CLINICAL INVESTIGATION PLAN

PROTOCOL

Clinical Investigation Plan number: ALMED-19-003

Acronym: CLOSE AP+

Title: Evaluation of a closed-loop insulin delivery system at home with tailored home care services in poorly controlled Type 2 diabetes: a randomized controlled trial vs usual care

ID-RCB Number: 2019-A02317-50

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SIGNATURE PAGE

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Date	Signature
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INVESTIGATOR STATEMENT

SIGNATURE PAGE

Study title: Evaluation of a closed-loop insulin delivery system at home with tailored home care services in poorly controlled type 2 diabetes: a randomized controlled trial vs usual care.

By my signature below, I hereby confirm that I agree:

- To conduct the trial described in the protocol, in compliance with the ICH Harmonized Tripartite Guidelines for Good Clinical Practice (ICH E6), the provisions of the Declaration of Helsinki (Appendix 3) and the European Directive 2001/20/EC as well as with applicable local regulatory requirements and with the study procedures
- To conduct the study in compliance with this protocol, any mutually agreed future protocol amendments, and with any other study procedures provided by the Sponsor
- To document the delegation of significant study-related duties and to notify the Sponsor of changes in site personnel involved in the study
- To dispense, track and retain the study medical device in accordance with Good Clinical Practice (GCP) and protocol
- To comply with procedures and all applicable regulations for data recording and reporting including Serious Adverse Event (SAE)
- To authorize direct access to source data for monitoring, auditing and inspection
- To retain the trial-related essential documents until the Sponsor informs these documents are no longer needed as detailed in section XIII.4
- To refrain from publishing all or part of the information concerning this study as defined in section XIII.8.

Furthermore, I hereby confirm that I will have and will use the availability of adequate resources, personnel and facilities for the conduct of this trial and to fulfill my obligation as principal investigator.

Name & Title **Address & Tel.**

Date **Signature**

___/___/_____

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SYNOPSIS

Title	**Evaluation of a closed-loop insulin delivery system at home with tailored home care services in poorly controlled Type 2 diabetes: a randomized controlled trial vs usual care**
Acronym	CLOSE AP+
Sponsor's protocol code number	**ALMED-19-003**
Sponsor	AIR LIQUIDE SANTE INTERNATIONAL
Clinical Phase	Interventional study
Coordinating Investigator	Professor Yves REZNIK
Medical/Scientific Experts	[redacted]
Study centres	Approximately 10 investigational centres located in France specialized in Type 2 Diabetes care
Number of patients	A total of 56 randomised patients, i.e., 28 patients in each of the 2 study arms, in order to have 42 evaluable patients.

Context and rationale of the study	In Type 2 Diabetes (T2D), the pathophysiological process results in an inadequate production of insulin and an inability of the body to respond fully to insulin, defined as Insulin Resistance (IR). The number of T2D cases is expected to increase in all countries as a result of population aging, changes in dietary habits and a sedentary lifestyle that have led to an increasing prevalence of obesity. The burden of the diabetes disease represented 7.9 Bn€ in France in 2014. Diabetes was thus the fourth item of expenditure of the Health Insurance. In addition, the management of diabetes-related complications represented 7.7 Bn€. The treatment of T2D usually starts with oral antidiabetic drugs (OAD). If patients are not able to reach their glucose target, they are prescribed the first line of T2D therapy – Metformin. Poor glycaemic control on metformin can lead to dual and even triple therapy including injectable GLP1 analog. For patients who are refractory to basal therapy in addition to previously prescribed antidiabetic agents, treatment intensification requires the addition of prandial insulin therapy to target the control of postprandial hyperglycaemia. The resulting regimen of multiple injections of rapidacting insulin with basal insulin achieves target glycaemia in > 70% of patients but carries an increased risk of hypoglycaemia and body weight gain.

	Full compliance with insulin therapy regimens remains challenging, and injection anxiety, quality of life disruption, and discomfort are well documented obstacles. A subgroup of T2D patients on an intensified multiple daily injection insulin regimen failed to reach glycemic targets, and pump therapy was proven to safely improve glucose control. Unfortunately, about half of the patients treated with insulin pumps in the OpT2mise trial still did not reach the objective of achieving a HbA1c level < 8%. This observation together with the inability of disabling patients to manage their insulin treatment and their glucose control system i.e. SMBG/CGM, argues for the development of new optimization strategies for insulin therapeutic administration. Using an Artificial pancreas (AP) for closing the loop may constitute a reliable solution to further improve T2D insulin treatment outcomes and diabetes complications in a subgroup of T2D patients with poor glucose control, risk of hypoglycemia, and inability for selfmanaging their diabetes treatment so that home nurse intervention becomes a prerequisite for implementation of an intensified insulin regimen. The automated insulin delivery system has the potential to improve the condition of many poorly controlled insulin-treated T2D patients, in particular those needing home nursing care for their daily insulin treatment. The aim of this interventional study, therefore, is to investigate whether a therapeutic solution combining an automated insulin delivery system (Closed-loop) with tailored Home Healthcare Provider (HHP) services can improve blood glucose control, reduce the rate of acute metabolic complications (hypoglycaemia and hyperglycaemia), improve both the patients quality of life and experience, and reduce the global healthcare related costs in patients with uncontrolled Type 2 Diabetes needing home nursing care for their daily insulin treatment versus usual care.

Objectives	Primary objective The primary objective is to determine whether the therapeutic strategy, composed of an automated insulin delivery system and home healthcare provider services, will improve the glycaemic control, measured by the Time In Range (TIR) at the end of the study, in patients with uncontrolled Type 2 Diabetes needing home nursing care for their daily insulin treatment, compared to usual care (including multiple daily injection regimen). Secondary objectives - To assess glycaemic control, - To assess safety, [redacted] - [redacted]

Endpoints	Primary endpoint Time In Range, defined as the percentage of time spent with glucose measurements at 70-180 mg/dL (3.9–10.0 mmol/L) recorded by continuous glucose monitoring (CGM), during the last 14 days completed CGM recording from days 70 to 90. The TIR will be computed considering the full 24-h day. In a complementary way, the TIR will also be computed considering the diurnal period (from 06.00 H to 23.59 H) and the nocturnal period (from 00.00 H to 05.59 H) separately. Secondary endpoints - Efficacy endpoints ● HbA1c absolute change from baseline, ● Absolute change of glucose variability from baseline (i.e., %CV Coefficient of Variation) considering (1) the full 24-h day, (2) the diurnal period (from 06.00 H to 23.59 H) and (3) the nocturnal period (from 00.00 H to 05.59 H), ● Absolute change of Time In Range from the 14 days completed CGM recording at baseline to the 14 days completed CGM recording between D70 and D90. The change from baseline in TIR will be analyzed considering the full 24-h day. ● Time below target range, defined as the percentage of time spent with CGM glucose (1) <70 mg/dL (3.9 mmol/L), and (2) <54 mg/dL (3.0 mmol/L), during the last 14 days CGM completed recording from days 70 to 90. The time below target range will be analyzed considering the full 24-h day and in a complementary way, by splitting the diurnal period (from 06.00 H to 23.59 H) and the nocturnal period (from 00.00 H to 05.59 H), ● Time above target range defined as the percentage of time spent with CGM glucose (1) >180 mg/dL (10.0 mmol/L) and (2) ≥250 mg/dL (13.9 mmol/L), during the last 14 days CGM completed recording from days 70 to 90. The time above target range will be analyzed considering the full 24-h day and in a complementary way, the diurnal period (from 06.00 H to 23.59 H) and the nocturnal period (from 00.00 H to 05.59 H), ● Total daily insulin dose change from baseline to D90, ● Body weight absolute change from baseline to D90, ● The number of discontinuations and their causes.

	- [redacted]

[redacted]

- Safety endpoints
  - Number of diabetes-related hospital admissions, and duration
  - Number of hypoglycaemic events, number of diurnal hypoglycaemic events (i.e., occurring from 06.00 H to 23.59 H) and number of nocturnal hypoglycaemic events (i.e., occurring from 00.00 H to 05.59 H),
  - Number of severe hypoglycaemic events, number of severe diurnal hypoglycaemic events (i.e., occurring from 06.00 H to 23.59 H) and number of severe nocturnal hypoglycaemic events (i.e., occurring from 00.00 H to 05.59 H),
  - Number of severe hypoglycaemic events having led to hospitalisation,
  - Number of severe hypoglycaemic events having required a third party assistance,
  - Number of severe hyperglycaemic events ≥ 300 mg/dL for over 1 hour.

Adverse events and product technical complaints will be collected from the signature of the informed consent to study end.

A Data Safety Monitoring Board (DSMB) will review the safety data of the five first patients of each group, then 25 patients having completed the study, and more frequently if judged necessary by the DSMB.

- [redacted]

[redacted]

	[redacted]

	[redacted]
Methodology	Randomised, national, multi-centre, open-label, prospective, controlled, parallel group clinical trial The randomization will be stratified on the HbA1c level at baseline (<10.0% or ≥10.0%). The randomization will be done centrally, based on a computergenerated randomization scheme.
Study duration	The total study duration from 1st selection to last completion visit is expected to last approximately 29 months (From Q4 2019 to Q2 2022). Study duration for each patient is approximately 18 weeks +/- 2 weeks.

Patient selection	**Target population:** Patients with uncontrolled Type 2 Diabetes needing home nursing care for their daily insulin treatment <u>Selection criteria</u> 1. Male or female patient aged 18 years or older, 2. Type 2 Diabetes diagnosed for at least 6 months with a stable authorized antidiabetic therapeutic regimen for 3 months, 3. Treated with insulin for at least 6 months, 4. Patient with 8.0% ≤ HbA1c <12.0% within the last 3 months before selection, 5. Patient with a current minimum of 2 daily insulin injections and who would benefit of an optimisation, 6. Patient requiring long term family nurse's daily assistance at home for performing insulin injections and/or glucose monitoring, 7. Total daily insulin dose < 1.5U/kg, 8. Patient willing and able to complete the requirements of the study,

	9. Patient living with a caregiver or a diabetes care partner, or patient living alone but with a caregiver living nearby who has a telephone and a key to his or her home, 10. Patient living in an area covered by a GSM (Global System for Mobile Communications) network and not considering a trip outside of France or out of an area covered by a GSM network within the planned dates corresponding to the 30 days of the installation of the pump (to cover the open-loop period and first 15 days of the closed-loop period), and the last 20 days of the study. <u>Inclusion criteria</u> 1. Patient having demonstrated ability to understand the benefits and harms of the automated insulin delivery system and to continuously and safely wear a CGM, as per investigator's judgement, 2. Family nurse having demonstrated ability to use the automated insulin delivery system, as per HHP judgement, 3. Patient able to use basic technology such as a cell phone and having demonstrated ability to use the automated insulin delivery system, as per Home Healthcare Provider (HHP) judgment. In case the patient has not demonstrated ability to use the automated insulin delivery system, his (her) caregiver has to demonstrate ability to use basic technology such as a cell phone and the automated insulin delivery system instead as per Home Healthcare Provider (HHP) judgment. The caregiver has to be an adult person able to speak and read French, having demonstrated ability to use the automated insulin delivery system, with no known medical condition that in the judgment of the investigator might interfere with the completion of the protocol. The caregiver must have committed to maintain uninterrupted availability via personal cell phone and to provide assistance to the patient and must be knowledgeable at all times of the participant's location during the day when closed loop is in use. 4. 14 days completed (ie ≥ 70% of the daily data points non missing) CGM data from the selection period (the CGM period may be repeated only once if uncompleted data), 5. Patient covered by healthcare insurance (in accordance with French regulation), 6. Patient who has received verbal and written information about the study and who signed the informed consent form before any study related procedure.

	7. Patient under curatorship must have received the agreement of their legal guardian to participate to the study. Exclusion criteria 1. Pregnant or breastfeeding woman, 2. Patient who experienced a severe hypoglycaemic event having led to a hospitalisation or having required a third party assistance within the past 6 months, 3. Patient who experienced a diabetic ketoacidosis within the past 6 months, 4. Patient who has demonstrated a marked decrease in hypoglycaemia perception defined by a Gold score > 4, 5. Patient who has disabilities which could compromise the compliance to the study, in the investigator's opinion, 6. Patient with severe health impairment resulting in short life expectancy (< 1 year) as assessed by the investigator, 7. Patient participating in another interventional or observational clinical trial or who participated in another interventional clinical trial within 30 days before selection, 8. Patient known allergy to any component of the automated insulin delivery system compounds, 9. Proliferative retinopathy (assessed with a fundus examination or retinal photography performed within 6 months before selection or before the randomisation at the latest) with visual impairment which could compromise the safety of rapid glucose control normalisation and the compliance to the study, 10. Planned initiation of a treatment that would impact the blood glucose levels (such as steroids) during the study period, 11. Patient deprived of liberty by a judicial or administrative decision, patient admitted to a social institution, patient hospitalized without consent or who is in an emergency situation, 12. Lack of effective contraception in women of childbearing potential, 13. Subject with a history of hearing or vision impairment hindering perception of glucose display and alarms (as this point is a contra-indication stated in the user's manual of the investigational medical device), 14. Severe impairment of renal function (Creatinine Clearance < 30 mL/min),

	15. Patient on dialysis (as the user's manual of Dexcom G6 states that G6 readings may be inaccurate in this population),

	16. Conditions which may increase the risk of induced hypoglycemia as per the investigator's judgment, 17. Inpatient psychiatric treatment in the past 6 months, 18. Current or recent abuse of alcohol or recreational drugs, 19. Patients that have frequent exposure to magnetic resonance imaging (MRI), computed tomography (CT) scan, or highfrequency electrical heat (diathermy) treatment (as this point is a contra-indication stated in the user's manual of the investigational medical device and Dexcom G6.

Investigational Plan	1/ Selection Period: After patient eligibility has been assessed by the investigator and the automated insulin delivery system has been presented to the patient, and caregiver, the patient gives his/her written consent to participate in the study. A 14 days blinded CGM use is initiated for patient baseline evaluation of his (her) glycaemic control and acceptance of the CGM device sensors. The home healthcare provider provides family nurse training on CGM and visits the patient at home, in presence of the family nurse, to provide patient and caregiver instructions and training on CGM. The family nurse, under HHP supervision will set up the first blinded CGM and will change the sensor after 10 days. The HHP will set up the connection of the CGM to the cloud-based CLARITY® platform, through a dedicated laptop, to ensure remotely data access to the Investigator. The family nurse continues to visit the patient daily as usual to perform glucose monitoring and insulin injections. The home healthcare provider visits the patient after 14 days of CGM recording to upload the data to the visualisation platform. In case of incomplete CGM data after 14 days recording, a new CGM could be set up to repeat this period. At the end of this period and upon validation of the selection / inclusion / exclusion criteria by the investigator based on written information provided by the home healthcare provider, the patient is randomly assigned to one of the 2 study groups. 2/ Initiation Period: **For the patients randomized to the investigational group**: A pump is set up for 2 days use (including 2 nights) in open mode at hospital and a new CGM is installed to monitor glucose levels for insulin dose adjustments if needed. Those adjustments will be performed at hospital according to the investigator's instructions.

	The home healthcare provider will provide family nurse and caregiver training on Tandem pump (Tandem-control IQ) and will visit the patient at home in presence of the family nurse, to provide patient and caregiver instructions. The home healthcare provider will set up the connection of the Tandem pump, through a dedicated laptop, to the cloud-based t:connect® platform to ensure the Investigator has a remote access to data following patient hospital discharge. The patient will be followed, for 2 weeks, by the family nurse for his/her daily glycaemic controls and insulin injections (bolus) through the pump and for uploading the data of the CGM and pump to the cloud-based t:connect® platform. **For the patients randomized to the control group**: During the hospital visit, patients randomized to the control group will receive instructions from the investigator for optimization of their usual insulin therapy (multi injection basal and bolus) to be performed at home by their family nurse. 3/ Run-In Period **(Patients allocated to investigational group only)**: Patients allocated to investigational group will be hospitalized for 2 nights. The automated insulin delivery system will be switched from open to closed-loop mode. Patients will be monitored during those days by the hospital medical team and any insulin dose adjustment will be performed according to investigator's judgement during the hospitalization. The HHP will verify the connection of the automated insulin delivery system, through a dedicated laptop, to the cloud-based t:connect® platform to ensure the Investigator has a remote access to data following patient hospital discharge. Patients and caregivers will receive instructions and training from Home Healthcare Provider on Tandem Control-IQ technical usage at hospital. A validation of their learning will be performed at that time. 4/ Follow-Up Period: During that period, the patient will receive his/her allocated therapeutic strategy. **For patients in the investigational group**: - Following the hospital discharge, between 7 to 10 days at the time of the next CGM change Specific to the study and for safety purpose, the patient will be followed by the family nurse twice a day at minimum 6 hours interval to ensure the patient uses the automated insulin delivery system properly and to upload the data to the visualisation platform. The investigator will perform a twice daily follow-up by remote monitoring of patient's data and will call the family nurse as needed.

	In addition, the home healthcare provider will visit the patient at home the day after the hospital discharge (at day 3) and the day of the 1st CGM change (day 9) for reminders on the automated insulin delivery system training and instructions on how to manage any trouble, and to ensure the patient uses the automated insulin delivery system properly. - For the rest of the Follow-Up Period (after the 1st CGM change) The family nurse will visit the patient every 3 days for the insulin cartridge refilling, catheter replacement, battery charge and for uploading data from the pump to the cloud-based t:connect® platform and every 9 days for CGM replacement. The family nurse will inquire about any event, make sure that it is reported in the patient diary and report to the investigator and/or HHP as appropriate. The HHP will call the patient 5 days after his/her last visit (day 15) and then will visit the patient at home, at day 30 and day 60, for reminders on the automated insulin delivery system training and instructions on how to manage any trouble. At each visit, and whenever needed, the HHP will review the data and will inform the investigator of any abnormalities. The HHP will make sure the patient reports any event and will notify the investigator of any event recorded. **For patients in the control group**: The family nurse will perform the usual care i.e. daily glycaemic controls and insulin injections. The family nurse will also make sure the patient is reporting any event in his/her diary. The family nurse and HHP will visit the patient at home at day 70, to set up a CGM for 20 days blinded recording. The patient and/or caregiver will receive a training with reminders of the proper usage of the CGM. 5/ <u>Ending Period</u>: All patients come to the investigator site at day 90 for final data collection and evaluation. All patients will then return to their pre-study therapy.

Investigational Medical Device	The tested therapeutic strategy consists of an automated insulin delivery system and a tailored home healthcare provider service to ensure its proper use by the patient and family nurse. The automated insulin delivery system is made up of 2 medical devices, an insulin pump with a closed-loop algorithm, which is the Tandem t:slim X2 Insulin Pump with Control-IQ Technology (CE mark for T1D patients), and a CGM which is the Dexcom G6 system (CE mark).

	Tandem t:slim X2 Insulin Pump with Control-IQ Technology "The **Pump"** is made up of: - The t:slim X2 Insulin Pump and the t:slim 3mL (300 units) cartridge - The catheter (infusion set) which needs to be changed every 3 days. In addition, patients, their caregivers and investigating centre staff will have access to the t:connect® Diabetes Management Application in both home and clinical settings. This t:connect® Application (so-called cloudbased t:connect® platform) supports diabetes management through the display and analysis of information uploaded from the Pump and specified CGM. Thus, the data sharing functionality will keep the investigator remotely updated between the visits. Data will be uploaded by the healthcare professionals i.e., either the family nurse or the home healthcare provider or the investigator according to the study period. Data from CGM and Pump will be synchronized and displayed on the t:connect® Application during run-in and follow-up periods. Specific to the study, for safety purpose, following the patient's discharge after the run-in period and during the 7 to 10 days after patient hospital discharge (up to the next CGM sensor change) data will be uploaded by the family nurse to the visualization platform twice a day at 6 hours minimum interval to ensure the patient is using the automated insulin delivery system safely. **Dexcom G6 CGM system** includes 3 different components with a sensor that is to be changed every 10 days (at maximum): A: Simple auto-applicator - a one-touch applicator which easily inserts a small sensor just beneath the skin. B: Sensor and transmitter - a slim sensor which continuously measures glucose levels just beneath the skin and sends data every 5 minutes wirelessly through a transmitter to the display device or study pump when paired. Once installed, no calibration is required. C: Display device - a small touch screen receiver which generally displays glucose data. In addition, Dexcom CLARITY® is the dedicated Dexcom diabetes management application available on various platforms (smartphone, website) allowing the Healthcare professionals with the data sharing functionality the visualization of patients glycaemia data remotely keeping them updated between the visits. A blinded display device (blinded for control group and investigational group during selection and initiation periods) will be provided to the study patients to ensure the display of data on CLARITY® platform accessible to healthcare professionals only.

