, Urschitz M, Lehki B, Mader JK, Kojzar H, Ellmerer M, Pieber TR. Bolus Delivery with Insulin Pumps in Type 1 Diabetic Patients: Effect of Bolus Delivery Speed on Insulin Absorption from Subcutaneous Tissue. Submitted to Diabetes Technology and Therapeutics, 2016

PCDIAB has established the PCDIAB website www.pcdiab.eu in December 2012. This website contains information regarding the PCDIAB research project and the consortium partners. This website also contains a secured domain only accessible for consortium partners and this is used to distribute documents of general use within the consortium. See deliverable report D6.11 and D6.12 for more detailed information.

The PCDIAB project is published HorizonHealth.eu webportal: (http://www.horizonhealth.eu/project/portable-bihormonal-closed-loop-diabetes/192) which is an initiative by the CommHERE network to improve communication on the outcome of EU funded health research projects to the general public and the media.



PCDIAB was represented at the MDL-day (MDL stands for maag darm lever corresponding to gastroenterology and hepatology) in the AMC organized for the public at large on October 6th 2013. The picture below gives an impression of this event.

INR gave several presentations to a diverse range of stakeholders. At UT a presentation was

given to business administration students on the 11th of September 2013, and to technical medicine students on the 18th of December 2013. In September 2013, INR received a delegation of the Rabobank for the Herman Wijffels Innovation Award 2013. On the 7th of November 2013 INR won the Herman Wijffels Audience Award. On the 2nd of November, INR hosted a visit of approximately 20 diabetes patients who filled in the online questionnaire. During the International Diabetes Day on November 14th 2013 INR gave a presentation. In February 2014, INR gave a presentation to the local government of Goor.

An open PCDIAB conference: 'Bihormonal Closed Loop' was organized by AMS, GRZ and INR and combined with the closed PCDIAB conference in month 45. The open PCDIAB conference was organized with invited speakers from within and outside the consortium, including young scientists, with all major groups working on the bihormonal pancreas represented, that is groups from Boston, MA and Portland, OR, USA, Montreal, Canada and Copenhagen, Denmark. The open PCDIAB conference took place during the ATTD conference in Milan on February 5th 2016 (http://www.attd2016.com).