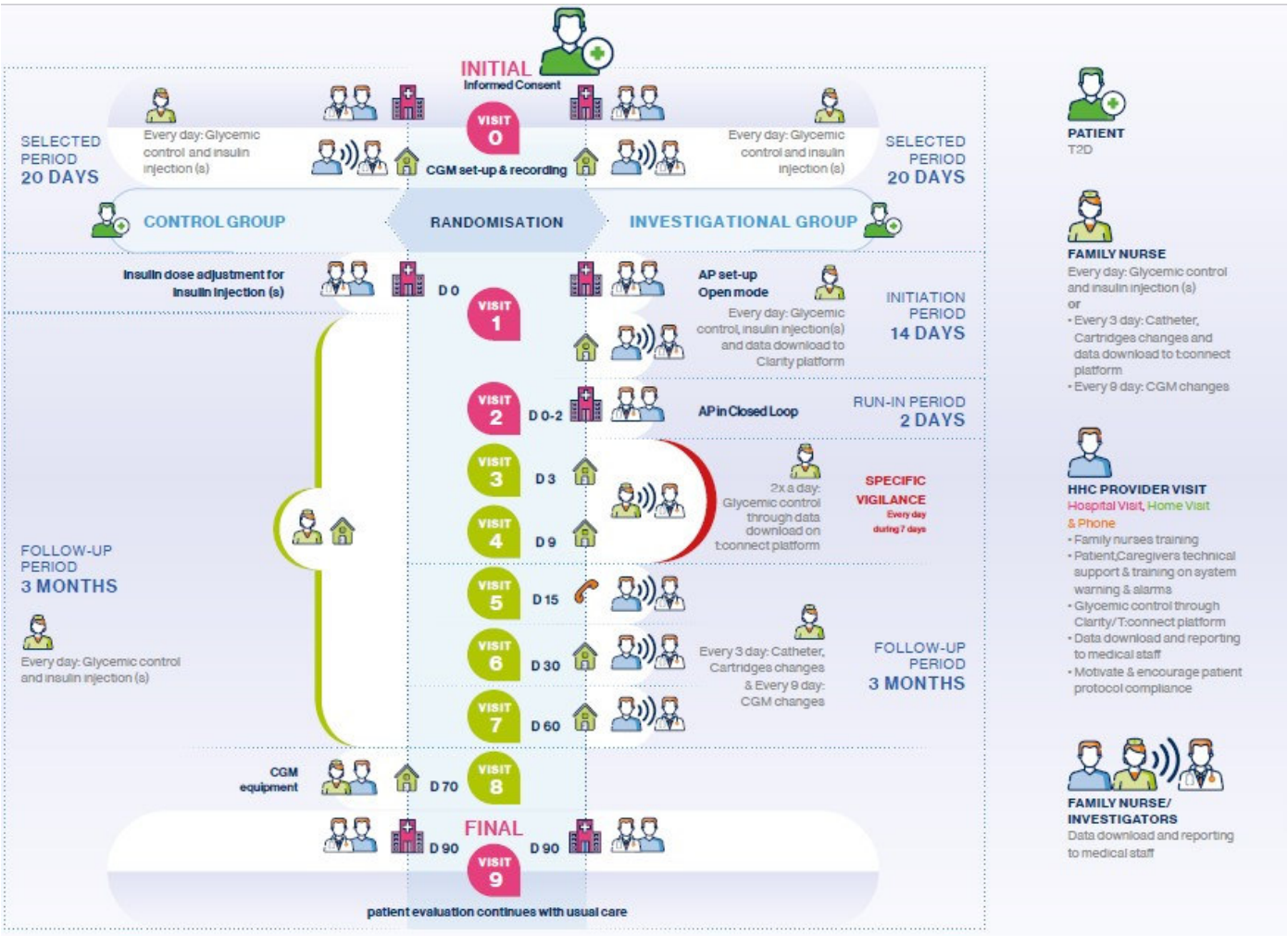
	Data will be uploaded by the healthcare professionals i.e., either the home healthcare provider or the investigator. Data from CGM will be synchronized and displayed on the CLARITY® platform during selection period for all patients and during the end of follow-up period for patients in the control group. During the initiation, run-in and follow-up periods, CGM data will be displayed to the t:connect® platform via the insulin pump. **Home Healthcare Provider role** consists: ● In education and training sessions of the patients, caregivers and family nurses, ● In assessment of patients', caregivers', and family nurses' knowledge acquired, ● In supplying the medical devices and consumables, ● In coordination between patients, caregivers, family nurse and investigating center staff, ● In follow-up by visiting patients, by uploading the Pump and/or CGM data and providing written feedback to the investigator, ● In synchronizing the CGM data to the CLARITY® platform for patients in the control group, ● In motivation and encouragement of the patient to the study compliance, ● In providing technical assistance for patients, caregivers and family nurses by providing Hotline 24/24h -7 days in case of technical complaints, ● In providing technical intervention at home in case of any technical complaint within 12 hours. The Home Healthcare Provider will apply the Code of Practice for Home Healthcare Providers, set out in Appendix 2, for its stipulations that would be applicable to the CLOSE AP+ study. Accordingly, the home healthcare provider is present at the patient home/hospital for CGM and Pump training during selection and initiation periods. **In the investigational group**, the home healthcare provider will be present at home at D3 (at the time of the 1st bolus), at D9 (at the 1st CGM sensor change), at D28 and at D56. In addition, HHP will call the patient at D15 and more if judged necessary. Specific to the study for safety purpose, CGM and Pump data are synchronized to the remote server of the t:connect® application twice daily at 6 hours minimum intervals during the first 7 to 10 days after

	switching to closed-loop mode (up to 1st CGM sensor change) by the family nurse.

	In the control group, the home healthcare provider will perform a refresh training to the family nurse and patient before set-up of a new CGM at D70. In addition, the home healthcare provider is present at the hospital for the study end visit at D90.
Concomitant treatments	**Non-authorized concomitant treatments** Glinides, sulfonylurea, glucocorticoids*, any other medication that could interfere with glycaemic levels. *To note: glucocorticoids are not authorized with the exception of patients treated with stable prednisolone < at 10 mg equivalent per day since 3 months **Authorized glycaemic control concomitant treatments** Metformin, DDP4 inhibitors, GLP1-receptor agonists. **First aid kit** In the event of any deficiency of one or more of the components of the automated insulin delivery system, the patient should have immediate access to a first aid kit including replacement therapy (fast-acting insulin and insulin pen).
Statistical analyses	Analyses will be adjusted on the HbA1c level at baseline (<10.0% or ≥10.0%) if the study recruitment allows it. Thorough description of all parameters recorded will be presented separately by study group, using the observed case approach (apart from the primary endpoint). Summary tabulated results will be provided by group and assessment time/visit, if relevant or they will be replaced by the corresponding individual data listings if too few patients are concerned. Quantitative variables will be summarized in tables displaying number of patients, means, standard deviations, medians and percentiles when appropriate, and extreme values. When applicable, the Wald two-tailed 95.0% Confidence Interval (95%CI) of the means will be provided. Qualitative variables will be described in terms of frequencies and percentages of the total number of non-missing recordings described. When applicable, the Agresti-Coull 95%CI of the percentages will be provided. The statistical analysis of the primary endpoint (TIR at D90) will be based on modified Intention To Treat (ITT) efficacy and Per Protocol (PP) data sets with the PP analysis considered as a sensibility analysis. The modified ITT efficacy data set will include all randomised patients with at least 3 days with ≥ 70% of non missing CGM data points recording at baseline (selection period), as well as at the end of the study (planned from D70 to D90).

	The TIR at D90 will be compared between groups using a parametric analysis of covariance model adjusted on the HbA1c stratification factor and the TIR value at baseline. This analysis will be performed (1) considering the full 24-h day (primary efficacy analysis), (2) diurnal period (from 06.00 H to 23.59 H) and (3) nocturnal period (from 00.00 H to 05.59 H).

Figure 1: STUDY FLOW CHART



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LIST OF ABBREVIATIONS AND DEFINITIONS

Abbreviation	Definition
AE	Adverse Event
ADA	American Diabetes Association
ADE	Adverse Device Effect
ADR	Adverse Drug Reaction
ALT	ALanine aminoTransferase
ANCOVA	ANalysis of COVAriance
ANSM	Agence Nationale de Sécurité du Médicament et des produits de santé
AP	Artificial Pancreas
ASADE	Anticipated Serious Adverse Device Effect
AST	ASpartate aminoTransferase
ATC	Anatomical Therapeutic Chemical
CA	Competent Authority
CGM	Continuous Glucose Monitoring
CNEDiMTS	(French) Commission Nationale d'Evaluation des Dispositifs Médicaux et des Technologies de Santé
CNIL	Commission Nationale de l'Informatique et des Libertés
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organisation
CS	Clinically Significant
CV	Coefficient of Variation

DRM	Data Review Meeting
DSMB	Data Safety Monitoring Board
EC	Ethics Committee
ENCC	Echelle Nationale de Coûts à méthodologie Commune
FDA	Food Drug Administration
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
HAS	(French) Haute Autorité de Santé
HbA1c	Haemoglobin A1c
HCP	HealthCare Provider
HDL	High-Density Lipoprotein
HHP	Home Healthcare Provider
ICF	Informed Consent Form
iCGM	Integrated Continuous Glucose Monitoring
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IFU	Instructions For Use
IMD	Investigational Medical Device
IR	Insulin Resistance
ISF	Investigator Site File
ITT	Intention To Treat
IWRS	Interactive Web Randomization System

LDL	Low-Density Lipoprotein
MD	Medical Device
MDI	Multi Drug Injections
MedDRA	Medical Dictionary for Regulatory Activities
MMSE	Mini Mental State Examination
MoCA	Montreal Cognitive Assessment
NGAP	Nomenclature Générale des Actes Professionnels
OAD	Oral Antidiabetic Drug
PP	Per Protocol
PT	Preferred Term
QALY	Quality-Adjusted Life Year
QoL	Quality of Life
RBC	Red Blood Cell
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDV	Source Data Verification
SEAE	Study Emergent Adverse Event
SOC	System Organ Class
SOP	Standard Operating Procedure
SADE	Serious Adverse Device Effect
SUSAR	Suspected Unexpected Serious Adverse Reaction

T2D	Type 2 Diabetes
TIR	Time In Range
TMF	Trial Master File
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
WBC	White Blood Cell
WHO	World Health Organization

I - INTRODUCTION

I.1 - BACKGROUND

I.1.1 - PATHOPHYSIOLOGY OF TYPE 2 DIABETES

In Type 2 Diabetes (T2D), the pathophysiological process results in an inadequate production of insulin and an inability of the body to respond fully to insulin, defined as insulin resistance (IR). Due to insulin resistance in muscle and liver tissue, the body's ability to metabolize glucose becomes compromised. IR is widely recognized as one of the earliest steps in the progression of T2D. Although a genetic component to this condition exists in many patients, environmental conditions (lifestyle) are thought to be key players in the disease's emergence [8].

One of the characteristic features of T2D is the progressive nature of the disease. In patients with prediabetes and early T2D, the pancreatic beta cells can compensate for insulin resistance by secreting greater amounts of insulin to maintain normal glycaemic control. Prediabetic state turns to a diabetic state as pancreatic beta cells gradually become exhausted and can no longer meet the demands of insulinresistant tissues. Increasing insulin resistance combined with worsening of beta-cell dysfunction, and eventual failure, lead to loss of glycaemic control. The consequence of such continued disease progression is the increased risk of diabetic complications, with macrovascular complications being the most frequent comorbidity associated with T2D. Similarly, microvascular complications, such as neuropathy, nephropathy, or retinopathy, are likely to occur. Moreover, multiple pathophysiologic abnormalities including defects in functioning in α-cells, adipocytes, gastrointestinal tract, kidney, and brain play important roles in the development of glucose intolerance in T2D as well [9].

I.1.2 - EPIDEMIOLOGY OF T2D

Type 2 Diabetes is the most common type of diabetes with a population approximately 10 times larger than the T1D population with a fast growth rate [10]. T2D most commonly affects older adults, but rates of T2D are increasing in children, adolescents and younger adults [10]. Indeed, the prevalence of T2D is strongly associated with aging and obesity. The number of T2D cases is expected to increase in all countries as a result of population aging, changes in dietary habits and a sedentary lifestyle that have led to an increasing prevalence of obesity [1-4]. The World Health Organization (WHO) has estimated that Type 2 Diabetes will affect over 366 million people by 2030 [4]. Given the high mortality associated with the disease, primarily due to macrovascular complications, Type 2 Diabetes is a major public health concern worldwide [11]. Like many other countries in the world, T2D is a major public health issue in France, facing to an increasing number of patients with T2D, and thus an increasing burden of diabetes-related complications [21]. Moreover, diabetes is the principal cause of terminal renal insufficiency, adult-onset blindness and lowerlimb amputation in Western Europe [2].

Improvement in T2D care has led to a significant increase in life expectancy of T2D patients during the last decades [13]. However, a large number of T2D patients do not achieve an optimal HbA1c level.

I.1.3 - BURDEN OF THE DISEASE

In 2014, diabetes was the 4th reason of healthcare expenditure in France with 7.9 Bn € out of a total of 155 Bn€. Diabetes comes after psychiatric diseases, neuro-cardiovascular diseases and cancers. Healthcare

expenses affected 3 Million patients: 83% of expenses were related to primary care, 10% to hospital care and 7% to other care. Expenses directly related to diabetes were of 2.3 M€: antidiabetic drugs at 48%, medical devices (strips, insulin pens and other medicines such as insulin pumps, CGMs) at 35%, and hospitalizations for diabetes as the main reason of admission at 12%. The increase of the prevalence of diabetes in France from 2012 to 2014 was of 2.9% [50].

I.1.4 - T2D TREATMENTS AND CARE

The goal of diabetes treatment is the prevention of the onset and progression of micro- and macrovascular complications, as well as the achievement of quality of life and longevity equivalent to people without diabetes. The UK Prospective Diabetes Study (UKPDS), Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) and Kumamoto Study [48] have established the importance of glycaemic control [3, 14, 15].

Poor glycaemic control is a significant challenge in the management of Type 2 Diabetes, with 36% to 69% of patients failing to reach glycaemic control targets. These individuals are at an increased risk of developing diabetes-related complications, which impact negatively on their quality of life and have cost implications for healthcare providers [16].

Glucose control in Type 2 Diabetes deteriorates progressively over time, and, after failure of diet and exercise alone, needs on average a new intervention with glucose-lowering agents every 3-4 years in order to obtain/retain good control [17].

The management of the T2D patient is carried out on the front line by the general practitioner. It often requires multidisciplinary cooperation with dieticians, physical activity professionals, nurses, ... Diabetologists and other specialists may be needed.

I.1.5 - INITIAL TREATMENT

As long as a residual beta-cell function is retained, the therapy of T2D is designed to support the natural regulatory system instead of replacing it completely [13]. The treatment of T2D usually starts with oral antidiabetic drugs (OAD). Indeed, if patients are not able to reach their glucose target, they are prescribed the first line of T2D therapy – Metformin. Poor glycaemic control on metformin can lead to dual and even triple therapy where a patient is given an additional (or two additional) therapeutic(s). This can be a SGLT2 inhibitor or an incretin-based therapy (DPP4 inhibitor or GLP1 receptor agonist). If the patient also fails to achieve tight glycaemic control following this, they may expect to be prescribed insulin [18, 19]. Usually one or two daily injections of basal insulin are sufficient for an extended period [20]. The addition of basal insulin improves glycaemic control and achieves the target HbA1c level in over 50-60% of patients.

I.1.5.1 - INTENSIFICATION

For patients who are refractory to basal therapy in addition to previously prescribed antidiabetic agents, treatment intensification requires the addition of prandial insulin therapy to target the control of postprandial hyperglycaemia. The resulting regimen of multiple injections of rapid-acting insulin with basal insulin achieves target glycaemia in > 70% of patients but carries an increased risk of hypoglycaemia and body weight gain. Full compliance with insulin therapy regimens remains challenging, and injection anxiety, quality of life disruption, and discomfort are well documented obstacles [5].

I.1.5.2 - INSULIN PUMP AND CGM

In the OpT2mise trial, it was shown that for insulin-treated T2D patients with unsatisfactory glycaemic control on Multi Drug Injections (MDI) therapy a significant improvement (in terms of HbA1c, but also Time In Range) could be achieved by using an insulin pump [5-7].

In the Diamond trial, it was found that CGM use could help to improve glycaemic control on MDI therapy (HbA1c and Time In Range) for insulin-treated T2D patients [21].

It can be estimated that today T2D patients account for 17 to 20% of the total insulin pump users in France among an estimated total of 60 000 patients in 2018 (extrapolation from Air Liquide Healthcare data through its different affiliates like Orkyn, Vitalaire, LVL, and Dinno Santé). This estimated ratio is unique in Europe and may be explained by existing pump funding for T2D patients in France which is not the case in some other European countries where pump use is only funded for T1D patients.

A higher frequency of treatment discontinuation by T2D patients versus T1D can been observed at 6 months after treatment initiation, as well as 3 years afterwards. Most of treatment discontinuations before 6 months are associated with psychological issues regarding the acceptability of the device. Clearly T1D / T2D patients differ in many ways, and mainly in the fact that most T2D persons are not insulin dependent for several years.

This type of patients is usually older (an average age of 59 years for T2D patients). Therefore, these patients might see the pump as a new constraint associated with a new and invasive step in their disease. Moreover, using this device can induce some stress, for it involves comprehension and an active participation from the patients to make it effectively work. In this regard, it is key to educate patients and to train healthcare professionals, so they can provide the necessary help to ensure the proper and safe use of therapeutic tools, and empower the patients so they can manage their glycaemic control.

I.1.5.3 - CLOSED-LOOP SYSTEMS

The development of a closed-loop system that combines CGM with computer-based algorithm to determine the amount of insulin to be delivered by the pump may provide further improvements in both glycaemic control and reduction in the risk of hypoglycaemia. Hybrid closed-loop systems are characterized by automated insulin delivery system, apart from when the user administers insulin boosts at meal time. Superior control may delay the onset of macro- and microvascular complications of diabetes [22].

Several closed-loop (Artificial Pancreas (AP)) systems have been developed and successfully evaluated in people with type 1 diabetes leading to improved glucose control and less time in hypoglycaemia [23].

Opposed to the multitude of clinical trials in T1D, there is far less data with AP solutions in patients with T2D [24-28]. In those studies, it was found that AP had the potential to significantly improve Time In Range and to reduce time in hyperglycaemia for patients with T2D in hospital settings [13].

A closed-loop insulin delivery system has also been shown to be safe and feasible in insulin-naïve patients with T2D in a controlled research facility setting [28].

I.1.5.4 - OUTCOME MEASUREMENT

The ease and accuracy with which glycated haemoglobin A1c (HbA1c) can be measured has made it an invaluable clinical tool for the evaluation of the treatment effect for patients with diabetes. However, HbA1c has some inherent drawbacks. While HbA1c reflects average blood glucose over the last 2–3 months,

its limitation is the lack of information about acute glycaemic excursions and the acute complications of hypo- and hyperglycaemia events. HbA1c also fails to identify the magnitude and frequency of intra- and interday blood glucose variation [29]. Moreover, HbA1c is unreliable in patients with anemia, haemoglobinopathies or iron deficiency and in female patients who are pregnant [30, 31].

The introduction of CGM has provided an opportunity to develop metrics of glycaemic control that provide valuable information beyond that furnished by glycated haemoglobin A1c (HbA1c). Time In Range refers to the time an individual spends within the glucose target range (70 to 180 mg/dL) [31].

Up to now, HbA1c was considered as the surrogate marker of interest in diabetes.

Despite its perceived clinical value by clinicians and patients alike, the Food and Drug Administration (FDA) has not yet recognized TIR as a valid outcome in order to prove efficacy [32]. In France, the Haute Autorité de Santé (HAS) / Commission Nationale d'Evaluation des Dispositifs Médicaux et des Technologies de Santé (CNEDiMTS) is willing to consider a surrogate endpoint if validated for the prediction of the expected clinical outcome in a scientific paper [33].

Time In Range (TIR) may be used as an appropriate clinical endpoint in diabetes research and as a measure of glycaemic control in patients. Evidence suggests that TIR is inversely correlated to risk of developing vascular complications in patients with diabetes [32]. TIR is associated with the prevalence of diabetic retinopathy and/or microalbuminuria in T2D [21, 31, 32].

In 2019, the International Consensus panel at the American Diabetes Association (ADA) [49] identified "Time in Range" as a metric of glycaemic control that provides more actionable information than A1c alone. The panel agreed that establishing target percentages of time in the various glycaemic ranges with the ability to adjust the percentage cut points to address the specific needs of special diabetes populations (e.g., pregnancy, high-risk) would facilitate safe and effective therapeutic decision making within the parameters of the established glycaemic goals.

I.1.5.5 - AUTONOMY AND GLOBAL CARE OF PATIENTS

Patients play a central role in diabetes care because of their daily responsibility for a large number of behavioural choices and activities. More concretely, patients have to take into account their diet, exercise, medication administration, blood glucose testing, smoking behaviour and medical examinations, including inspections of eyes and feet. Such self-management is a complex activity and includes the ability to monitor one's condition and affects the cognitive, behavioural and emotional responses necessary to maintain a satisfactory Quality of Life (QoL).

Although modern care and education are becoming more patient-centred, many patients find it difficult to maintain adequate self-management. High-quality care is therefore needed, to better support patients' self-management abilities [15].

In France, approximately 25% of home-based T2D patients require assistance to manage their treatment. Most of them are elderly patients with several comorbidities requiring private visiting nurses paid by the National Social Security for assistance in the management of their T2D.

For some patients in need of intensification, logistics may be challenging as family nurse is expected to visit at meal times.

I.2 - INVESTIGATIONAL MEDICAL DEVICE

The investigated automated insulin delivery system is made up of 2 medical devices.

The medical devices components are:

- The Dexcom G6 Continuous Glucose Monitoring (CGM) system (CE marking, class IIb),
- The Tandem t:slim X2 Insulin Pump with Control-IQ Technology. The Control-IQ algorithm is implemented into the Tandem t:slim X2 Insulin Pump (CE marked for T1D patients).

The Tandem t:slim X2 Insulin Pump with Control-IQ Technology system allows automated glycaemia recording every 5 minutes and comparison to the pre-set target glucose range. The need for insulin subcutaneous infusion or carbohydrates consumption is automatically calculated if the glucose level rises above the pre-set glycaemia upper limit or drops below the pre-set glycaemia lower limit, respectively. If the upper limit is exceeded, the required amount of insulin is automatically delivered by the insulin pump. If the lower limit is dropped below, the required amount of carbohydrates to be ingested is indicated to the patient. However, for optimal performance of the system, carbohydrates announcements have to be performed before each meal. The performance of the Tandem t:slim X2 Insulin Pump with Control-IQ Technology system in T1D patients (adults and infants) has been demonstrated in several trials [25, 34, 35]. A FDA approval is expected by the end of 2019. However, the performance of the Tandem t:slim X2 Insulin Pump with Control-IQ Technology system in T2D has not been yet established while closed-loop algorithms have already been evaluated [24, 26, 27, 36]. An in silico study was performed to assess the performance of the University of Virginia (UVA) closed loop glucose control algorithm (as implemented in the Tandem t:slim X2 Insulin Pump with Control-IQ technology) in T2D patients data and using replay simulation methodologies [47]. More specifically, the objectives of this in silico study were to determine:

- The most appropriate mode of the Tandem t:slim X2 Insulin Pump with Control-IQ technology i.e., exercise or standard, for T2D patients,
- The basal insulin rate,
- If an insulin bolus fixed dosage could be used for every meal announcement.

This study has showed that all controller modes were safe and superior to open loop therapy. For both standard and exercise modes, a basal rate at 100% of the open loop values, associated with fixed meal bolus between 10 % to 20% of the total daily dose led to above 75% time between 70 and 180 mg/dL (versus 62% in open loop) with similar exposure to low glucose (below 70 mg/dL) at around 2.2% (or 30 min a day). Therefore, standard mode of Control-IQ algorithm including a fixed bolus between 10% to 20% of the total insulin daily dose (to be modulated based on clinicians observation in real-life use) and a basal insulin dosage at 100% of the initial value were identified as the recommended association of values for the setup and instructions during the conduct of the CLOSE AP+ study.

I.3 - RATIONALE OF THE STUDY

Closed-loop insulin delivery system has the potential to improve the condition of many poorly controlled insulin-treated T2D patients.

A wide acceptance of the AP usage in T2D care will strongly depend on the identification of subpopulations and care settings where the AP could significantly improve the risk- and cost-benefit balances of T2D management as compared to established practice [36].

The aim of this interventional study, therefore, is to investigate whether a therapeutic solution combining an automated insulin delivery AP system with a tailored HHP service can improve blood glucose control, reduce the rate of acute metabolic complications (hypoglycaemia and hyperglycaemia), improve both the patients quality of life and experience, and reduce the healthcare related costs in patients with uncontrolled Type 2 Diabetes needing home nursing care for their daily insulin treatment versus usual care.

I.4 - RISK AND BENEFITS OF THE INVESTIGATIONAL DESIGN AND CLINICAL INVESTIGATION

The **main benefit** for the patient that can be anticipated from the investigational design and clinical investigation is an improvement of his/her glycaemic control.

For the control group, an improvement may be expected from the insulin dosage adjustment based on the data collected by CGM. For the investigational group, an improvement is expected from the automated insulin delivery AP system with a tailored HHP service.

All **possible risks** identified from the investigational design and clinical investigation have been listed hereunder with the mitigation actions.

Item	Explanation	Mitigation details & actions
Inappropriate insulin dosage delivery	Wrong calculation of the insulin dosage by the algorithm (not performant) Failure of the automated delivery system	- An in-silico study was performed to assess the performance and efficiency of the algorithm on Type 2 patients' data (as mentioned in section I.2). The study concluded to the superiority of the closed-loop versus the open loop with TIR at 75% vs 62% respectively with no severe events. - A dedicated training of the patient and caregiver in case of hyper/hypoglycaemia (detailed in Appendix 4) and system failure/deficiency will be set up; - A hotline 24/24h by the HHC for medical devices support and issues will be implemented; - A hotline 24/24h by the investigator center for medical support is available; - Access to a first-aid kit including replacement insulin therapy will be ensured; - Same algorithm i.e. Control IQ used into 2 recent trials: The NIH-funded DCLP3 study (NCT03563313) and the French paediatric study Freelife Kid AP study (NCT03739099).

Item	Explanation	Mitigation details & actions
Inappropriate and suitable technology for T2D patients	Bad performance No medical benefits for patients No acceptability by patients	- Already existing published studies with Closed loops for Type 2 showing improved glycaemia controls [24, 26, 27, 36]. - An in silico study was performed to assess the performance of the University of Virginia (UVA) closed loop glucose control algorithm that is implemented in the Tandem t:slim X2 Insulin Pump with Control-IQ technology) in T2D patients. This study has showed that all controller modes were safe and superior to open loop therapy.

Insufficient Training and patients' monitoring	Complex home return Patients safety issues	- Training and care will be provided to patients, caregivers and healthcare professionals by the HHC with knowledges and skills assessment (Appendix 1); - The data monitoring during the first week following patient hospital discharge (pump in closed-loop) will be performed twice a day at minimum 6 hours interval by the family nurse at home and remotely by the investigator. - The family nurse will be present at patient home every day during the initiation period (pump in open mode). - The HHC will be present at home with the family nurse for the 1st medical devices set-up by the family nurse and the day of the patient will be back home. - The use of the devices (CGM, pump and pump with Control IQ technology) will be optimised with simplified instructions. - A dedicated training of the patient and caregiver in case of hyper/hypoglycaemia / system failure will be set up; - A hotline 24/24h by the HHC for medical devices support and issues will be implemented; - A hotline 24/24h by the investigator center for medical support is available; - Access to a first-aid kit including replacement insulin therapy (back-up solution).
Inappropriate Interface with family nurses	Lack of coordination and followup around patients at home	- HHC will ensure good interface and appropriate coordination with family nurse and all investigating center staff. - Family nurse will get all detailed contacts and information relating to the role and mission of each participating personnel. - Family nurse will be present every day during the initiation period, every 3 days during follow-up period reinforced by a twice daily visit during the first week of the follow-up period i.e. 1st week following patient hospital discharge; - The HHC will be present at home with the family nurse for the 1st medical devices set-up by the family nurse and the day of the patient will be back home; - The patient will be asked to mention in a specific diary all adverse events and device deficiencies/failure. Diary will be controlled at each visit of the family nurse and/or HHC.
Item	**Explanation**	**Mitigation details & actions**

Patient unable to use the device - lack of patients' support	Patients requiring one daily visit of family nurse at home at least	- Patients skills assessed for study's inclusion by the investigator; - Technical training as well as family nurses support will be provided to patients by HHC. The HHC will evaluate the patient's knowledge acquisition and skills after its technical training during each visit (Appendix 1); - Sequential plan (CGM, then Pump in open mode, then closed-loop system) and periods (selection, initiation, run in) for the set-up of the IMD system to patient including hospital stays (2 nights for open mode set-up and 2 nights for closed-loop set-up) and monitoring before home returns will be implemented; - Simplified process to enter a fix value for meal announcement with a dedicated and simplified instruction; - Each meal value entered in the Pump, as well as schedule and date will be taken back by the patient in his/her dedicated diary and checked by the family nurse during each visit; - Strong support provided at home including family and HHC nurses visits; - Usual visits provided by the family nurse at home during the first week then every 3 days for pump's consumables replacement and every 9 days for CGM sensor change; - A hotline 24/24h 7 days/7 by the HHC for medical devices support and issues will be implemented; - A hotline 24/24h by the investigator center for medical support is available - Regular feedbacks including alerts will be given to investigators by the HHC nurse in connection with the family nurse about the patient's knowledge acquisition and the control of his/her treatment. - Remote monitoring of connected IMD access possible by the investigators through dedicated web-based platforms (CLARITY® and t:connect®).
Study deviations - Lack of process to detect problems in the patient	Lack of reactivity to take appropriate measures	- Alert and recommendation from Sponsor Pharmacovigilance Department; - A DSMB will be put in place during the whole study duration with independent members. Definition of stopping rules and review of the safety data of the five first patients of each group, then after the 25 patients having completed the study, and more frequently if judged necessary by the DSMB. - Progressive patients recruitment (recruitment period during 13 months) with the support of approximately 10 centers.
Material safety issues	Device failure or misuse by the patient	- The educational materials are aimed at risk minimisation and will support safe and effective use of the product by the patient. The HHC will evaluate the patient's knowledge acquisition after each training (Appendix 1). - The Tandem t:slimX2 insulin pump basal-IQ is CE marked and ControlIQ algorithm was investigated into two recent trials, i.e. the NIH-funded DCLP3 study (NCT03563313) and the French paediatric study Freelife Kid AP study (NCT03739099).

Of note, where training is required and knowledges and skills assessed as described in Appendix 1, the level "en cours" or "acquis" must be obtained for each item by the patient. Otherwise, these levels must have been obtained by the caregiver.

II - STUDY OBJECTIVES

II.1 - PRIMARY OBJECTIVE

The primary objective is to determine whether the tested therapy strategy, composed of an automated insulin delivery system and home healthcare provider services, will improve glycaemic control, measured by the Time In Range (TIR) at the end of the study, in patients with uncontrolled Type 2 Diabetes needing home nursing care for their daily insulin treatment, compared to usual care (including multiple daily injection regimen).

II.2 - SECONDARY OBJECTIVES

The secondary objectives are the following:

- To assess glycaemic control,
- To assess safety,

[redacted]

III - OVERVIEW OF STUDY DESIGN

This is a randomised, national, multi-centre, open-label, prospective, controlled study performed in two parallel groups.

Approximately 10 public hospitals located in France and specialized in T2D care management will be recruited to enroll a targeted total number of 56 randomized patients with Type 2 Diabetes needing home nursing care for their daily insulin treatment (number of patients per group 28 with 1:1 ratio and estimated dropout of 25%). The randomization will be stratified according to the level of HbA1c at baseline (<10.0% or ≥10.0%). The patient recruitment period will last approximately 24 months and the individual patient study duration will be approximately 18 weeks +/- 2 weeks (including a selection, initiation and run-in period of 6 weeks +/-2 weeks and a follow-up period of 12 weeks). The total study duration from 1st selection to last completion is thus expected to last approximately 29 months.

IV - STUDY PATIENTS

IV.1 - ELIGIBILITY CRITERIA

Patient selection is based on the selection, inclusion and exclusion criteria listed below. Patients who meet each of the selection and inclusion criteria and none of the exclusion criteria are eligible to participate in this study.

All patients will receive oral and written information on the study and will sign a written Informed Consent Form (ICF) prior to any study specific assessments and before any data collection is performed.

IV.1.1 - SELECTION CRITERIA

During the selection visit (V0) detailed in section VI.2, the investigator will check that study eligible patients meet all the following selection criteria:

1. Male or female patient aged 18 years or older,
2. Type 2 Diabetes diagnosed for at least 6 months with a stable authorized antidiabetic therapeutic regimen for 3 months,
3. Treated with insulin for at least 6 months,
4. Patient with 8.0% ≤ HbA1c <12.0% within the last 3 months before selection,
5. Patient with a current minimum of 2 daily insulin injections and who would benefit of an optimisation,
6. Patient requiring long term family nurse's daily assistance at home for performing insulin injections and/or glucose monitoring,
7. Total daily insulin dose < 1.5U/kg,
8. Patient willing and able to complete the requirements of the study,
9. Patient living with a caregiver or a diabetes care partner, or patient living alone but with a caregiver living nearby who has a telephone and a key to his or her home,
10. Patient living in an area covered by a GSM (Global System for Mobile Communications) network and not considering a trip outside of France or out of an area covered by a GSM network within the planned dates corresponding to the 30 days of the installation of the pump (to cover the open-loop period and first 15 days of the closed-loop period) and the last 20 days of the study.

IV.1.2 - INCLUSION CRITERIA

Before randomisation, the investigator will check that study eligible patients meet all the following inclusion criteria:

1. Patient having demonstrated ability to understand the benefits and harms of the automated insulin delivery system and to continuously and safely wear a CGM, as per investigator's judgement,
2. Family nurse having demonstrated ability to use the automated insulin delivery system, as per Home Healthcare Provider (HHP) judgement,
3. Patient able to use basic technology such as a cell phone and having demonstrated ability to use the automated insulin delivery system, as per Home Healthcare Provider (HHP) judgment. In case the

patient has not demonstrated ability to use the automated insulin delivery system, his (her) caregiver has to demonstrate ability to use basic technology such as a cell phone and the automated insulin delivery system instead as per Home Healthcare Provider (HHP) judgment. The caregiver has to be an adult person able to speak and read French, having demonstrated ability to use the automated insulin delivery system, with no known medical condition that in the judgment of the investigator might interfere with the completion of the protocol. The caregiver must have committed to maintain uninterrupted availability via personal cell phone and to provide assistance to the patient and must be knowledgeable at all times of the participant's location during the day when closed loop is in use.

4. 14 days completed (i.e.≥ 70% of the daily data points non missing) CGM data from the selection period (the CGM period may be repeated only once if uncompleted data),
5. Patient covered by healthcare insurance (in accordance with French regulation),
6. Patient who has received verbal and written information about the study and who signed the informed consent form before any study related procedure.
7. Patient under curatorship must have received the agreement of their legal guardian to participate to the study.

IV.1.3 - EXCLUSION CRITERIA

During the selection visit (V0) detailed in section VI.2, the investigator will check that study eligible patients do not meet any of the following exclusion criteria:

1. Pregnant or breastfeeding woman,
2. Patient who experienced a severe hypoglycaemic event having led to a hospitalisation or having required a third party assistance within the past 6 months,
3. Patient who experienced a diabetic ketoacidosis within the past 6 months,
4. Patient who has demonstrated a marked decrease in hypoglycaemia perception defined by a Gold score > 4,
5. Patient who has disabilities which could compromise the compliance to the study, in the investigator's opinion,
6. Patient with severe health impairment resulting in short life expectancy (< 1 year) as assessed by the investigator,
7. Patient participating in another interventional or observational clinical trial or who participated in another interventional clinical trial within 30 days before selection,
8. Patient known allergy to any component of the automated insulin delivery system compounds,
9. Proliferative retinopathy (assessed with a fundus examination or retinal photography performed within 6 months before selection or before the randomisation at the latest) with visual impairment which could compromise the safety of rapid glucose control normalisation and the compliance to the study,
10. Planned initiation of a treatment that would impact the blood glucose levels (such as glucocorticoids, sulfonylurea, glinide) during the study period,
11. Patient deprived of liberty by a judicial or administrative decision, patient admitted to a social institution, patient hospitalized without consent or who is in an emergency situation,
12. Lack of effective contraception in women of childbearing potential,

13. Subject with a history of hearing or vision impairment hindering perception of glucose display and alarms (as this point is a contra-indication stated in the user's manual of the investigational medical device),
14. Severe impairment of renal function (Creatinine Clearance < 30 mL/min),
15. Patient on dialysis (as the user's manual of Dexcom G6 states that G6 readings may be inaccurate in this population),
16. Conditions which may increase the risk of induced hypoglycemia as per the investigator's judgment,
17. Inpatient psychiatric treatment in the past 6 months,
18. Current or recent abuse of alcohol or recreational drugs,
19. Patients that have frequent exposure to magnetic resonance imaging (MRI), computed tomography (CT) scan, or high-frequency electrical heat (diathermy) treatment (as this point is a contra-indication stated in the user's manual of the investigational medical device and Dexcom G6.

IV.2 - ROLE OF CAREGIVER

Patients who are not capable to follow all protocol instructions on their own as per investigator's judgment or who have not acquire all knowledge and skills required by the protocol as per Home Healthcare Provider (HHP) judgment (as described in Appendix 1), must have a caregiver who should be able to follow protocol instructions instead of the Patient.

The caregiver will assist the patient in the observance of the protocol instructions and in the management of his diabetes treatment.

The caregiver has to be an adult person, with no known medical condition that in the judgment of the investigator might interfere with the completion of the protocol and who committed to maintaining uninterrupted availability via personal cell phone and to provide assistance to patient. The caregiver must have demonstrated the ability to use basic technology such as a cell phone and to use the automated insulin delivery system as per Home Healthcare Provider (HHP) judgment.

IV.3 - STUDY DURATION FOR THE PATIENT

Trial termination is defined by the date of the last completed visit (actual or planned to be performed at the time of premature withdrawal if applicable) by the last participating patient. The maximum patient's individual study duration will be of 20 weeks.

IV.4 - PREMATURE STUDY DISCONTINUATION

The study could be interrupted temporarily or definitively by the Sponsor and/or the Ethics Committee (EC) and/or the Competent Authority (CA). If such a situation occurs, the investigator should promptly inform the patients and complete the study electronic Case Report Form (e-CRF) with all available data at that time. Study temporary or definitive discontinuation must be declared to Competent Authority (and EC if applicable) in accordance with French local requirements, including its reason such as:

- The investigational intervention is considered as too noxious (as per Ethics Committee (EC) and/or Competent Authority (CA) and/or DSMB (detailed in section IX.3) and/or Sponsor Pharmacovigilance Department recommendation);
- A new fact occurs that modifies Sponsor/Competent Authority approval on the trial, such as benefit/risk ratio for instance;
- Any unethical reason;
- Sponsor decision to discontinue the IMD development.

Also, patients have the right to withdraw from the study at any time for any reason, without prejudice to further treatment. All the data collected until then will be kept in the study, but not the data collected afterwards.
In addition, the Sponsor or the Investigator may decide to stop the trial or part of the trial at any time for a given patient.
Reasons for individual premature withdrawal recorded by the investigator in the e-CRF will include:

- At least 1 selection or inclusion criterion not met,
- Any lack of compliance to the study procedures which can compromise the safety of the patient and/or study progress and, in particular, for the investigational group only, the lack of safe and competent use of the automated insulin delivery system in both open and closed-loop features.
- Discontinuation of one of the investigational medical devices during the initiation and/or run-in periods.
- Less than 70% of CGM data recorded during selection period after having retried for an additional 14 days period of CGM recordings.
- Patient's inability to attend study visits, - Patient's consent withdrawal, - Death.

In these above mentioned cases, the patient will be withdrawn and replaced by another patient who will undergo the study protocol in the same study group if the withdrawal occurs before D3. The "end of study" module of the e-CRF (detailed in section VI.6) will be completed accordingly by the investigator and the date and reason of premature withdrawal will be reported in both the e-CRF and the patient's medical file. These withdrawn patients will return to their usual care therapy i.e., multiple daily injection insulin therapy and nursing care.

V - INVESTIGATIONAL THERAPEUTIC STRATEGY

The study investigational therapy is composed of an automated insulin delivery system made up 2 medical devices and of a tailored home healthcare provider service.

V.1 - OVERVIEW OF IMD: AN AUTOMATED INSULIN DELIVERY SYSTEM

An automated insulin delivery system uses an automated insulin delivery pump with an automated insulin delivery algorithm and an integrated CGM (iCGM) data to adjust basal insulin delivery and deliver automatic insulin correction boluses. The study automated insulin delivery pump is the Tandem t:slim X2 insulin pump in which the automated insulin delivery algorithm is directly implemented into the pump to form one medical device: the Tandem t:slim X2 insulin pump with the Control-IQ technology. The iCGM data will be transmitted from the Dexcom G6 Continuous Glucose Monitoring (CGM) system. Thus, the study automated insulin delivery system made up of 2 medical devices are:

- The Tandem t:slim X2 Insulin Pump with Control-IQ technology, hereafter entitled the "Pump".

- The Dexcom G6 Continuous Glucose Monitoring (CGM) system (CE marking, class IIb), hereafter entitled the "CGM".

The automated insulin delivery system allows automated glycaemia recording every 5 minutes and comparison to the pre-set target glucose range. The need for insulin subcutaneous infusion or carbohydrates consumption is automatically calculated if the glucose level rises above the pre-set glycaemia upper limit or drops below the pre-set glycaemia lower limit, respectively. If the upper limit is exceeded, the required amount of insulin is automatically delivered by the Pump. If the lower limit is dropped below, the required amount of carbohydrates to be ingested is indicated to the patient.

Insulin is not part of the automated insulin delivery system. The automated insulin delivery system is intended to be used with U100 Humalog® or NovoRapid® rapid-acting insulin analogues only. Use of insulin with lesser or greater concentration can result in under delivery or over delivery of insulin. This can cause a very high or a very low blood glucose.

V.1.1 - TANDEM T:SLIM X2 INSULIN PUMP WITH CONTROL-IQ TECHNOLOGY

This medical device consists of the Tandem t:slim X2 insulin pump with the Control-IQ algorithm system implemented to the pump.

The Tandem t:slim X2 Insulin Pump with Control-IQ technology package includes the following items:

- t:slim X2 Insulin Pump with Control-IQ Technology. The t:slim X2 Insulin Pump is made up of the t:slim X2 Insulin Pump (English product with units of insulin designated in mg) and the t:slim 3mL (300 units) cartridge.
- Pump Case.
- t:slim X2 Insulin Pump with Control-IQ Technology current user guide in English and the previous one in French with a summary of differences.
- USB Cable.
- Wall Power USB Adapter and plug adapter suitable for French electrical outlets.
- Cartridge Removal Tool.
- Assortment of infusion sets.

The infusion set will be changed by the family nurse every 3 days at the same time the cartridge is refilled.

V.1.1.1 - CONTROL-IQ ALGORITHM SYSTEM

The Control-IQ algorithm system is implemented in the pump. It includes automated insulin correction boluses for high blood glucose in addition to basal rate modulation and it has a dedicated hypoglycaemia safety system. The algorithm is initialized based on the patient's body weight and estimated total daily insulin dose. It calculates the required insulin infusion rate or suspends insulin delivery when low blood glucose is predicted, aiming at a predefined target glucose level by continuously adapting model parameters.

V.1.1.2 - T:CONNECT® DIABETES MANAGEMENT APPLICATION

The cloud-based t:connect® Diabetes Management Application is intended for patients with diabetes mellitus who use Tandem Diabetes Care® insulin pumps, their caregivers and healthcare providers in both

home and clinical settings. This t:connect® Application supports diabetes management through the display and analysis of information uploaded from Tandem Diabetes Care® insulin pumps and specified blood glucometers and/or CGM's.

The t:connect® Diabetes Management Application includes the following components:

The t:connect® HCP Portal which is used by HealthCare Providers (HCP) having collected patient's consent to view patient data that have already been uploaded by either the provider or the patient. Once an account is created, users can sign in to the HCP Portal without installing any additional software.

The t:connect® HCP Software which is an additional application for healthcare providers that must be installed on each computer that will be utilized to upload device data in HCP office. This software provides the computer a means to upload data successfully to the t:connect® Application through the HCP Portal, and does not need to be opened or started separately from the HCP Portal once installed. During the trial, the t:connect® HCP Software will not be used.

The t:connect® Patient Application which is used by patients to upload device data outside of HCP office, and to generate and view reports. Once patients upload their data, authenticated and authorized healthcare providers can view the patient's reports in the t:connect® HCP Portal. During the trial, the t:connect® Patient Application will be used by the family nurse and the HHP to upload device data at home.

During the CLOSE AP+ trial, patient glycaemic and insulin data will be uploaded at home from the Pump, through a dedicated laptop, to the web-based t:connect® platform by either the family nurse, or HHP or the investigator according to the study periods (further detailed in section VI).

V.1.2 - DEXCOM G6 CGM SYSTEM

The Dexcom G6 CGM medical device allows the continuous measuring of the glucose levels in the interstitial fluid.
The Dexcom G6 CGM is composed by:

- An auto-applicator: a one-touch applicator which easily inserts a small sensor just beneath the skin.
- A glucose sensor inserted under the skin which continuously measures glucose levels in interstitial fluid. The sensor is recommended to be fixed to a smooth surface in the abdomen, at least 8 cm far from insulin pump. The glucose sensor is calibrated according to the manufacturer's instruction. Once installed, no further calibration is required. The sensor is to be changed every 10 days (at maximum). In case of sensor wire rupture or detachment, the patient should contact the healthcare provider to avoid any infection or inflammation at the insertion site.
- A transmitter that is attached to the sensor after sensor's insertion. The Dexcom G6 CGM transmitter can only be paired with one medical device at the same time.
- A dedicated receiver: glucose measurements are generally displayed on the receiver (it will set in blind mode for all patients during the selection period) and updated every 5 minutes. Data are sent wirelessly (Bluetooth Low Energy) to the receiver (during the selection period for all patients and during the end of follow-up period for patients in the control group) or to the Pump (during the open-mode and closed-loop periods for patients in the Intervention group) through the transmitter. Pairing of the receiver to the transmitter can only be achieved if the distance between them does not exceed 6 meters.

Of note, any contact of sunscreens, insect repellents and/or skin care products should be avoided.

The following items are provided with the Dexcom G6 CGM medical device:

- USB Cable,
- Wall Power USB Adapter.

Accessory to Dexcom G6 CGM medical device, the cloud-based Dexcom CLARITY® has data interface capabilities. It is intended for use by both home users and healthcare professionals to assist people with diabetes and their healthcare professionals in the review, analysis, and evaluation of historical CGM data to support effective diabetes management.

During the CLOSE AP+ trial, the web-based Dexcom CLARITY® will be used by the healthcare professionals only during periods where patient is equipped with a blinded CGM. Patient glycaemic data will be uploaded at home, from the receiver through a dedicated laptop by the HHP to the Dexcom CLARITY® platform (further detailed in section VI).

V.2 - HOME HEALTHCARE PROVIDER (HHP) SERVICES

All referring HHP involved in the CLOSE AP+ trial will be trained to the protocol, study procedures and automated insulin delivery system use and management before starting their study participation.

HHP role consists in:

- delivering the investigational medical devices and associated consumables,
- training session of family nurses to study protocol including procedures, roles and responsibilities, and knowledge assessment,
- education and training sessions of family nurses on medical devices (Dexcom G6 CGM and t:slim X2 Insulin Pump with Control-IQ Technology) functioning, alert management, rescue medication, and knowledge assessment,
- performing education and training sessions of patients and caregivers on how to carry / wear the CGM and/or t:slim X2 Insulin Pump with Control-IQ Technology and how to manage alerts

  and alarms; giving instructions for 24/24 hours and 7/7 days support; performing knowledge assessments of the patients and their caregivers,
- motivating and encouraging the patient to respect the study procedures,
- creating the patient Dexcom CLARITY® account, pairing and blinding the CGM device components and uploading the data to the Dexcom CLARITY® platform,
- uploading the glycaemic and insulin data from t:slim X2 Insulin Pump with Control-IQ Technology, through the dedicated laptop, to t:connect® platform,
- visualizing and downloading (if needed) insulin and glycaemic data (from Dexcom G6 CGM or t:slim X2 Insulin Pump with Control-IQ Technology) and providing report to the investigational site,
- ensuring coordination between patients, caregivers, family nurse and investigating center staff,

- providing technical assistance for patients, caregivers and family nurses by providing Hotline 24/24h -7 days in case of technical complaints or device failure,
- providing technical intervention at home in case of any technical complaint and/or device replacement within 12 hours.

The Home Healthcare Provider will apply the Code of Practice for Home Healthcare Providers, set out in Appendix 2, for its stipulations that would be applicable to the CLOSE AP+ study.

Accordingly, the HHP is present:

In the investigational group:

- at patient home for Dexcom G6 CGM training and set-up procedure supervision (selection period)
- at hospital for t:slim X2 Insulin Pump with Control-IQ Technology set-up/take off (initiation, run_in and ending periods)
- at patient home for t:slim X2 Insulin Pump with Control-IQ Technology and/or Dexcom G6 CGM refreshing trainings (initiation and follow-up periods), at D3 (ideally at the time of the 1st bolus following the hospital discharge of the run-in period), at D9, D30, D60 and any time the patient requires it.

In the investigational group, and specific to the study for safety purpose, the Tandem Pump with ControlIQ Technology system data are uploaded to the t:connect® platform twice daily at 6 hours minimum interval during the first week (Day 3 to Day 9) by the family nurse (if the patient/caregiver is not able to do it) to allow the investigator to closely monitor the patient.

In the control group:

- at patient home for CGM trainings, at selection and follow-up (at D70) periods.

In addition, **for both study groups**, the HHP is present at the hospital for the study end planned at D90 as detailed in section VI.6.

V.3 - COMPARATOR INTERVENTION

In the control group, patients continue to receive their usual care which will be composed, according to the investigator's prescription, of basal-bolus multiple daily injection insulin treatment and glycaemic controls performed by family nurse during usual daily home visit(s).

In addition, glucose will be monitored through a Dexcom G6 CGM for 14 days at the selection period and for 20 days (to ensure exhaustive data capture for at least 14 days) at the follow-up period ending. The initial 14-day monitoring period can be extended by an additional 14-day selection period in case of missing CGM data points (corresponding to less than 70% of the data points available over the 1st CGM recording as per inclusion criterion detailed in section IV.1.2).

V.4 - USE OF THE INVESTIGATIONAL MEDICAL DEVICE

The automated insulin delivery system is to be used according to instructions given during the investigators, family nurses and patients training sessions. Knowledge assessment will be performed at the end of each training session.

All referring study sponsor and representative personnel, as well as the home healthcare providers nurses involved in the CLOSE AP+ trial will be trained to the automated insulin delivery system use and management before the study start.

Investigators have to refer to user guide of medical devices used in the clinical trial regarding contraindications, warnings and precautions.

V.4.1 - MANAGEMENT AND DISPENSING OF MEDICAL DEVICE

The two medical devices components of the study automated insulin delivery i.e. Dexcom G6 CGM and the Tandem t:slim X2 Insulin Pump with Control-IQ technology will be provided by their manufacturers.

The Sponsor will order the medical devices to each manufacturer separately. The manufacturers will send the medical devices already labelled for clinical trial to the HHP central office.

The medical devices will be distributed by the HHP nurses to patients and collected at the end of the study to return the used and unused medical devices back to the manufacturers.

Insulin is not provided by the manufacturer and will be purchased directly by the patients at their pharmacy.

V.4.2 - STUDY MEDICAL DEVICE: AUTOMATED INSULIN DELIVERY SYSTEM PACKAGING AND LABELLING

The Dexcom G6 CGM system will be provided in its commercial form (initial kit, consumables and replacement equipment) and labelled according to the needs of the clinical study by the manufacturer.

The Tandem t:slim X2 Insulin Pump with Control-IQ technology will be packaged in the form of an initial kit as described below and each box will be identified by a serial and/or batch number.

Initial kit components:

- t:slim X2 Insulin Pump with Control-IQ Technology. The t:slim X2 Insulin Pump is made up of the t:slim X2 Insulin Pump (English product with units of insulin designated in mg) and the t:slim 3mL (300 units) cartridge.
- Pump Case.
- t:slim X2 Insulin Pump with Control-IQ Technology current user guide in English and the previous one in French with a summary of differences.
- USB Cable.
- Wall Power USB Adapter and plug adapter suitable for French electrical outlets.
- Cartridge Removal Tool.
- Assortment of infusion sets.

Each of the components of the Pump may be provided independently of each other as replacement and/or consumable material.

Thus, throughout the study and according to the needs of the patients and following orders from the HHP, the manufacturer will send to the HHP central office the consumables and/or the replacement equipment.

V.4.3 - STUDY MEDICAL DEVICE: AUTOMATED INSULIN DELIVERY SYSTEM STORAGE

Upon receipt, the HHP central office will electronically record the received kits and will identify them by a unique number. The date of receipt will be also recorded. An acknowledgment of receipt will be sent to the Sponsor or its representative and kept in the sponsor's Trial Master File (TMF).

In case of anomaly or damage to the boxes provided, including packaging, the HHP central office will inform the manufacturer(s) within 24 business hours.

In case of batch recall, the manufacturer will warn the Sponsor and HHP central office. The HHP central office will follow its recall procedures and will inform the investigators.

The medical devices will then be stored in a ventilated room, in a dedicated location for the study and in accordance with their particular storage conditions (see storage conditions in the MD's operating manual).

The HHP central office will document any temperature excursions or non-compliance with the storage conditions required for the medical devices provided in their file, as well as corrective and preventive actions as appropriate.

V.4.4 - DISPENSATION OF STUDY MEDICAL DEVICE: AUTOMATED INSULIN DELIVERY SYSTEM

The investigator, the family nurse and the HHP nurse should use the study medical devices (MDs) only for patients who have consented to participate in the study. They will not use or authorize the use of the study MDs in circumstances other than those described in this protocol.

During the selection and inclusion visits, the investigator entrusts the management and initiation of the MDs to HHP. If the patient is deemed to be motivated and able to use the automated insulin delivery system as per investigator’s judgement, then the HHP will assign a Pump and CGM to the patient as per his/her randomisation group allocated.

The Dexcom G6 CGM system previously labelled for use in a clinical study is provided by the HHP nurse and delivered to patients at home for its set-up during the selection period. Additional consumables will be provided to allow sensor replacement up to the initiation visit at the hospital.

The Pump initial kit previously labelled for use in a clinical study is provided by the HHP nurse and delivered to the randomised patients in the investigational group on the first day of hospital at the initiation visit.

Those patients will also be provided with Dexcom G6 CGM consumables to cover the need up to the run-in visit at the hospital.

The MDs replacement can be performed either at the hospital by the investigator (run-in period) or at the patient's home by the family nurse or the patient’s caregiver trained by the HHP nurse. The HHP nurse will bring the assigned sensor box(es) to the patient's home.

The HHP nurse will maintain a record of the Pump and CGM kits provided to patients included in the study, including the following information:

- Identification of the study,
- Identification of the patient (including patient number in the study) to whom automated insulin delivery system under study is distributed,

- Date(s) of delivery to the patient, quantity(ies), batch/serial number(s) and number of kit(s) delivered to the patient (initial shipment, replenishment or replacement),
- Date(s) of return, quantity(ies), batch/serial number(s) and number of kit(s) used, partially used or not used by the patient (see section V.4.5). This information will also be recorded in the e-CRF.

V.4.5 - MANAGEMENT OF USED AND UNUSED IMD

Used kits (boxes and empty packaging) or partially used kits are retrieved and stored by the HHP until their inventory and reconciliation with the registration of kits administered to patients included in the study.

During the study, the Home Healthcare Provider will be responsible for the recycling of Dexcom receiver.

At the end of the study, the HHP will also recover all unused kits (MDs and consumables). He/she will then perform an accurate inventory and reconciliation of kits administered to patients with used or partially used kits and unused kits.

Once the reconciliation is done and after explicit agreement of the Sponsor, the HHP will be responsible for the return of the MDs to the manufacturer. The manufacturers will be responsible for the destruction and/or recycling. The Sponsor will capture a certificate of destruction / recycling, including the following information:

- Identification of destroyed / recycled study kits (batch number or patient number)
- Quantity of destroyed / recycled study kits
- Date and method of destruction / recycling
- Name and signature of the person (or company) responsible for the destruction / recycling of the MDs and consumables of the study.

The reconciliation forms and certificates of destruction/recycling will be kept in the HHP, Investigator Site File (ISF) and sponsor's Trial Master File (TMF).

Any laptop given during the clinical study to patient may be cleaned (hardware) and given to another patient. This recycling process guarantees the laptop does not contain any patient data.

V.5 - IMD ALLOCATION-RANDOMIZATION

At the end of the selection period, as detailed in section VI.2.1, study patients will be randomly assigned in a 1:1 ratio to either investigational group or control group according to a central computer-generated randomization scheme upon confirmation of their randomisation by their investigator.

The study randomisation numbers will be allocated sequentially according to a central allocation system, i.e., an Interactive Web Response System (IWRS), to limit the possible study group allocation bias. Before confirming the patient randomization, the investigator should record the patient's birth date (month and year), the informed consent signature date, the gender, the HbA1c level and the confirmation of the inclusion/exclusion criteria met.

The randomization will be performed by block and stratified on the HbA1c level (either <10.0% or ≥10.0%).

The patient will be equipped by the IMD attributed by the IWRS according to his/her randomization number. The randomization number will be automatically registered in the e-CRF at the end of the selection period. The patient will be informed by phone by the Investigator of the allocated group (control/investigational). IMD serial number allocated to each patient will be recorded in the e-CRF at the initiation visit (V1) as per the planned IMD dispensation procedure (see section V.4.4).

The randomization list will be generated via SAS® software by an independent statistician (i.e. out of the study team) of the Clinical Research Organization (CRO) delegated by the Sponsor. One signed paper copy and one electronic copy of the randomization list will be stored at the Quality Assurance Unit of the CRO. The randomization list and individual codes will be kept in the strictest confidentiality until the database lock. They will not be accessible to any study team member before the randomisation of a given patient by his (her) investigator. Especially, the randomisation blocks size(s) will not be revealed to any study team member until the database lock, keeping in mind that this block size may be unique for the whole randomisation list or that a combination of 2 or more variable block sizes may have been introduced in the randomization list prior to its computer-generation.

In case of screening failure prior to patient's randomization, the investigator will specify in the patient's eCRF the date and reason for his (her) non-randomization.

If a patient withdraws prematurely for any reason after D3, the attributed randomization code and attributed IMD will not be reused nor will the patient be allowed to re-enter in the study afterwards.

V.6 - INTERVENTION DURATION

Total duration of the intervention will be of approximately 15 weeks from initiation visit (V1) detailed in section VI.3 to end of study visit (V9) detailed in section VI.6 for patients randomised in the study investigational group.

For patients randomised in the control group, the total duration will be approximately 12 weeks from initiation visit (V1) detailed in section VI.3 to end of study visit (V9) detailed in section VI.6.

V.7 - OBSERVANCE/COMPLIANCE

All patients will receive appropriate training in the safe use of the automated insulin delivery system in both open and closed-loop features for investigational group, and training of CGM only for control group.

Patient ability to follow instructions for use of the automated insulin delivery system required by the protocol will be assessed by the investigator during the selection, initiation and run-in periods. The investigator reserves the right to withdraw patients who would not be able to follow the instructions.

Patients will then come back to their initial treatment. These patients will be replaced if the withdrawal occurs before D3.

Observance of patients during the follow-up period will be assessed by patient's family nurse, HHP and investigator, based on the quality of the glycaemic data and information provided by the patient in the patient's diary. Observance data will be collected in the e-CRF.

All patients will have regular contacts with the operational study team during the home study periods including 24/24 hours 7/7 days telephone support by home healthcare providers. In addition, a hotline 24/24h by the investigator center for medical support will be available.

V.8 - CONCOMITANT MEDICATIONS

Any initiation of medication that could interfere with the automated insulin delivery system or with insulin therapy **will not be authorized** during the course of the study. These medications include:

- Glinides,
- Sulfonylurea,
- Glucocorticoids* (*with the exception of patients treated with stable prednisone < at 10 mg equivalent per day since 3 months)
- Or any other medication that could interfere with glycaemic levels.

Authorized glycaemic control concomitant treatments are:

-Metformin, DDP4 inhibitors, GLP1-receptor agonists.

-First aid kit

In the event of any deficiency of one or more of the components of the automated insulin delivery system, the patient should have immediate access to a first aid kit including replacement therapy (fast-acting insulin and insulin pen).

Of note, acetaminophen is compatible (up to 1 g every 6 hours) with the study automated insulin delivery system.

VI - SCHEDULE OF ASSESSMENTS

VI.1 - STUDY FLOWCHART

Ten visits are planned in the study:

- A Selection visit (Visit 0)
- An Initiation visit (Visit 1)
- A Run-In visit (Visit 2)
- Six follow-up visits over a 3-month period (Visits 3 to 8) - An end of study visit (Visit 9).

The study flowchart is available and presented in Figure 1 and Figure 2 with detailed contents per study group allocated.

VI.2 - SELECTION VISIT (V0) AND SELECTION PERIOD

The selection will include two different steps: the patient will first be invited to participate in the trial during a consultation visit to his (her) diabetes specialist, performed at hospital. The second step consists of a 14- to 28-day blinded continuous glucose monitoring period at patient's home, including regular home visits performed by the HHP and the family nurse. Each step of this selection period is detailed below according to the healthcare professional in charge of its performance.

VI.2.1 - ROLES OF THE INVESTIGATOR

Before any inclusion, the Investigator will be trained to the use of the automated insulin delivery system by the HHP.

- At patient's selection visit (Visit 0), the Investigator will:
  - Perform a first verification of selection, inclusion and exclusion criteria to check the potential eligibility of the patient to the study, including resource person details for isolated patients.
  - Give an overview of the protocol to the patient. If the patient is interested in participating in the trial, the automated insulin delivery system will be presented and the different periods of the trial explained in detail to the patient and caregiver (if applicable).
  - Give the information letter to the patient and the patient will sign the informed consent form if he/she agrees to participate.
  - Perform the following evaluations:
    - Blood pregnancy test for women of child-bearing potential.
    - Review of the current treatment(s) including T2D treatments and nonauthorized concomitant medication (as mentioned in section V.8).
    - Physical examination including cognitive assessment (MoCA and/or MMSE), blood pressure, body weight and height.
    - Visual examination (fundus examination or retinal photography) except for patients with fundus examination or retinal photography examination performed within the 6 months before selection.
    - Laboratory data performed within the last 3 months: HbA1c, blood glucose, total cholesterol, triglycerides, HDL-Cholesterol, LDL-Cholesterol, serum albumin, AST, ALT, gamma GT and serum Creatinine, blood counts (Red Blood Cells (RBC), White Blood Cells (WBC), platelets, haemoglobin, hematocrit) with their sampling date, fasting status, unit and normal range in use in the local laboratory.
  - Give the schedule of home and hospital visits, [redacted] and the patient diary to the patient. The diary will be used by the patient to collect any adverse events and device failure/deficiencies occurring during the trial.
  - Collect the contact details of the family nurse and caregiver of the patient and forward contact details information of the patient (and caregiver if applicable) and family nurse to the HHP.
  - Plan the date of the initiation visit (Visit 1).
  - Complete the e-CRF.
- After CGM set-up and 14 days of blinded CGM monitoring at the patient's home, the Investigator will:
  - Receive the HHP report including information related to study conduct and CGM data collected over the 14-day continuous recording period.

- Control CGM data and determine if a second 14-day monitoring period is required in case of insufficient data collection.
- If collected data are suitable with study continuation, randomize the patient via IWRS.
- Inform the patient by phone of the allocated randomization group.
- Inform the HHP of the patient allocated randomization group.

[redacted]

VI.2.2 - ROLES OF THE HOME HEALTHCARE PROVIDER (HHP)

- Before the first visit at the home of the patient, the HHP will:
  - Acknowledge receipt of contact information of the patient (caregiver if applicable) and family nurse sent by the investigator.
  - Contact the family nurse by phone to explain the protocol and get his/her oral agreement for participation in the study. In case of refusal, all efforts will be made to identify another nurse who would be interested in participating in the study. The investigator may have previously contacted the family nurse to introduce the protocol.
  - Upon oral agreement, send the written contract to the family nurse and plan an appointment for training of the family nurse to the Dexcom G6 CGM. Of note, the family nurse will designate a substitute family nurse who will take over from him/her in case of absence. The same trainings will be performed for the family nurse and his/her substitute.
  - Collect the contract signed by the family nurse.
  - Train the family nurse to the use of the Dexcom G6 CGM system according to user guide, hotline number in case of product deficiencies or any questions regarding the product.
  - Plan subsequent training sessions with the family nurse.
  - Plan patient's home visit with the family nurse for installation of the Dexcom G6 CGM system.
- The HHP will visit the patient at home a first time to:
  - Deliver the Dexcom G6 CGM devices for 14 days data collection.
  - Provide a dedicated laptop for data uploading. All laptops will be collected by the HHP after the clinical study needs.
  - Train the patient and caregiver to the use of the Dexcom G6 sensor.
  - Supervise the insertion of the Dexcom G6 sensor, pairing of transmitter and receiver, configuration of the CLARITY® account on the dedicated laptop, and training of the family nurse to data upload. *Of note, display device will be set up as blinded device by the HHP.*

- Instruct the patient, the caregiver and the family nurse to precaution for use, e.g., maximal distance between sensor and receiver to be observed, handling of technical and emergency problems and adherence issues.
- Remind the patient of the next hospital visit date and of the schedule of the next visit (potential 2-nights hospitalization requirement, study design, etc.).
- Answer patient's and caregiver's questions.
- Remind the patient [redacted] to report adverse events and technical complaints in the patient diary.

- At the end of the 14-day recording period, the HHP will visit the patient at home for:
  - Uploading the Dexcom G6 CGM data to the CLARITY® platform.
  - Control of uploaded data. If quality requirements of recorded data are fulfilled (≥ 70% non missing data points), the Dexcom G6 CGM system will be kept in place and removed at hospital during the initiation visit. Otherwise, an additional 14-day recording period will be required and the Dexcom G6 CGM system will be changed.
  - Reporting of safety issues and technical complaints from the patient to the study investigator.
  - Immediately after the visit, a written report on validity of Dexcom G6 CGM recorded data and on patient ability to follow instructions for study continuation will be sent by the HHP to the investigator to proceed to randomisation. The report will also include information on all serious adverse events, non-serious adverse events and device deficiencies.
- After randomisation, the HHP will acknowledge receipt of information on randomization group (from e-CRF notification) and next visit schedule.
- **If the patient is randomized to the investigational group**, the HHP will organize an appointment for training of the family nurse to the automated insulin delivery system. The HHP will train the family nurse on the installation and use of the Pump in open mode. The family nurse will also be reminded of the procedure to change the Dexcom G6 sensor.
- After each visit, the HHP will complete the e-CRF [redacted].

VI.2.3 - ROLES OF THE FAMILY NURSE

- **Before the first study visit** at the home of the patient and after information on patient's participation to the trial, introduction to the study protocol by the investigator or HHP, and agreement for participation to the study (contract signature), the family nurse will:
  - Be trained to the use of the Dexcom G6 CGM by the HHP, problems management (emergency procedures, Dexcom G6 CGM replacement and hotline numbers to be called for either technical or medical issues) and upload of Dexcom recordings on the CLARITY® platform.
  - Plan the upcoming training sessions with the HHP.
  - Plan the visit for Dexcom G6 CGM installation at the patient's home with the HHP.

- **Visits at the patient's home**:
    - The frequency of family nurse visit(s) at the patient's home for standard diabetes care will remain the same as before initiation of the selection period.
    - The family nurse will visit the patient with the HHP nurse for installation of the Dexcom G6 sensor. During this visit, the family nurse will be reminded by the HHP on precautions of use of the Dexcom G6 CGM system, on emergency procedures, Dexcom G6 CGM replacement, and hotline numbers to be called (both technical and medical ones).
    - At each visit, the family nurse will remind the patient of the date of the scheduled visit at hospital of the study (potential 2-nights hospitalization requirement, study design, etc.), answer the questions of the patient (and caregiver if applicable) and control the information in the patient diary.
    - 10 days after Dexcom G6 CGM installation, the family nurse will change and replace the Dexcom G6 sensor.
    - If an additional 14-day recording period is required (> 30% missing data points), tasks listed above will be repeated during this additional CGM period.
    - The family nurse will be informed on randomization group by the HHP. If the patient is randomized to the investigational group, the family nurse will be trained to the automated insulin delivery system by the HHP.
- The family nurse will inform the HHP of any serious adverse events, any non-serious adverse events, and the device deficiencies/failure.
- [redacted]

VI.3 - INITIATION VISIT (V1) AND INITIATION PERIOD

The purpose of Visit 1 is to initiate the studied diabetes therapies in both randomized groups. The initiation period will start with a visit of the patient at hospital for data analysis of the Dexcom G6 CGM system. The proceedings of the initiation period will differ depending on the assigned group. **Patients randomized to the control group** will return to their usual T2D care with possible insulin dosage adjustment prescribed by the investigator further to CGM data review. **Patients randomized to the investigational group** will be provided with a new Dexcom G6 CGM sensor and a Tandem t:slim X2 insulin pump with control-IQ technology that will be installed at the hospital in open-mode for 14 days after a 48h observation period at the hospital.

VI.3.1 - ROLES OF THE INVESTIGATOR

- Based on CGM data collected during the last 14 days of CGM monitoring, the Investigator will define the basal and bolus settings of the pump for the investigational group patients and adjust insulin treatment prescription for the control group patients.

- During the visit of the patient at hospital:
  - **For all patients:** [redacted] ○ The investigator will fill in the e-CRF. In addition, the Investigator will check the patient diary, report in the e-CRF any adverse event or device deficiency reported by the patient in his/her diary or during the interview and report SAE and device deficiency according to section VIII.2.2.
    - ○ The following evaluations will be performed:
      - Adverse events and device failure/deficiencies
      - Physical examination, blood pressure and body weight
      - Concomitant medications
      - Laboratory data: HbA1c, blood glucose, total cholesterol, triglycerides, HDL-Cholesterol, LDL-Cholesterol, serum albumin, AST, ALT, gamma GT and serum Creatinine, blood counts (Red Blood Cells (RBC), White Blood Cells (WBC), platelets, haemoglobin, hematocrit) with their sampling date, fasting status, unit and normal range in use.
  - **For patients randomized to the control group**: ○ The Dexcom G6 sensor will be removed and other parts i.e., receiver and transmitter, collected.
    - ○ The patient will be reminded of the installation of a CGM for 20 days at Day 70. ○ The patient will be provided with the schedule of visits at home and at the hospital, with the patient diary [redacted]
  - **For patients randomized in the investigational group**: ○ Pump will be installed.
    - ○ Patient visit will include 2 nights at hospital for patient observation following the set-up of the Dexcom G6 CGM system with the Pump in open mode.
    - ○ The patient (and the caregiver if applicable) will be trained to the use of the Pump and CGM in open mode, specifically on the management of alarms or alerts on the pump and on meal information entry into the pump for bolus insulin delivery (always the same value to facilitate the entry and avoid carbohydrate calculation). Patients will be provided with a short notice describing the management of meals announcement before leaving hospital.
    - ○ After 48h of observation, the Investigator will ensure that the patient (or the caregiver) is able to go back home and follow the instructions for study continuation, and plan the date of the next visit at the hospital to initiate the

Run-in period. Otherwise, the patient will be withdrawn from the study and replaced.

- The patient will be reminded of the next steps of the protocol and will be provided with the schedule of visits at home and at the hospital, with the patient diary [redacted]
- The investigator will fill in the e-CRF.
- During the next weeks, the investigator will have access to patient's glycaemic data through the cloud-based t:connect® platform and will be trained by the HHP to the display and exploitation of data on the t:connect® platform. The investigator will receive the report from the HHP following his/her visit at patient home.
- After Visit 1, the investigator will complete the e-CRF [redacted]

VI.3.2 - ROLES OF THE HOME HEALTHCARE PROVIDER (HHP)

- **Patients randomized in the control group**:
  - The HHP will attend the visit at the hospital to collect the Dexcom G6 CGM devices, the dedicated laptop and fill the related certificate.
  - The HHP will contact the family nurse to plan the date for the installation of the Dexcom G6 CGM system at Day 70 at the patient's home.
  - The HHP will remind the patient to report adverse events and/or device deficiencies/failure in the patient diary.

- **Patients randomized in the investigational group**:
  - The HHP will attend the visit at the hospital for: ○ Installation of a Dexcom G6 CGM system with the Tandem t:slim X2 insulin pump in open mode.
    - ○ Training of the patient (and the caregiver if applicable) to the use of the Tandem t:slim X2 insulin pump, to the management of alarms, alerts, hotline numbers, contact details in case an HHP intervention would be required.
  - A dedicated training session for the family nurse(s) will be organized before his (her) visit to the patient. The family nurse will be trained to the use of the Tandem t:slim X2 insulin pump especially in open mode, to the management of alarms, alerts and instructions in case of issues and/or required materials replacements. At the end of the training session, a validation of knowledge acquired will be performed.
  - The HHP nurse will attend the visit during which the family nurse will change the catheter and refill the cartridge of the Pump for the first time for:
    - Delivery of all required supplies for the following 2 weeks.
    - Reminders on the instructions for the use of the Tandem t:slim X2 insulin pump in open mode if required.
    - Reminders to the patient (and the caregiver if applicable) and the family nurse on the management of alarms, alerts, hotline numbers (both technical and medical ones), contact details in case an HHP intervention would be required.
    - Upload of Dexcom G6 CGM and pump data on the cloud-based t:connect® platform.

- Reminders to the patient of the date and duration of the next visit at hospital.
- Reminders to the patient to report adverse events and device deficiencies in the patient diary [redacted]

- After each visit, the HHP will send a report to the investigator including the glycaemic/insulin data observed, a notification of any adverse events and device failure/deficiencies observed or reported by the patient, as well as any additional relevant information.

- The HHP nurse will complete the e-CRF [redacted].

VI.3.3 - ROLES OF THE FAMILY NURSE

- **For patients of the control group**:
  - The frequency of family nurse visits at patient home will remain unchanged: the family nurse will visit the patient at home for standard diabetes care, as prescribed by the Investigator.
  - The family nurse will remind the patient to report adverse events and device failure/ deficiencies in the patient diary and the date of the Dexcom G6 CGM system future set-up (D70).
  - The family nurse will immediately inform the HHP nurse of any adverse events or device failure/deficiencies occurring during the trial period.
- **For patients of the investigational group**:
  - The family nurse(s) will be trained to the use of the Tandem t:slim X2 with control IQ technology system and to the upload of data and to data visualisation on the t:connect® platform.
  - The family nurse will administer the insulin bolus during his (her) visit at the patient's home using the Tandem t:slim X2 insulin pump as instructed during his (her) training. The frequency of the daily home nurse visit(s) will remain the same as for standard diabetes care during the initiation period.
  - The family nurse will replace the catheter and refill the insulin cartridge of the Pump every 3 days at home.

    The family nurse will change and replace the Dexcom G6 sensor every 9 days and upload the Dexcom G6 CGM and pump data on the cloud-based t:connect® platform.
  - The family nurse will be reminded of the date of the next visit at the hospital and of the procedures to be performed until then.
  - During each visit at the patient's home, the family nurse will ensure that any adverse events and device failure/deficiencies will be reported by the patient in his/her diary. The family nurse will immediately inform the HHP nurse of any adverse events or device deficiencies/failure occurring during the trial.

[redacted]

VI.4 - RUN-IN VISIT (V2)

The run-in visit purpose will be to finalize the installation of the automated insulin delivery system studied in the investigational group. Thus, this visit will be the starting point of the evaluation of the tested strategy

therapy. The run-in visit is performed at the hospital **for patients of the investigational group only**. It will consist in a 2-night hospitalization for the automated insulin delivery system to be initiated (closed-loop mode), the settings adjusted and the patient trained to the management of the automated insulin delivery system in closed-loop mode.

VI.4.1 - ROLES OF THE INVESTIGATOR

- The Investigator will be trained to the automated insulin delivery system in closed-loop mode and to the display and exploitation of data on the t:connect® platform.
- The Investigator will set up the automated insulin delivery system and define the settings based on insulin pump and CGM data collected during the initiation period, using the standard mode of the algorithm. The patient will be closely monitored to ensure the settings and mode chosen are safe.
- Depending on the date of the last change of the Dexcom G6 sensor, the sensor should be changed during the run-in visit.
- The patient (and the caregiver if applicable) will be re-trained to enter meal information in the pump for bolus insulin delivery (always the same value to facilitate the entry and avoid carbohydrate calculation). The Investigator must ensure and confirm that the patient (or the caregiver) will be capable to handle the automated insulin delivery system and follow instructions on tasks to be performed at home for continuation of the study. Otherwise, the patient will be withdrawn from the study and replaced if the withdrawal occurs before D3.
- The investigator will perform a confirmatory fingerstick blood glucose measurements during the first 12 hours after closed-loop mode activation.
- The investigator will instruct the participant or their caregiver to perform a confirmatory fingerstick blood glucose measurements in the following situations:
  - In case of symptoms of hypoglycemia although CGM glucose is > 80 mg/dL ● If 20 minutes after fast-acting oral glucose intake, CGM glucose is still < 80 mg/dL ● If 2 hours after bolus insulin, CGM glucose is still > 250 mg/dL.
- The following assessments will be performed:
  - Adverse events and device deficiencies/failure collection ● Physical examination, blood pressure and body weight ● Concomitant medications.
- Before leaving the hospital:

  [redacted]The patient and/or his (her) caregiver will be provided with: [redacted]
    - Guide on the management of alarms, alerts, hotline numbers,
    - Contact details in case of technical intervention required with emergency and replacement procedures,
    - Contact details in case of a medical emergency, ○ Roles of the investigator, the HHP and the family nurse, ○ The patient diary including a specific section for bolus reporting, ○ The date of the end of study visit planned.

- The Investigator will complete the e-CRF [redacted]

[redacted]

VI.4.2 - ROLES OF THE HOME HEALTHCARE PROVIDER (HHP)

The HHP will attend the run-in visit at hospital for the switch to the automated insulin delivery system from open to closed-loop mode.

During this visit, the HHP will:

- Train the patient (and the caregiver if applicable) to the use of the automated insulin delivery system in closed-loop mode.
- Identify, with the Investigator, the strengths and weaknesses in the patient (and caregiver if applicable) understanding of the management of the closed-loop system and re-explain the tasks that are not fully understood.
- Verify the connection of the Pump to the t:connect® platform to ensure the Investigator has access to data.

After the visit, the HHP will complete the e-CRF [redacted]

VI.4.3 - ROLES OF THE FAMILY NURSE

The family nurse will not be directly involved in the run-in visit. The HHP will contact the family nurse to schedule an appointment at patient home the day after hospital discharge.

VI.5 - FOLLOW-UP VISITS (V3 TO V8)

The Investigator will not attend the follow-up visits at patient's home, but he/she will receive the reports of each of them and he/she will be alerted if needed by the HHP. These visits will be performed at the patient's home by the HHP to ensure that the patient manages safely the automated insulin delivery system, that all procedures are performed according to the protocol, to control the upload of data on the t:connect® platform and to resupply the patient with all materials required i.e., Dexcom G6 CGM sensors and transmitter and Tandem t:slim X2 insulin pump catheters and cartridges.

VI.5.1 - ROLES OF THE INVESTIGATOR

During the follow-up period, the Investigator will perform a remote follow-up of glycaemic and insulin data.

Specific vigilance during the first 10 days

During the first 10 days: the Investigator will verify glycaemia on the t:connect® platform twice a day at 6 hours minimum interval to ensure optimal settings of the pump and patient's safety. If pump settings have to be modified, the Investigator will contact the family nurse who will modify the pump settings according to the new written prescription received. Changes in pump settings and safety information must be entered by the Investigator in the e-CRF.

From 11th day onwards, the Investigator will analyze the report sent by the HHP after each visit.

The Investigator will be immediately notified by the HHP of any adverse event, and/or device deficiencies/failure occurring during this period. Safety information will be reported by the Investigator in the e-CRF.

VI.5.2 - ROLES OF THE HOME HEALTHCARE PROVIDER (HHP)

- **For patients of the investigational group (Visits 3 to 7)**:
  - The HHP will visit the patient at home the day after the end of hospitalization (Day 3, visit 3) in the presence of the family nurse, the day of the first CGM sensor change (Day 9, visit 4), 1 month (Day 30, visit 6), and 2 months (Day 60, visit 7) after the set-up of the automated insulin delivery system in closed-loop mode.
  - In addition, the HHP will call the patient at Day 15 (Visit 5). The visits 3 to 7 and the phone call at day 15 are intended to:
    - Ensure that the patient enters meal information in the Pump for bolus insulin delivery and knows how to do it.
    - Remind the patient of the management of alerts, alarms and emergency issues. The contact details of the persons to be contacted in case of safety or technical issues will be reminded to the patient. The HHP will ensure that adverse events and/or device deficiencies will be reported by the patient in his/her diary. Any mismanagement of the system will be reported to the Investigator.
    - Ensure that data are uploaded on the t:connect® platform and remind the family nurse of the procedures for data upload (performed twice a day with 6 hours minimum interval during the first 10 days following patient hospital discharge and at each visit afterwards).
  - In addition, the HHP will provide the patient every month with required supplies for automated insulin delivery system.
  - [redacted]
  - During the follow-up period, the HHP will also perform a remote follow-up of glycaemia and insulin data. Serious adverse events, non-serious adverse events possibly related to the IMD, to investigation procedures or to diabetes and device deficiencies/failure will be immediately notified to the Investigator.

- **For patients of the control group (Visit 8)**:
  - An appointment for Visit 8 will be planned 20 days before the study end visit to set up a new Dexcom G6 system for a 20-day continuous glucose monitoring period. This visit will be performed with the family nurse.
  - The patient will be reminded of the precautions of use of the Dexcom G6 CGM, on management of emergency problems and device deficiencies/failure. The HHP will also

remind the patient of completing the patient diary, of the date of the next visit at hospital (Visit 9) [redacted]

- The HHP will configure the CLARITY® account and remind the family nurse of the process of data upload on the CLARITY® platform. The family nurse will also be reminded to check that the patient fills in the patient diary and to report any adverse event or device deficiencies/failure to the HHP.

[redacted]The HHP will complete the e-CRF [redacted]

VI.5.3 - ROLES OF THE FAMILY NURSE

- **For patients of the investigational group**:

On Day 3, the family nurse will be trained by the HHP to the upload of data and to data visualisation on the t:connect® platform.

Specific vigilance during the first 7 to 10 days

From the first day after patient discharge (Day 3) to the day of first CGM sensor change, the family nurse will visit the patient at least twice a day at 6 hours minimum interval to ensure the patient uses the pump safely, to upload data from the pump to the t:connect® platform, to ensure the patient enters the fixed bolus corresponding to 10% to 20% of his(her) total insulin daily dose as the meal value in the Pump as instructed by the investigator, and to ensure more globally the patient uses the automated insulin delivery system in a right way.

- From 11th day onwards (after the first CGM sensor change), the family nurse will visit the patient every 3 days.
  - At each visit, the family nurse will:
    - change the Pump catheter and refill the cartridge,
      - control the charge of the battery and charge it if necessary,
      - ensure that the patient enters meal value in the pump,
      - ensure that adverse events and device deficiencies/failure are reported by the patient in his/her diary. Any adverse event and/or device deficiencies/failure must be reported by the family nurse to the HHP. **Every 3 visits**, the family nurse will change the CGM sensor.
    - upload data from the Pump to the t:connect® visualisation platform.

- **For patients of the control group**:
  - The frequency of visit(s) at the patient's home will remain the same as before study initiation, as defined by the medical prescription. In addition to usual diabetes care, the family nurse will ensure that adverse events and device deficiencies are reported by the patient in his/her diary.

    The family nurse will immediately inform the investigator of any adverse event occurring during the trial. [redacted]

- Visit 8 at the patient's home will be planned with the HHP.
- Twenty days before the study end (D70, visit 8), a new Dexcom G6 CGM system provided by the HHP will be installed for a 20-day continuous glycaemia recording period. During Visit 8, in addition to usual care, the family nurse will:
  - Install the new blinded Dexcom G6 CGM system,
  - Be trained by the HHP to the procedure of data upload and data visualisation on the CLARITY® platform,
  - Be reminded by the HHP on the precautions to use the Dexcom G6 CGM system and on the procedures in case of emergency or technical issues.

[redacted]

- [redacted]

VI.6 - END OF STUDY VISIT (V9)

The end of study visit will be performed at the hospital to unequip and remove the devices, and perform the evaluations required by the protocol. All patient materials will be collected and the patient will be switched back to MDI T2D care as per investigator's prescription.

VI.6.1 - ROLES OF THE INVESTIGATOR

At the end of study visit, the Investigator will:

- Remove the Dexcom G6 CGM (**for every patient**) and the Tandem t:slim X2 Insulin Pump (**for patients of the investigational group only**). Before removing the devices, the Investigator will ensure that data have been collected by the HHP.
- Perform the following evaluations:
  - Adverse events and device deficiencies/failure.
  - Concomitant medications.
  - Physical examination, blood pressure and body weight.
  - Laboratory data: HbA1c, blood glucose, total cholesterol, triglycerides, HDL-Cholesterol, LDL-Cholesterol, serum albumin, AST, ALT, gamma GT and serum Creatinine, blood counts (Red Blood Cells (RBC), White Blood Cells (WBC), platelets, haemoglobin, hematocrit) with their sampling date, fasting status, unit and normal range in use.
- Collect [redacted], the patient diary and study documentation.

[redacted]

VI.6.2 - ROLES OF THE HOME HEALTHCARE PROVIDER (HHP)

The HHP will attend the end of study visit at the hospital to:

- Upload data from the Dexcom G6 receiver to the CLARITY® platform for patients of the control group, and data from the Tandem t:slim X2 Insulin Pump to the t:connect® platform for patients of the investigational group,
- Collect and return Dexcom G6 CGM, Tandem t:slim X2 Insulin Pump devices and dedicated laptop (as detailed in section V.4).

VI.6.3 - ROLES OF THE FAMILY NURSE

The family nurse will not attend the end of study visit at the hospital. The HHP will contact the family nurse to provide her (him) with information regarding the new patient MDI T2D care as per investigator's prescription. [redacted]

VI.7 - ASSESSMENTS AND PROCEDURES

VI.7.1 - PATIENT'S ASSESSMENTS AND PROCEDURES

Figure 2: STUDY FLOWCHART of EXAMINATIONS and EVALUATIONS Figure 2A-Investigational Group

EXAMINATIONS AND EVALUATIONS	SELECTION	INITIATION	RUN-IN	FOLLOW-UP					
	VISIT 0	VISIT 1	VISIT 2 D0-D2	VISIT 3 D3	VISIT 4 D9	VISIT 5 D15	VISIT 6 D30	VISIT 7 D60	VISIT 9 D90
Information letter + Informed consent form	X								
Demographics child-bearing potential (blood pregnancy test)	X								
Medical and surgical history	X								
Physical examination, blood pressure and body weight (and height at Selection)	X	X	X						X
Cognitive assessment MOCA and/or MMSE	X								
Concomitant medication	X	X	X	X	X	X	X	X	X
Fundus examination	X								
Selection, Inclusion and Non Inclusion criteria	X	X							
Randomisation	X								
Laboratory data: HbA1c, blood glucose, total cholesterol, triglycerides, HDL-C, LDL-C, serum albumin, creatinine, AST, ALT, blood counts, gamma GT	X	X							X
CGM system									
Patient equipment & training		X							
CGM replacement by family nurse	X	X		X	X	X	X	X	
CGM removal									X
Remote monitoring	X	X							
Pump System									
Patient equipment & training		X Open mode	X Closed-loop						
Catheter changes & cartridge fill in, battery charge		X	X	X	X	X	X	X	X
Remote monitoring				X	X		X	X	X
Pump system removal									X
Home Healthcare Provider Services									
Patient 24/7 technical support and motivation	X	X	X	X	X	X	X	X	X
Family nurse training	X	X		X					
Patients, Caregivers training and motivation	X	X	X	X					
Pump data upload and follow-up			X	X by family nurse	X by family nurse		X	X	X
CGM data upload and follow-up	X	X							
Prescriber reporting	X	X		X	X	X	X	X	

Figure 2B: Control Group

EXAMINATIONS AND EVALUATIONS	SELECTION	INITIATION	FOLLOW-UP	
	VISIT 0	VISIT 1 D0	VISIT 8 D70	VISIT 9 D90
Information letter + Informed consent form	X			
Demographics child-bearing potential (blood pregnancy test)	X			
Medical and surgical history	X			
Physical examination, blood pressure and body weight (and height at Selection)	X	X		X
Cognitive assessment MOCA and/or MMSE	X			
Concomitant medication	X	X	X	X
Fundus examination	X			
Selection, Inclusion and Non Inclusion criteria	X	X		
Randomisation	X			
Laboratory data: HbA1c, blood glucose, total cholesterol, triglycerides, HDL-C, LDL-C, serum albumin, creatinine, AST, ALT, blood counts, gamma GT	X	X		X
CGM system				
Patient equipment & training	X		X	
CGM replacement by family nurse	X		X	
CGM removal		X		X
Remote monitoring	X		X	
Home Healthcare Provider Services				
Patient 24/7 technical support and motivation	X			
Family nurses, Caregivers training and motivation	X		X	
CGM data upload and follow-up	X	X		X
Prescriber data reporting	X			

VI.7.1.1 - DEMOGRAPHICS AND CHILD-BEARING POTENTIAL

Patients' demographics (age, gender) will be collected at selection visit.
A blood pregnancy test will be performed at selection visit for women of child-bearing potential to verify that no pregnant female patient is included in the study. Breastfeeding information will also be collected.

VI.7.1.2 - MEDICAL AND SURGICAL HISTORY

Relevant medical and surgical history and comorbidities will be collected at selection visit. The T2D must have been diagnosed for at least 6 months prior to the selection visit.

VI.7.1.3 - PHYSICAL EXAMINATION, BLOOD PRESSURE, BODY WEIGHT AND HEIGHT

The following examinations and assessments will be performed at each visit at hospital:

- Height (**at selection visit only**)
- Body weight
- Blood pressure: both systolic and diastolic resting blood pressures will be measured after 5 minutes rest in supine position. The arm with the highest mean diastolic blood pressure at selection will be recorded in the e-CRF and used for all subsequent measurements
- Physical examination including cognitive assessment (MoCA and/or MMSE score **at selection visit only**).

VI.7.1.4 - TREATMENTS

- **T2D treatment history**

History of T2D treatments (trade name, start/end date) will be collected at selection visit. Patients must have been treated with insulin for at least 6 months prior to their selection visit. Patients prescription for daily insulin treatment and glycaemic control by a home family nurse will be collected at selection. Patients must require daily home nurse care for their insulin treatment at the time of their selection visit.

- **Concomitant medication**

Current treatments (trade name, start/end date) for comorbidities will also be collected at each visit performed at hospital.

- **Insulin**

Insulin (trade name, start/end date) used during the study will be collected. Of note, the automated insulin delivery system is intended to be used with U100 Humalog® or NovoRapid® rapid-acting insulin analogues only.

- **IMD use (for patients in the investigational group only)**

Time on auto-mode defined as the percentage of time spent with activated closed-loop of the insulin administration system over 24-h day will be computed based on the data continuously recorded into the Pump. In addition, patient compliance to the IMD will be collected at each visit by the investigator both on patient medical file and in the e-CRF by asking questions to the patients and checking the patient diary. The reason for any non-compliance, including treatment and/or study discontinuation will be recorded in both patient medical file and e-CRF by the Investigator.

VI.7.1.5 - FUNDUS EXAMINATION OR RETINAL PHOTOGRAPHY

Patients with proliferative retinopathy can not be included in the study. If the last fundus examination or retinal photography examination is dated more than 6 months, a new fundus examination or retinal photography will be requested by the investigator. The examination must be performed before randomisation.

VI.7.1.6 - PREGNANCY TEST

A blood pregnancy test will be performed at selection visit for women of child-bearing potential.

VI.7.1.7 - LABORATORY DATA

The following assessments will be performed at Selection, Initiation and End of study visits:

- Glycaemic control: blood HbA1c, blood glucose.
- Lipid profile: total cholesterol, triglycerides, HDL-Cholesterol, LDL-Cholesterol.
- Hepatic function: serum albumin, AST, ALT, gamma GT.
- Kidney function: serum creatinine.

- Blood counts (Red Blood Cells (RBC), White Blood Cells (WBC), platelets, haemoglobin, and hematocrit).

VI.7.1.8 - GLYCAEMIC CONTROL AND GLYCAEMIC VARIABILITY

In addition to HbA1c assays, the glycaemic control and variability will be computed based on the continuous measurement of the glucose values recorded after wearing the CGM device in blinded mode during the 14 consecutive days of the selection period and every day from D70 to D90.

VI.7.1.9 - ADVERSE EVENTS/DEVICE DEFICIENCIES/FAILURE

Safety assessments will consist in evaluating all serious and non-serious adverse events (AE), and device deficiencies/failure occurring from the Informed Consent Form (ICF) signature until the end of the study.

At each visit, occurrence of AEs and device deficiencies/failure should be inquired and follow-up of previously reported AEs and device deficiencies/failure should be performed. Related essential data should be recorded in the patient's medical file and in the e-CRF by the Investigator.

For the AEs, the following data will be recorded in the e-CRF:

- Description of the AE
- Seriousness of the event
- Onset and resolution dates of the AE
- Severity of the AE (mild, moderate or severe)
- Causality with regards to IMD
- Causality with regards to investigation procedures
- Action(s) taken regarding the IMD - Corrective treatment/therapy given - Event outcome.

In addition, the following parameters will be considered for assessment of the safety profile of automated insulin delivery system:

- Hypoglycaemic events defined as at least 10 min of continuous CGM readings below the thresholds of (1) 70 mg/dL (3.9 mmol/L) or (2) 54 mg/dL (3.0 mmol/L),
- Non severe hypoglycaemic events, being defined by CGM readings between < 70 mg/dL (3.9 mmol/L) and ≥ 54 mg/dL (3.0 mmol/L),
- Severe hypoglycaemic events being defined by CGM readings < 54 mg/dL,
- Severe hypoglycaemic events requiring third party assistance,
- Severe hypoglycaemic events requiring hospitalization,
- Severe hyperglycaemic events being defined by CGM readings ≥ 300 mg/dL for over 1 hour, - Device incidents and deficiencies.

A Data Safety Monitoring Board (DSMB) will review the safety data of the five first patients of each group, then 25 patients having completed the study, and more frequently if judged necessary by the DSMB.

VI.7.1.10 - [redacted]

[redacted]

[redacted]

https://www.usability.gov/how-to-and-tools/methods/system-usability-scale.html

[redacted]

[redacted]

[redacted]

VII - ENDPOINTS

VII.1 - PRIMARY ENDPOINT

The primary endpoint will be Time In Range (TIR) at D90, defined as the percentage of time spent with CGM glucose measurements at 70-180 mg/dL (including boundaries), during the last 14 days completed of CGM recording between D70 and D90 at the end of the study period.

For any of the 14 days to be eligible, ≥ 70% of the data points have to be non missing. Full 24-hour periods available only will be used, thus excluding from the calculation all days with CGM sensor installation or desinstallation.

For data analysis and calculation of the TIR at baseline and at D90, gaps in the CGM recording for incomplete days will be imputed using a linear interpolation approach of the planned 14 days [51].

The primary endpoint will be computed at D90 for the full 24-h day. In a complementary way, the TIR will also be computed separately considering the diurnal period (from 06.00 H to 23.59 H) and the nocturnal period (from 00.00 H to 05.59 H).

VII.2 - SECONDARY ENDPOINTS

VII.2.1 - EFFICACY ENDPOINTS

- HbA1c absolute change from baseline: HbA1c will be assayed for all patients at baseline and D90. The absolute change from Baseline, i.e., HbA1c at D90 – HbA1c at $D_{baseline}$ will be calculated for each patient.
- Absolute change of glucose variability from baseline:
  - The percentage coefficient of variation (%CV) will be computed at baseline ($\%CV_{Basl}$) and D90 ($\%CV_{D90}$), as well as the absolute difference ($\%CV_{D90}$ -$\%CV_{Basl}$) for each patient [52]. For a given patient, the $\%CV_{Basl}$ will be calculated by dividing the Standard Deviation (SD) by the corresponding mean of the CGM recordings during the 14 days at the end of the selection period.

In the same manner, for each patient, the $\%CV_{D90}$ will be calculated by dividing the Standard Deviation (SD) by the corresponding mean of the CGM recordings during the last 14 days of the D70 to D90 period.

For each patient, $\%CV_{Basl}$, $\%CV_{D90}$ and the ($\%CV_{D90}$ -$\%CV_{Basl}$) difference will be computed 3 times:

- ⇨ Considering the full 24-h day,
- ⇨ the diurnal period (from 06.00 H to 23.59 H),
- ⇨ or the nocturnal period (from 00.00 H to 05.59 H) separately,

- Absolute change of Time In Range from the 14 days completed CGM recording at the end of the selection period (baseline) to the last 14 days completed CGM recording from D70 to D90 at the end of the study period: time in range is defined in section VII.1 as the percentage of time spent in target range of glucose level (CGM measurements in 70-180 mg/dL (including boundaries)). At baseline, as well as from D70 to D90, any day of the considered period need to have ≥ 70% non missing data points to be eligible for the TIR computation. The absolute change in TIR from Baseline, i.e., D90– D0 will be calculated 3 times for each patient: (1) for the full 24-h day, (2) for the diurnal period (from

06.00 H to 23.59 H) and (3) for the nocturnal period (from 00.00 H to 05.59 H),

- Time below target range is defined as the percentage of time spent with CGM glucose measurements (1) <70 mg/dL, and (2) <54 mg/dL, during the last 14-day CGM completed recording from days 70 to 90. The time below target range will be computed for the full 24-h day, the diurnal period (from 06.00 H to 23.59 H) and the nocturnal period (from 00.00 H to 05.59 H) separately,
- Time above target range is defined as the percentage of time spent with CGM glucose measurements (1) >180 mg/dL, and (2) ≥250 mg/dL, during the last 14-day CGM completed recording from days 70 to 90. The time above target range will be computed for the full 24-h day, the diurnal period (from 06.00 H to 23.59 H) and the nocturnal period (from 00.00 H to 05.59 H) separately,
- Total daily insulin dose change from baseline to D90 (sum of basal and bolus insulin injection), -
  Body weight absolute change from baseline (end of period of selection) to D90.

[redacted]

[redacted]

VII.3.1 - SAFETY PARAMETERS

Safety assessments are detailed in section VI.7.1.9. They include:

- Number of diabetes-related hospital admissions and their length of stay: the frequency of scheduled and unscheduled diabetes-related hospital admissions will be calculated for each study patient from baseline to D90.
- Number of hypoglycaemic events
- Number of diurnal hypoglycaemic events (i.e., occurring from 06.00 H to 23.59 H)
- Number of nocturnal hypoglycaemic events (i.e., occurring from 00.00 H to 05.59 H)
- Number of non severe hypoglycaemic events
- Number of severe hypoglycaemic events
- Number of severe diurnal hypoglycaemic events (i.e., occurring from 06.00 H to 23.59 H)
- Number of severe nocturnal hypoglycaemic events (i.e., occurring from 00.00 H to 05.59 H)
- Number of severe hypoglycaemic events requiring third party assistance
- Number of severe hypoglycaemic events requiring hospitalization
- Number of severe hyperglycaemic events (≥ 300 mg/dL for over 1 hour).

Adverse events and device deficiencies/failure will be collected from the signature of the informed consent to study end.

A Data Safety Monitoring Board (DSMB) will review the safety data of the five first patients of each group, then 25 patients having completed the study, and more frequently if judged necessary by the DSMB.

Composition, role and frequency of DSMB meetings will be detailed in the separate DSMB Charter.

VII.3.2 - [redacted]

[redacted]

[redacted]

VIII - SAFETY AND DEVICE DEFICIENCIES

VIII.1 - DEFINITIONS

Adverse Event (AE)

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including clinically significant abnormal laboratory findings) in patients, users or other persons, whether or not related to the investigational medical device.

This definition includes events related to the procedures involved (see definition below).

For users or other persons, this definition is restricted to events related to investigational medical devices.

Investigation Procedure

Any procedure specific to the clinical investigation. All activities related to the use of a medical device may be considered investigation procedures.

Note: "Preceding investigation procedure" shall be understood as a procedure which is imposed by the Clinical Investigation Plan and which has taken place before (or coincided in time) with the serious adverse event.

Adverse Device Effect (ADE)

Adverse Event related to the use of an investigational medical device.

This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

Abnormal laboratory value

All abnormal laboratory values that the investigator is aware of will be reported as Adverse Events if the investigator categorizes their values as « Clinically Significant » (CS).

Serious Adverse Device Effect (SADE)

Adverse Device Effect that has resulted in any of the consequences characteristic of a Serious Adverse Event.

SAEs related to procedures imposed by the clinical investigation plan but not with the use of the device should not be considered Serious Adverse Device Effects.

Serious Adverse Event (SAE)

Adverse Event that led to any of the following: -

death

- serious deterioration in the health of the patient, that either resulted in:

- a life-threatening illness or injury, or

- a permanent impairment of a body structure or a body function, or
- in-patient or prolonged hospitalization, or
- medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, or
- chronic disease,
- foetal distress, foetal death or a congenital physical or mental impairment or birth defect.

Note: planned hospitalization for a pre-existing condition, or a procedure required by the protocol, without serious deterioration in health, is not considered as a Serious Adverse Event.

The following reasons for hospitalization are exempted from being reported:

- Hospitalization for social and/or convenience reasons.
- Hospitalization for pre-planned (i.e., planned prior to signing informed consent) surgery or standard monitoring of a pre-existing disease or medical condition that did not worsen.

However, complications that occur during hospitalisation are AEs or SAEs (for example, if a complication prolongs hospitalization).

Use Error

Act or omission of an act that results in a different medical device response than intended by the manufacturer or expected by the patient.

Use Errors include slips, lapses, and mistakes.

Note: an unexpected physiological response of the patient does not in itself constitute a Use Error.

Device Deficiency

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.

Note: Device Deficiencies include malfunctions, use errors, and inadequate labelling.

Unanticipated Serious Adverse Device Effect (USADE)

Serious Adverse Device Effect which by its nature, incidence, severity or outcome has not been identified in the current version of the Risk Analysis report.

Note: Anticipated Serious Adverse Device Effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the Risk Analysis report.

VIII.2 - COLLECTION, ASSESSMENT AND FORWARDING/REPORTING BY THE INVESTIGATOR

VIII.2.1 - COLLECTION AND ASSESSMENT

All Adverse Events (serious and non-serious, related and not related) and device deficiencies occurring during the study from the informed consent signature until the end of study i.e., the last study evaluation will be reported by the investigator in the e-CRF. Related SAEs may be reported at any time.

Adverse Events, ADEs and Device Deficiencies will be entered by the Investigator in the corresponding section of the e-CRF. SAEs, ADEs and Device Deficiencies will be reported by the Investigator by the means of specific forms. Depending on the situation, both forms may have to be used for a single event.

- The Investigator will assess the seriousness of every Adverse Event.
- The Investigator will assess the causal relationship between each adverse event and the Investigational Medical Device and/or investigation procedures. That causal relationship is assessed as being a reasonable possibility or not. A reasonable possibility of a causal relationship between the event and the Investigational Medical Device and/or investigation procedures means that there are facts (evidence) or arguments to suggest a causal relationship. If a causal relationship is suggested between the event and the Investigational Medical Device, the Adverse Event meets the definition of the Adverse Device Effect.
- The Investigator will assess, for every device deficiency, if it could have led to a SADE, if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate.

VIII.2.2 - REPORTING TO THE SPONSOR

The investigator reports to the sponsor, immediately and no later than 3 calendar days of his/her being aware, all SAEs, ADEs and Deficiencies of the Investigational Device and/or investigation procedures, by the means of, respectively the “SAE/ADE Form” and/or the “Device Deficiency Form”, that will be sent by email to:

AIR LIQUIDE Santé INTERNATIONAL, Pharmacovigilance Department:
Email: vigilance.alsi@airliquide.com

The investigator will answer within 48 hours to any safety query sent by the sponsor.

VIII.2.3 - ASSESSMENT BY THE SPONSOR

For each Serious Adverse Event, the sponsor (Study Physician) will assess the causal relationship between the investigational medical device and/or investigation procedures and the event.

For each device deficiency, the sponsor (Study Physician) will assess if that device deficiency could have led to a SADE, if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate.

The assessments given by the investigator cannot be downgraded. In case of disagreement, both opinions are provided.

VIII.2.4 - REGULATORY SAFETY SUBMISSIONS BY THE SPONSOR

Regulatory safety submissions (individual cases, annual safety reports) will be done by the sponsor according to legal requirements.

VIII.3 - NEW SAFETY EVENTS

A new safety event is any new data which might lead to:

- A reassessment of the benefit-risk balance of the study or of the IMD,
- A change in the use of the IMD, in the conduct of the study, or in the study documents,
- The interruption, discontinuation or modification of the study protocol or other study conducted on the same IMD.

Any new safety event occurring during the study period will be notified by the Sponsor according to legal requirements to the French Competent Authority and Ethics Committee.

IX - DATA HANDLING

IX.1 - ELECTRONIC CASE REPORT FORM (E-CRF)

An electronic data capture system will be used for this study. An electronic CRF (e-CRF) will be designed to collect all the data required by the protocol apart from the automatic recordings of the study IMDs. The e-CRF will be developed by the Information Technology Department of ICTA (Dijon, France), in compliance with Sponsor specifications and regulatory requirements.

Data entry will be performed by the Investigator or by the designated person from his/her team at the investigator site and by the HHP with two different connection profiles, using the e-CRF screens designed with web technologies.

[redacted]

Patients will be identified with a unique identification code. Two letters for the country code, three digits for the site number, dash then the patient number on 3 digits. The last 3 digits will be attributed according to the chronological order of selections within each centre.

Data entered *via* the Internet will be directly recorded in the SQL study database.
The investigator or the designated personnel from his/her team agrees to complete all documents provided by the Sponsor at each patient's visit and complete the e-CRF as close as possible from the patient's visit.

All corrections of data on the e-CRF must be made by the investigator (or the designated person from his/her team) or by the HHP according to the provided instructions. Any data modification will be recorded in chronological order using the audit trail feature of SQL Server database, including who, when and why the modification was done.

In order to ensure confidentiality and security of the data, usernames and passwords will be used to restrict system access to authorized personnel only, whether investigator and authorized site members, HHP, Sponsor or third parties.

The monitors must make certain that all data are completed on the e-CRF and are according to source.

After comparing the data to the source documents, the monitor will request corrections/clarifications from the investigator using functionalities on line for Source Data Verification (SDV).

Before the lock of the database by the Data Management Department, the investigator must attest by entering his/her username and password:

- The authenticity of the data collected in the e-CRF,
- The coherence between the data in the e-CRF and those in the source documents.

IX.2 - DATA MANAGEMENT

SAS® software version 9.2 or later will be used for data management process and data will be recorded in the clinical study database stored in a secure folder.
For the study results evaluation (including the calculation of the primary endpoint as detailed in section VII.1), pseudonymised IMDs recordings uploaded from CGM and pumps throughout the patients' study participation periods will be transferred electronically to the study database.

The Data Management Department of ICTA (Dijon, France) is responsible for data processing including drafting of Data Management Plan, development of database structure, drafting the Data Validation Plan (list of edit checks and cleaning listings), data transfers and data coding. Medical and surgical history and adverse events will be coded using the latest available version of the Medical Dictionary for Regulatory Activities (MedDRA). Prior and concomitant medications will be coded using World Health Organization drug dictionary (latest version available). A review of the data will be performed according to the CRO Standard Operating Procedure (SOP).

Database status will be declared as final when all data have been entered, cleaned by the Data Manager, validated by the monitor and the investigator or delegate. After declaration of a final database, the data will be exported from the SQL source database and converted into SAS datasets in the final database, and both databases will be locked and protected from changes. All statistical analyses for the final analysis will be performed on the locked SAS database.

IX.3 - STUDY COMMITTEES

A Data Safety Monitoring Board (DSMB) will be established prior to study start (first visit of first patient). All members will be independent from the Sponsor.

A Data Safety Monitoring Board (DSMB) will review the safety data of the five first patients of each group, then 25 patients having completed the study, and more frequently if judged necessary by the DSMB. The DSMB will make recommendations regarding the continuation, temporary suspension or definitive termination of the clinical study.

Composition, role and frequency of DSMB meetings will be detailed in the separate DSMB Charter.

X - STATISTICAL METHODS

X.1 - SAMPLE SIZE

The primary study objective is to demonstrate that the tested therapeutic strategy is superior to the usual care strategy on the TIR at D90.

The required number of assessable patients can be assessed using the standard formula of comparison of 2 means:

$$n_A = 2 \times \frac{s^2}{\Delta^2} \times \left(z_{\alpha/2} - z_{power}\right)^2,$$

With n_A= number of assessable patients/group, s=standard deviation, and Δ= expected difference between both groups

Based on previous studies [53], the difference between the investigational group and the control group is expected to be between 14% and 24%, and the standard deviation corresponding to the mean TIR is expected to be equal to 16 (identical in both groups).

Based on a difference of 17% in the mean TIR at D90 between the investigational group and the control group, a standard deviation = 16 (identical in both groups) for the mean TIR at D90, a type 1 error (α) = 5.0%, a type 2 error

(β) = 10.0% (statistical power = 90.0%), the sample size estimation yields n=21 valid patients per study group including a 10.0% account for the adjusted analysis (primary analysis adjusted on HbA1c value at baseline and TIR at baseline). Allowing for a 25.0% rate of non-evaluable patients, a total of 56 patients needs to be randomized (28 patients in each study group).

Table 1: Estimated sample size needed to show the statistical significance of a difference Δ in TIR at D90 varying from 14% to 24% at the 5% level with a power of 90%

Δ	Number of assessable patients (+10.0%)	% Loss	Number of patients to recruit by group
14%	31	25.0%	42
15%	27	25.0%	36
16%	25	25.0%	34
17%	**21**	**25.0%**	**28**
18%	19	25.0%	26
19%	17	25.0%	23
20%	16	25.0%	22
21%	15	25.0%	20
22%	14	25.0%	19
23%	13	25.0%	18
24%	11	25.0%	15

X.2 - DATA SETS ANALYSED

X.2.1 - PATIENTS DATA SETS

The five following data sets analysed will be considered and exhaustively defined prior to the database lock:

[1] **The Selected data set** will include all patients who signed an informed consent.

[2] **The Randomised Intention-to-treat (ITT) data set** will include all patients who were randomised to study IMD.

[3] **The Safety data set** will include all randomised patients continuing their study participation at the end of their initiation visit (V1).

[4] **The modified Intention-To-Treat (ITT) efficacy data set** will include all patients from the safety data set with at least 3 days with ≥ 70% of non missing data points recording at baseline (selection period), as well as at the end of the study (planned from D70 to D90).

[5] **The Per Protocol (PP) data set** will include all patients in the modified ITT efficacy data set who completed the 90-day study period without any major protocol deviation.

Safety analysis will be performed on the safety data set.

Efficacy parameters [redacted] will be analysed in the modified ITT efficacy data set. The primary efficacy endpoint will also be analysed in the PP data set, the PP analysis serving as sensibility analysis.

According to ICH recommendation, modified ITT efficacy and PP analyses will be conducted according to the IMD **assigned** by the IWRS.

Safety analyses will be conducted according to the IMD **actually equipped with** rather than according to the IMD assigned.

The definition of the data sets analysed will be finalized during the final Data Review Meeting (DRM), before the database lock. During this DRM, all protocol deviations encountered throughout the study will be reviewed and their consequences on the efficacy evaluations performed will be evaluated.

A deviation will be considered major and thus, resulting to the exclusion of the concerned patient from the Per Protocol data set, when it is likely to bias significantly the interpretation of the efficacy results, especially the primary efficacy endpoint *(i.e., the TIR at D90)*. All other protocol deviations will be considered minor.

A listing of all protocol deviations will be provided for all randomised patients, including the type *(major/minor)* of protocol deviations according to the decisions made during the DRM. The number and percentage of patients with protocol deviations will be tabulated by study group *(and overall)* and type of protocol deviations on the modified ITT efficacy data set.

Protocol deviations which will be evaluated will include, but will not be limited to:

- deviations in selection, inclusion and exclusion criteria,
- deviations in dates of visits and assessments, including study premature withdrawals, - deviations in the allocation and/or the schedule of the study IMDs equipment.

[redacted]

[redacted]

X.3 - STATISTICAL ANALYSES

A Statistical Analysis Plan (SAP) will be prepared by the CRO and validated by the Sponsor. Its final version will be approved after the DRM. After database lock, statistical analyses will be performed by the CRO under the supervision of the Sponsor with SAS® version 9.2 or higher (SAS institute, North Carolina, USA).

X.3.1 - GENERAL CONSIDERATIONS

Analyses will be adjusted on the HbA1c level at baseline (<10.0% or ≥10.0%) if the study recruitment allows it.

Thorough description of all parameters recorded will be presented separately by study group, using the observed case approach *(apart from the primary endpoint as detailed in section VII.1)*. Summary tabulated results will be provided by group and assessment time/visit, if relevant or they will be replaced by the corresponding individual data listings if too few patients are concerned.

Quantitative variables will be summarized in tables displaying number of patients, means, standard deviations, medians and percentiles when appropriate, and extreme values. When applicable, the Wald two-tailed 95.0% Confidence Interval (95%CI) of the means will be provided.

Qualitative variables will be described in terms of frequencies and percentages of the total number of non-missing recordings described. When applicable, the Agresti-Coull [54] 95%CI of the percentages will be provided.

The primary analysis of the primary efficacy endpoint is detailed in section X.3.3. All other efficacy [redacted] and safety statistical results provided will be exploratory and exclusively descriptive. They may not lead to any causal interpretation. As a consequence, the statistical significance level of the various two-sided tests performed will be 5.0%. No adjustment for multiplicity will be made.

Gaussian quantitative variables will be analysed using parametric ANCOVA model and HbA1c category level at baseline as a cofactor.

Non-gaussian quantitative variables and ordinal qualitative variables will be analysed using a non-parametric ANCOVA model and HbA1c category level at baseline as a cofactor (performed on ranks).

Depending on the analysed parameter and its frequency of collection in both study groups, ANCOVA will be performed with or without repeated measures.

Nominal qualitative variables will be analysed using Cochran-Mantel-Haenszel (CMH) chi-squared tests.

X.3.2 - DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographic and other baseline characteristics recorded up to D0 will be tabulated by study group (**and IMD actually equipped with)** and overall in the safety data set. No systematic statistical test will be performed to compare both groups at baseline.

Comorbidities, as well as medical and surgical history separately at selection will be summarised by study group and overall using the MedDRA codes of System Organ Classes (SOC) and Preferred Terms (PT).

Clinical laboratory evaluation at selection and Visit 1 separately will be summarised by study group and overall as both quantitative parameters *(raw values converted in international units, if necessary)* and qualitative parameters *(relative positions regarding normal ranges in use in each laboratory involved)*.

All concomitant treatments with start date at the latest on the day before the initiation visit will be tabulated descriptively by study group and overall using the WHO_DRUG dictionary and the Anatomical Therapeutic Chemical (ATC) classification. Three (3) tables will be provided:

- one table showing the number and percentage of patients with at least 1 concomitant treatment with start date at the latest on the day before the initiation visit, by therapeutic area *(ATC1 code corresponding to ATC system main group)*,
- one table by both ATC1 code and ATC system subgroup *(ATC2 code)*,
- and one table showing the number and percentage of patients with at least 1 metabolic system concomitant treatment with start date at the latest on the day before the initiation visit, by ATC system subgroups *(ATC2, ATC3 and ATC4 codes)*.

X.3.3 - PRIMARY EFFICACY ENDPOINT ANALYSIS

The primary efficacy endpoint is the TIR at D90 for the full 24-h day *(as detailed in section VII.1)*.

The primary analysis of this primary endpoint will be performed on the modified ITT efficacy data set *(defined in section X.2.1)*. The TIR at D90 will be compared between both study groups using a parametric ANalysis of COVAriance (ANCOVA) model with 3 factors: HbA1c category level at baseline, TIR value at baseline as covariate and study group **assigned** by the IWRS.

This ANCOVA model corresponding to the primary analysis of the primary efficacy endpoint will allow testing the following set of hypotheses:

- H_0 *(the null hypothesis of interest)*: mean TIR values at D90 are equal in the two groups,
- against H_1 *(the alternative two-sided hypothesis)*: mean TIR values at D90 differ between the two groups.

This primary ANCOVA model will be repeated in a secondary supportive step, including the interaction between the HbA1c category level at baseline and the study group as fixed effect, if the study recruitment allows further exploration of the HbA1c category level effect on the TIR at D90.
If this interaction term is significant *($p \leq 0.10$)* and if it appears potentially relevant from a clinical point of view, further analyses and/or graphs might be produced to interpret this statistically significant interaction.

Both ANCOVA models with and without interaction term *(if relevant)* will be repeated on the TIR at D90 considering the diurnal period *(from 06.00 H to 23.59 H)* and the nocturnal period *(from 00.00 H to 05.59 H)* separately as supportive analyses of the primary efficacy endpoint.

Moreover, all 3 ANCOVA models with and without interaction term *(if relevant)* will be performed in the PP data set to check their robustness.

X.3.4 - SECONDARY EFFICACY ENDPOINTS ANALYSIS

The secondary efficacy endpoints [redacted] will be analysed in the modified ITT efficacy data set.

Each secondary efficacy endpoint will be summarised at each time point using descriptive statistics and compared between study groups using Cochran-Mantel-Haenszel chi-squared tests adjusted on the HbA1c level at baseline (2-categories stratification variable) or analyses of covariance with or without repeated measures (depending on the analysed parameter and its frequency of collection in both study groups) adjusted on the HbA1c level at baseline.

When appropriate, analyses based on CGM measures will be performed considering (1) the full 24-h day, (2) diurnal period (from 06.00 H to 23.59 H) and (3) nocturnal period (from 00.00 H to 05.59 H) separately.

When relevant, continuous, longitudinal endpoint data (e.g. HbA1c, Total daily insulin dose, body weight) will be analysed using the mixed effects model for repeated measures method based on the restricted maximum

likelihood for estimation with several prespecified fixed effects, including first-order interactions with time, and the corresponding endpoint as the dependent variable in the model. ANCOVA will be used for analyses of measures taken at a single time point post baseline in both study groups.

X.3.5 - SAFETY EVALUATION

Safety data will be tabulated descriptively by study group and assessment time, when relevant. Extent of exposure and Adverse Events will be tabulated in the Randomised ITT and the safety data sets *(defined in section X.2.1)*. No statistical test will be performed.

X.3.5.1 - EXTENT OF EXPOSURE

Duration of the 4 study periods *(Selection, Initiation, Run-in and Follow-up periods)* and overall study duration will be tabulated *(expressed in days)* by study group *(and globally)*, as both quantitative and categorical data.

Overall study duration is defined as the time interval between the actual date of the selection visit *(V0 included)* and the actual date of the end of study visit *(V9 excluded)* whether the end of study occurred at the time of premature withdrawal or on visit date corresponding to D90 as planned, i.e., as the time interval equal to "date of end of study visit (V9) - date of selection visit (V0)".

X.3.5.2 - ADVERSE EVENTS (AEs)

The time period for the recording of Adverse Events (AEs) is the time interval between selection (V0) and end of study (V9) divided in 2 periods, either before or after the initiation visit (V1). All reported AEs will be classified in one of these 2 periods, according to their start date.

AEs tabulated evaluations described below will be performed on Study Emergent Adverse Events (SEAEs). AEs occurring before the initiation visit (V1) will be tabulated in the Randomised ITT and the safety data sets separately, if relevant, or they will be listed if too few patients are concerned.

Each AE *(whether serious or not serious, according to their regulatory definition provided in section VIII.1)* having been reported throughout the study for a given patient will be classified by Preferred Term (PT) and corresponding primary System Organ Class (SOC), using the MedDRA terminology, prior to the study database lock.

An AE will be categorised as Study Emergent if it begins at the earliest on the day of the initiation visit (V1). In case of missing or partial AE start date, an AE will be considered as Study Emergent (SE):

(1) if the AE start date is unknown,

or (2) if the partial AE start date is on or after the date of the initiation visit (V1) *(i.e., 'year' or 'year and month' is/are 'the same as' or 'after' those of the date of Visit 1)*.

An overall summary of AEs will be provided by study group, including:

- the number and percentage of patients with at least 1 AE and the total number of AEs,
- the number and percentage of patients with at least 1 SEAE and the total number of SEAEs,
- the distribution of the number of SEAEs reported by patient *(in 5 categories, if relevant: 1 SEAE, [2 - 3] SEAEs, [4 - 6] SEAEs, [7 - 9] SEAEs or 10 or more SEAEs)*,
- the number and percentage of patients with at least 1 Serious SEAE and the total number of Serious SEAEs,

- the number and percentage of patients with at least 1 possibly IMD related SEAE *(possibly IMD related SEAEs being defined as SEAEs for which the investigator has reported at least once either 'Causal relationship' or 'Probable' or 'Possible' for the relationship to the IMD)* and the total number of those possibly IMD related SEAEs,
- the number and percentage of patients with at least 1 SEAE possibly related to investigation procedures *(SEAEs possibly related to investigation procedures being defined as SEAEs for which the investigator has reported at least once either 'Causal relationship' or 'Probable' or 'Possible' for the relationship to the investigation procedures)* and the total number of those SEAEs possibly related to investigation procedures,
- the number and percentage of patients with at least 1 AE leading to study premature withdrawal and the total number of those significant AEs.

This summary table will also be provided for Serious Adverse Events (SAEs) separately.

The number and percentage of patients with at least 1 SEAE will be tabulated by study group, System Organ Class (SOC) and Preferred Term (PT) on the safety data set, as well as:

- the number and percentage of patients with at least 1 most common SEAE *(defined as those occurring in at least 5.0% of the patients from the safety data set)*, if it appears to be relevant,
- the number and percentage of patients with at least 1 SEAE by most severe intensity,
- the number and percentage of patients with at least 1 SEAE by worst recorded relationship to the IMD,
- the number and percentage of patients with at least 1 SEAE by worst recorded relationship to investigation procedures.

The number and percentage of patients with at least 1 SEAE will also be tabulated by study group and SOC only on the safety data set.

For the overall evaluation of AEs *(including counting of the number of AEs reported)*, recurring AEs *(i.e., AEs classified under the same Preferred Term (PT))* for a given patient in a given period will be counted only once for the patient concerned in the period concerned.

If relevant, the number and percentage of patients with at least 1 SAE will be tabulated by study group, System Organ Class (SOC) and Preferred Term (PT), separately from all AEs, in a second step.

Moreover, SEAEs occurring during the Run-in period *(which only concerns patients allocated to the investigational group)* will be tabulated in the safety data set separately, if relevant, or they will be listed if too few patients are concerned.

All SAEs reported throughout the study *(i.e., from the date of the selection visit (V0) onwards),* all AEs leading to study premature withdrawal *(which constitute significant AEs)* and deaths if applicable will be listed separately by study group. They will be exhaustively described on an individual basis, including all reported information in the section devoted to AEs in the e-CRF, as well as their start date *(i.e., both (1) the time interval between the date of the selection visit (V0) and the occurrence of the AE and (2) the timing of onset of the AE in relation to D0)*, and duration of the AE.

Adverse Device Effects and Device Deficiencies will be listed separately and they will be exhaustively described on an individual basis, in a similar manner to SAEs, if relevant.

Unplanned hospitalisations whatever their reason *(which will be reported as SAEs)* will also be listed separately from all SAEs and they will be tabulated by study group, including the number and percentage of patients

hospitalised at least once during their study participation and the number of hospitalisations per patient *(as both quantitative and categorical data).*

X.3.5.3 - CLINICAL LABORATORY EVALUATION

In the safety data set, for each laboratory parameter *(apart from HbA1c which is part of the secondary efficacy endpoints described in section X.3.4)*, laboratory results and their absolute variations from baseline *(i.e., initiation visit (V1))* will be summarised as quantitative parameters using descriptive statistics by study group at the end of study visit (V9) planned to be performed at D90, using the observed case approach.

Number and percentage of patients above, below or within normal ranges in use in each laboratory involved will also be tabulated by study group for each parameter at study end.

A shift table will also be provided for each parameter at study end to depict the number and percentage of patients with post baseline decreased laboratory values *(from Within Normal Ranges to Below, from Above normal ranges to Within Normal Ranges or from Above normal ranges to Below)*, the number and percentage of subjects without changes *(either always Within Normal Ranges or Above or Below)* and the number and percentage of patients with post baseline increased laboratory values *(from Below to Within Normal Ranges, from Within Normal Ranges to Above or from Below normal ranges to Above)* by study group.

X.3.5.4 - VITAL SIGNS, PHYSICAL FINDINGS AND OTHER OBSERVATIONS RELATED TO SAFETY

For systolic and diastolic resting blood pressure separately, quantitative descriptive statistics will be tabulated on the safety data set by visit planned and study group, using the observed case approach.

For each parameter separately, the absolute variations "post-initiation period – baseline *(recorded at initiation visit (V1))*" will also be tabulated by visit planned and study group.

X.3.5.5 - CONCOMITANT TREATMENTS

All concomitant treatments with start date at the earliest on the day of the initiation visit will be tabulated descriptively by study group in the safety data set using the WHO DRUG dictionary and the Anatomical Therapeutic Chemical (ATC) classification. Three (3) tables will be provided:

- one table showing the number and percentage of patients with at least 1 concomitant treatment with start date at the earliest on the day of the initiation visit, by therapeutic area *(ATC1 code corresponding to ATC system main group)*,
- one table by both ATC1 code and ATC system subgroup *(ATC2 code)*,
- and one table showing the number and percentage of patients with at least 1 metabolic system concomitant treatment with start date at the earliest on the day of the initiation visit, by ATC system subgroups *(ATC2, ATC3 and ATC4 codes)*.

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QALYs per patient in both study groups will be compared.

X.4 - HANDLING OF DROPOUTS OR MISSING DATA

For data analysis and calculation of the TIR at baseline and at D90, gaps in the CGM recording for incomplete days will be imputed using a linear interpolation approach of the planned 14 days.

Missing observations at D90 will be imputed as “non-response” in the Cochran-Mantel-Haenszel analyses.

The number and percentage of patients prematurely withdrawn from the study after their randomisation will be provided by study group and overall in the Randomised ITT and the safety data sets *(defined in section X.2.1)*.

All withdrawn patients will be further described by study group and overall regarding their time to dropout, study period and reason for premature withdrawal. Particular attention will be paid to the description of Adverse Events *(either serious or not serious, according to their regulatory definition provided in section VIII.1)* leading to study premature withdrawal, as detailed in section X.3.5.2.

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X.5 HANDLING OF MODIFICATIONS TO THE INITIAL STATISTICAL METHODS

Any modification of the initial statistical method previously described and the reason why they were performed will be described in a specific section of the study Statistical Analysis Plan (SAP), as well as in the clinical study report.

XI - QUALITY CONTROL/MONITORING

Monitoring is the act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirements.

The study will be subjected to regular monitoring (visits and/or telephone monitoring) by the sponsor or any person appointed by the sponsor. During the monitoring visits, the Clinical Research Associate (CRA) will verify Investigators' adherence to the Good Clinical Practice and the protocol and that informed consent is obtained and recorded for all patients prior to implementation of any study procedure.

The CRA will contact and visit the Investigator at regular intervals during the study. He/she will compare the e-CRFs with medical records and other relevant documentation through direct access, during the on-site monitoring visits. He/she ensures the completeness, consistency and accuracy of the data being recorded in the e-CRF by the Investigator.

The sponsor or any person appointed by the sponsor (such as the CRA) will explain the protocol and study related procedures to all study staff, including the Investigator. If new collaborators are included during the course of the study, additional training sessions will be organised by the investigator and/or the CRA.

As part of the supervision of the study progress, other sponsor personnel or the CRO may, on request, accompany the CRA on visits to the study site. The investigator and his/her collaborators commit to cooperate with the CRA to resolve any problems, corrections, or possible misunderstandings concerning the findings detected in the course of these monitoring visits.

XI.1 - ACCESS TO SOURCE DATA

The Investigator must authorize the Clinical Research Associate (CRA) to have direct access to all source documents concerning the patient necessary for the verification of data listed in the e-CRF. The Investigator must authorize the manufacturer representative to have direct access to IMD data concerning the patient necessary for the verification of proper use of IMD.

In case of requests from the Health Authorities, it is also indispensable to have access to all study data.

According to ICH-GCP requirements, the patient will be informed in writing about the need for Source Data Verification (SDV) for quality control, and audits/inspections.

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XI.2 AUDIT AND INSPECTION

An inspection may be conducted by a regulatory authority. An audit might be carried out by the sponsor to ensure that the study is conducted as per the protocol and in accordance with the applicable regulatory requirements.

The audit consists of the visit of the facilities together with the review of the study related activities and documentation (subject's medical file, study specific records, case report forms, …). The investigational study team and documentation should be available for any audit and inspection.

Investigators will have to accept that participation in the study implies agreement with regard to inspection and audit.

In case of inspection, the Investigator will inform the Sponsor who can participate in the inspection at the investigator's request.

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XII RESPONSIBILITIES

XII.1 - SPONSOR'S RESPONSIBILITIES

The Sponsor will submit an application to Independent Ethics Committee and the French Competent Authority (ANSM) for approval of the clinical study. A copy of the Ethics Committee and Competent Authority approvals must be received by the sponsor before the study starts.

In accordance with the provisions of the law and the GCP, the Sponsor will have an insurance policy intended to guarantee against possible damage resulting from the research.

The studies and/or experiments performed on behalf of the sponsor will be specifically and expressly guaranteed. It is advisable to underline that noncompliance with the Research Legal Conditions is a cause for guarantee exclusion.

XII.2 - INVESTIGATOR RESPONSIBILITIES

The Investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be completed in a neat, legible manner and kept up-to-date to ensure accurate interpretation of data.

The Investigator will maintain adequate and accurate records in accordance with ICH Good Clinical Practice and this Clinical Investigation Plan to enable the conduct of the study to be fully documented and the study data to be subsequently verified for trial-related monitoring, audits, EC review, and regulatory inspection.

Agreement of the investigator to conduct and administer this study in accordance with the protocol will be documented in separate study agreements.

The Investigator will be responsible for giving information and training about the study to all staff members involved in the study or in any element of patients management, both before starting the practical performance of the study and during the course of the study (e.g., when new staff becomes involved).

The Investigator will maintain a record of all individuals involved in the study (medical, nursing and other staff) and will specify, for each person, the tasks delegated for the study. The investigator is responsible for ensuring the privacy, health, and welfare of the patients during and after the study.

The Investigator must be familiar with the background and requirements of the study and with the properties of the investigational medical device as described in the technical documentation and any relevant health product information.

XIII ADMINISTRATIVE AND REGULATORY ASPECTS

XIII.1 - GOOD CLINICAL PRACTICES/ DECLARATION OF HELSINKI

The study will be conducted in compliance with ICH Harmonized Tripartite Guidelines for Good Clinical Practice (ICH E6), the provisions of the Declaration of Helsinki (Appendix 3) and the European Directive 2001/20/EC, as well as with applicable local regulatory requirements.

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XIII.2 - INDEPENDENT ETHICS COMMITTEE AND COMPETENT AUTHORITY

Prior to the commencement of the study, the study protocol (and its substantial amendments if any) will be reviewed and approved by concerned Independent Ethics Committee (IEC) and competent authority(ies) of participating country(ies). The study protocol, informed consent form, subjects' recruitment procedures and any written information to be provided to the subjects will be reviewed by the IEC for opinion.

The study protocol cannot be implemented until the approvals by IEC and competent authority, in accordance with the applicable regulatory requirements, have been obtained.

During the study, the sponsor should notify the investigator, the IEC and the competent authority(ies) of any relevant information that could affect the safety of the subjects and/or could impact the conduct of the study.

XIII.3 - PERSONAL DATA PROTECTION AND CONFIDENTIALITY

The Investigator must assure that the personal data of patients, including their identity and all other personal medical information, will be kept confidential at any time.

Patient number and initials will identify the patients in the e-CRF. On other documents submitted to the sponsor, patients will not be identified by their names but by an identification code (e.g. patient number).

By signing this protocol, the Investigator undertakes that the protocol and all attached information are and will remain confidential. The Investigator agrees that after providing the protocol and all information necessary for the personnel involved, he/she remains responsible for their total confidentiality. Such obligation is detailed in the confidentiality agreement signed by the Investigator before the initiation of the study.

The Investigator agrees that, subject to local regulations and ethical considerations, a Sponsor representative or any regulatory agency may consult directly and/or copy study documents in order to verify a case report.

The Investigator undertakes to treat all patients data used or disclosed in connection with the conduct of study in compliance with European and local applicable laws relating to data protection.

The Investigator will be responsible for keeping a list of all enrolled patients including patient numbers, full names and dates of birth.

All data received during the study will be collected in a computer system and shall remain strictly confidential. Access to the database will only be allowed to the study team, persons duly authorized by the sponsor and if necessary, by the representatives of regulatory authority(ies), which are all subjected to professional secrecy.

The collected data will be analyzed in order to be able to achieve the objectives of the study.

Confidentiality will be guaranteed by the fact that the subject file number will appear in the written analyses/documents and that the complete name of the subject will never appear in the study documents.

The sponsor will be entitled to use and to analyze all of the data collected during this study. The information will be controlled, in accordance with the regulations in force and notably with the Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation – GDPR), in addition to the Loi n°78-17 "relative à l'informatique, aux fichiers et aux libertés" in its current version.

The contact details of the Data Protection Officer designated by the sponsor are:
[redacted]
AIR LIQUIDE
Déléguée à la Protection des Données
75, Quai d'Orsay 75007
Paris - France
https://www.airliquide.com/fr/groupe/contactez-nous-rgpd
The data may be passed on to companies that act on behalf of the sponsor and are in countries located in or outside European Union that could guarantee an adequate level of personal data protection to administer the study.

XIII.4 - COMMISSION NATIONALE DE L'INFORMATIQUE ET DES LIBERTES (CNIL)

Data will be recorded and analysed in agreement with the compliance commitment of the CNIL MR-001 (Méthodologie de référence 001).

ARCHIVING OF STUDY DOCUMENTS

The Investigator must maintain adequate and accurate records to enable the conduct of the study to be fully documented and the study data to be subsequently verified. The study documents, including patient e-CRFs, should be classified in the Investigator's file.

The Investigator's file will contain the protocol/amendments, independent ethics committee and health authorities with correspondence, sample informed consent, IMD records, staff curriculum vitae and authorization forms, correspondence, etc.

The Investigator must keep the Study File until the Sponsor authorization of destruction and by default during at least 15 years after the last publication of the study. However, this period may be extended in accordance with the applicable regulatory requirements.

Should the investigator wish to assign the study records to another party or move them to another location, the sponsor must be notified in advance.

XIII.5 - PATIENT'S INFORMATION AND CONSENT

The information note must be given to the patients before their decision to participate or abstain from participation, according to local requirements and Good Clinical Practice.

This information is based on the elements set out in the Declaration of Helsinki and the ICH-GCP Guideline (ICH E6). It must also describe the measures taken to safeguard patient's privacy and protection of personal data, according to European GDPR and French law.

Restraints and risks must be explained, as well as the right to discontinue participation in the study at any stage, without affecting their further relationship with the investigator and/or their future care.

The information note and written consent form must be submitted by the Investigator to the patient with an oral explanation. The investigator should provide the patient ample time and opportunities to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the patients.

The consent must be agreed, dated and signed by the patient before any study-related procedure starts.

The consent form is made in duplicate: the original copy is kept by the Investigator and one copy is given to the patient.

If any information becomes available during the trial that may be relevant to the patient's willingness to keep on participating in the trial, an updated written informed consent must be submitted to the patient to confirm his/her agreement to continue participating.

XIII.6 - CONSEIL NATIONAL DE L'ORDRE DES MEDECINS (CNOM)

A separate financial agreement will be signed between the sponsor and the investigator and/or the institution involved.

According to French national law (article R1121-3-1 du Code de la Santé Publique), the financial agreement related to the study will be submitted for information to the CNOM upon financial agreement signature.

According to French national law (article L.4113.6 du Code de la Santé Publique), the Sponsor will inform the CNOM of the agreement implementation.

According to the 2011-2012 French law dated December 29, 2011 and its implementing decree 2013-414 of 21 May 2013, the sponsor will publish the existence of this agreement, as well as benefits in kind or in cash provided directly or indirectly to the Investigator.

XIII.7 - PROTOCOL AMENDMENT

Neither the Investigator nor the Sponsor may alter the protocol without the authorization of the other party. Any amendment that may be issued, must be dated and signed by both parties and must appear as an amendment to the protocol before implementation.

Substantial amendments are submitted for authorization to Competent Authority (CA) and approval to EC before implementation.

Substantial amendments on safety measures are submitted for approval/authorization to EC and CA but could be implemented immediately under specific conditions defined with the sponsor.

XIII.8 - USE OF INFORMATION AND PUBLICATION OF STUDY RESULTS

The study data and study results are the exclusive property of the Sponsor. Nevertheless, the sponsor is aware that its property rights over the data must not prevent the investigator from communicating the study

results to the scientific community. Provided any such presentations do not prevent recognition of its industrial property rights, the Sponsor therefore authorises the investigator to draw up and present any scientific papers concerning the study after having received the written Sponsor authorization.

The study results will be reported into a final clinical study report that will be written according to the ICH E3 Guideline (Structure and Content of Clinical Study Reports) and according to all applicable regulations.

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XV - APPENDICES

APPENDIX 1- PATIENT VALIDATION OF KNOWLEDGES AND SKILLS ACQUIRED FORM

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APPENDIX 2- CODE OF PRACTICE FOR HOME HEALTHCARE PROVIDERS

CODE DE BONNES PRATIQUES DES PRESTATAIRES DE SANTÉ À DOMICILE (PSAD)

PSAD

FÉDÉRATION DES PRESTATAIRES DE SANTÉ À DOMICILE

Octobre 2013

Dans un environnement de la santé en mutation, le secteur d'activité des Prestataires de Santé à Domicile (PSAD) est en fort développement. Par une démarche commune, les membres de la Fédération des Prestataires de santé à domicile ont la volonté d'afficher leurs valeurs et une éthique dans l'exercice de leur profession, à travers des engagements clairement définis, au sein d'un Code de Bonnes Pratiques, conformément aux textes législatifs, réglementaires et conventionnels applicables et aux valeurs auxquelles la Fédération tient et qu'elle encourage. Il reste du devoir des adhérents de chaque syndicat membre de la Fédération de se tenir bien informés des dispositions et évolutions règlementaires qui leur sont applicables.
Cette version intègre les dispositions arrêtées au 29 mai 2013. Elle sera disponible auprès de la Fédération et sur l'espace adhérent du site internet.
Ce document fera l'objet de mises à jour en fonction de l'évolution de la réglementation.

Validation du Code
Ce code a été conçu par Valerie BLANDIN-MATAS et relu et mis à jour par Maître Thierry DUGAST, avocat associé du Cabinet Saint-Louis Avocats.

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CODE DE BONNES PRATIQUES DES PSAD

Sommaire

CODE DE BONNES PRATIQUES DES PSAD

Glossaire

AFD : Association française des diabétiques
AFM : Association française contre les myopathies
ALD : Affection de longue durée
ANSM : Agence nationale de sécurité du médicament et des produits de santé
AM : Assurance maladie
AMO : Assurance maladie obligatoire
APF : Association des paralysés de France
ARS : Agence régionale de santé
BO : Bulletin officiel
BPDO : Bonnes Pratiques de dispensation à domicile de l'oxygène à usage médical
CEPS : Comité Économique des produits de santé
CERAH : Centre d'études et de recherche appareillage des handicapés
CISS : Collectif inter associatif sur la santé
CMU : Couverture maladie universelle
CNAMTS : Caisse nationale de l'assurance maladie des travailleurs salariés
CNOM : Conseil national de l'ordre des médecins
CPAM : Caisse Primaire d'Assurance Maladie
CPF : Commission des Pénalités Financières
CPN : Commission Paritaire Nationale
CPR : Commission Paritaire Régionale
CSP : Code de la Santé publique
CSS : Code de la Sécurité sociale
DASRI : Déchets d'activites de soins a risques infectieux
DEEE : Déchets d'équipements électriques et électroniques

CODE DE BONNES PRATIQUES DES PSAD

DEP : Demande d'entente préalable
DM : Dispositif médical
DMOS : Diverses Mesures d'ordre social
EFPIA : European Federation of Pharmaceutical Industries and Associations (Fédération européenne des industries et associations pharmaceutiques)
FFAAIR : Fédération française des associations et amicales de malades, insuffisants ou Handicapés respiratoires
FNI : Fédération Nationale des Infirmiers
HAS : Haute Autorité de santé
IDE : Infirmier Diplômé d'Etat
JO : Journal officiel
LEEM : Les Entreprises du médicament
LPP : Liste des produits et prestations remboursables
PG : Polygraphie
PPC : Pression positive continue
PSAD : Prestataire de santé à domicile
PSDM : Prestataire de services et distributeur de matériel médical
PSG : Polysomnographie
RCP : Responsabilité civile professionnelle
SAV : Service après-vente
SNITEM : Syndicat national de l'industrie des technologies médicales
UNCAM : Union nationale des caisses d'assurance maladie
VPH : Véhicule pour personne handicapée

Première partie

Pourquoi un Code de Bonnes Pratiques ?

Un secteur d'activité et un cadre législatif, réglementaire et conventionnel en pleine évolution

La profession des PSAD a évolué au fil des années, bénéficiant des progrès des technologies médicales utilisables à domicile, des évolutions sociales ou des financements favorisant le retour à domicile. De nouveaux cadres législatif, réglementaire et conventionnel ont accompagné cette évolution : l'enrichissement constant de la LPP (Liste de produits et prestations remboursables) sur la base des avis de la Haute Autorité de Santé (HAS), un texte de loi (loi du 26 juillet 2005 relative au développement des services à la personne, appelée communément loi Borloo), un décret et un arrêté de professionnalisation qui en sont issus en décembre 2006 et qui ont été suivis par un arrêté du 23 décembre 2011 relatif à la formation des personnels garants et intervenants. En outre, le 16 décembre 2011, les Prestataires ont signé un accord-cadre avec le CEPS. Enfin, plusieurs textes concernant le secteur de la santé en général et des dispositifs médicaux en particulier ont des incidences sur les PSAD. On citera notamment la loi relative au renforcement de la sécurité sanitaire du médicament et des produits de santé dite « médicament » du 29 décembre 2011 et ses textes d'application sur la publicité des dispositifs médicaux, les dispositions sur la transparence des avantages consentis par les entreprises aux professionnels de santé élargis appelées « Sunshine Act à la française », un décret du 5 juillet 2012 sur les modalités de prescription et de délivrance des DM...

Des relations multiples, nécessitant d'afficher des pratiques transparentes

La diversité des contacts établis dans la réalisation des prestations est l'une des caractéristiques de la profession : le patient, sa famille et ses proches, les professionnels de santé en médecine de ville ou en établissement de santé, les organismes payeurs, Assurance maladie et organismes complémentaires, mais également les associations de patients, les autorités ou les pouvoirs publics. Tous ces acteurs ont des exigences spécifiques intégrant différents cadres législatifs ou réglementaires. À travers l'élaboration d'un Code de Bonnes Pratiques, la Fédération des Prestataires de santé à domicile témoigne, auprès de chacun d'eux, d'une volonté d'afficher des valeurs fortes et des pratiques transparentes qu'ils s'engagent à respecter.

Une rédaction en cohérence avec la Charte patients/prestataires

En 2008, les PSAD ont soutenu l'élaboration de la Charte de la personne prise en charge par un prestataire de santé à domicile, réalisée à l'initiative d'une fédération d'associations de patients insuffisants respiratoires, la FFAAIR. La charte décrit les droits des patients et les obligations des prestataires ; initialement destinée aux insuffisants respiratoires, elle s'adresse également aux patients sous pompe à insuline, depuis l'adhésion en 2009 par l'Association française des diabétiques (AFD). D'autres associations de patients sont pressenties pour adopter prochainement la Charte patients/prestataires. Le Code de Bonnes Pratiques de la Fédération est en totale cohérence avec l'esprit de la charte. Adhérer à la charte est pour un prestataire un acte individuel, le Code de Bonnes Pratiques se situe quant à lui à un échelon fédéral et est automatiquement applicable à l'ensemble de syndicats membres et de leurs adhérents.

Une démarche en phase avec les autres entreprises de santé

Ces dernières années, en complément de la loi n° 93-121 du 27 janvier 1993 portant diverses mesures d'ordre social (DMOS) appelée communément « loi anti-cadeaux », les entreprises du médicament ou les fabricants de matériel ont édité des recommandations, chartes ou codes, dans le cadre de leurs relations avec les professions de santé : Code EFPIA (Code des bonnes pratiques de promotion des médicaments) fin 2004, puis dans une nouvelle version en octobre 2007, document d'orientation d'interprétation et d'application de l'article L4113-6 du CSP du 21 juin 2007 rédigé par le LEEM, le CNOM et le SNITEM, Charte de la visite médicale du 22 décembre 2004 modifiée par avenants en juillet 2005 et juillet 2008.

Il n'est pas inutile que la Fédération participe également à ce type de démarche, en rappelant les principes qui doivent gouverner l'action des PSAD sous l'angle des spécificités du secteur.

Le Code des Bonnes Pratiques de la Fédération s'inscrit dans cette démarche.

Deuxième partie

Approbation et mise en œuvre du code

Approbation du contenu par le Comité Exécutif de la Fédération
Le Comité Exécutif de la Fédération a délibéré et adopté le contenu du Code ; dès lors, tout adhérent ou toute personne morale souhaitant adhérer aux syndicats membres de la Fédération doit s'engager par écrit à le respecter.

Principe d'opposabilité
Le refus de signer le Code doit être une cause de refus d'adhésion à chaque syndicat membre de la Fédération. Le défaut de respect du Code peut entrainer l'exclusion d'un adhérent à un syndicat membre de la Fédération dans les conditions prévues par les dipositions applicables.

Engagement des adhérents
Chaque adhérent à un syndicat membre de la Fédération s'engage dans une démarche volontaire et proactive pour veiller à la bonne application de chacun des points décrits dans le Code, au sein de sa structure et auprès de ses équipes.

Troisième partie

Sources juridiques législatives, réglementaires, conventionnelles applicables à la profession, fondements du présent code

La rédaction du code a été réalisée à partir des textes juridiques applicables à la profession. Il convient également de prendre en compte les dispositions communes, comme celles du Code de Commerce ou du Code de la Consommation applicables à toutes les entreprises commerciales (non spécifiquement rappelées dans le présent code) :

Le Code de la Santé publique (CSP) et notamment les articles
– L 1110-1 à L 1110-11 portant sur les droits de la personne, et les textes réglementaires correspondants ;
– L 1111-1 à L 1111-9 portant sur l'information des usagers du système de santé et l'expression de leur volonté, et les textes réglementaires correspondants ;
– L 5232-3 issu de la loi n° 2005-841 du 26 juillet 2005 relative au développement des services à la personne et portant diverses mesures en faveur de la cohésion sociale ; D 5232-1 à D 5232-15 issus du décret n° 2006-1637 relatif aux prestataires de services et distributeurs de matériels ;
– L 4113-6 sur les avantages en nature ou en espèces et L 4113-8 sur les intérêts et ristournes ; R 4113-104 à R 4113-110 sur les conventions et liens avec des entreprises ;
– L1453-1 et ; Décret 2013-414 du 21 mai 2013 fixant les règles de publication des conventions et avantages ;
– L 5213-1 et suivants sur la publicité pour les DM (et les textes réglementaires : articles R 5213-1 et suivants ; arrêtés des 24 septembre et 21 décembre 2012). (Pour les DMIV, sont applicables les articles L 5223-1et suivants).

Le Code de la Sécurité sociale (CSS), ainsi que la Liste des produits et prestations remboursables décrivant l'ensemble des produits et prestations à la vente et/ou à la location, leurs tarifs de remboursement par l'Assurance maladie et les obligations associées pour le prestataire (techniques organisationnelles, diplôme requis…), et notamment les articles :
– L 165-1 ayant pour application la Liste des produits et prestations remboursables (LPP) ;
– L 165-1-2 sur le contrôle des spécifications techniques et les pénalités financières et le décret d'application n°2012-1135 du 8 octobre 2012.

La Convention nationale organisant les rapports entre l'Uncam, l'Union nationale des organismes complémentaires d'assurance maladie et les Prestataires délivrant des produits et prestations inscrits au livre 7 de la liste prévue à l'article L 165-1 du Code de la Sécurité sociale, signée en août 2002. (Une révision de la Convention est actuellement en cours).

L'arrêté du 17 novembre 2000 relatif aux BPDO (Bonnes Pratiques de dispensation de l'oxygène) (JO du 25 novembre 2000) et annexes BO n° 2000-12 bis art. L4211-5 du CSP.(Une révision des BPDO est actuellement en cours).

Le décret n°2005-829 du 20 juillet 2005 relatif à la composition des équipements électriques et électroniques et l'élimination des déchets issus de ces équipements.

Le décret n°97-1048 du 6 novembre 1997 relatif à l'élimination des déchets d'activités de soins à risques infectieux et assimilés (articles R 1335-1 et suivants CSP).

L'accord-cadre entre le Comité économique des produits de santé (CEPS) et les organisations professionnelles, signataires, concernées par les produits et prestations inscrits sur la liste prévue à l'article L-165-1 du code de la sécurité sociale du 16 décembre 2011.

Le Code des Bonnes Pratiques des PSAD regroupe par thème, les principes fondamentaux issus de ces textes et a pour objet de permettre à ses adhérents une approche transversale de leurs obligations. La rédaction du présent code synthétise dans un esprit pratique les dispositions réglementaires et conventionnelles applicables, sans pouvoir les reprendre toutes textuellement.

Il n'a donc pas pour but de se substituer à la législation et la réglementation en vigueur ni à l'interprétation de ces textes émanant des autorités judiciaires ou administratives compétentes.

Les termes « **Prestataire** » ou « **PSAD (Prestataire de Santé à Domicile)** » sont utilisés de façon générique tout au long du Code, pour désigner la profession des adhérents aux syndicats membres de la Fédération d'après les statuts de cette dernière.

Dans le code, le principal texte de référence réglementaire se rapportant au sujet traité est signalé par un chiffre en « exposant » :

- [1] Convention nationale organisant les rapports entre les trois caisses de l'Assurance Maladie obligatoire et les Prestataires délivrant des dispositifs médicaux, produits et prestataions associées inscrits aux Titres I et IV de la L.P.P du 7 août 2002 ;
- [2] Liste des produits et prestations (LPP) ;
- [3] Bonnes Pratiques de dispensation de l'oxygène à domicile (BPDO) ;
- [4] Décret et arrêté du 19 décembre 2006 et l'arrêté du 23 décembre 2011 relatifs à la professionnalisation ;
- [5] Décret du 9 mai 2012 relatif à la publicité des DM ainsi que les arrêtés des 24 septembre et 21 décembre 2012 ;
- [6] Décret du 5 juillet 2012 relatif aux modalités de prescription et de délivrance des produits et prestations inscrits sur la LPP ;

- [7] Décret du 8 octobre 2012 fixant les modalités de contrôle du respect des spécifications techniques auxquelles sont soumis certains dispositifs médicaux remboursables ;
- [8] Décret du 21 mai 2013 sur la transparence des liens et circulaire d'interprétation du 29 mai 2013 ;
- [9] Autres parties applicables du Code de la Santé publique et de la Sécurité sociale ;
- [10] Accord cadre entre le CEPS et les organisations professionnelles concernées par les produits et prestations inscrits sur la LPP ;
- [11] Convention entre le Synalam et la FNI de mars 2012.

NB : En cas de difficultés rencontrées par un PSAD dans l'interprétation ou l'application du Code, la Fédération est à sa disposition pour lui apporter son aide ; dans tous les cas, c'est le texte réglementaire correspondant qui fait office de référence et qui est applicable.

Quatrième partie

Le Code des Bonnes Pratiques

Les différents chapitres :

1. Relations avec les patients et leur entourage
2. Relations avec les professionnels de santé
3. Relations avec les organismes payeurs
4. Relations avec les associations de patients
5. Relations entre Prestataires
6. Relations avec autres organisations professionnelles
7. Respect de l'environnement, développement durable

Chapitre 1

Relations avec les patients et leur entourage

Droits fondamentaux des patients

1/1 Respect de la personne, de sa famille et de ses proches

Le Prestataire doit toujours agir dans l'intérêt du patient. Il respecte sa dignité et son intimité, celle de sa famille et de ses proches[4].
Il agit sans discrimination vis-à-vis des personnes malades et sans chercher à exploiter leur confiance[4].

1/2 Libre choix du Prestataire

Le libre choix du Prestataire[1] par le patient est un principe fondamental dans l'exercice de la profession.
Le Prestataire ne doit pas chercher à influencer de façon déloyale un patient pour être choisi ou pour obtenir un changement de Prestataire.
Le PSAD respecte, par ailleurs, le libre choix du patient concernant son infirmier libéral[11].

1/3 Information du patient adaptée, intelligible et loyale

Le Prestataire doit délivrer au patient et à son entourage toutes les explications et informations relatives au service ou au matériel fourni[1], [2] et [4]. Pour cela, il doit :

- **Être en mesure de présenter un ou plusieurs matériels adaptés au besoin du patient et notamment :**
  - leurs avantages et leurs inconvénients,
  - leur coût et leur niveau de prise en charge par les organismes sociaux,
  - à défaut, avertir le patient ou son entourage de la faculté d'avoir recours à un autre Prestataire.

Le Prestataire devra délivrer au patient le conditionnement du produit le plus économique, dans le respect de l'ordonnance[6].
Le PSAD s'engage à ne pas encourager des produits et/ou des prestations en fonction du niveau de prise en charge par les assurances santé complémentaires.

- **Informer sur les conditions de garantie et de durée de fonctionnement ;**

Remettre une notice d'utilisation et un document d'information concernant le matériel comprenant :
  - le mode d'emploi,
  - l'adresse et le téléphone du Prestataire.

- **Expliquer les conditions d'utilisation du DM et des consommables concernant :**
  - la sécurité,
  - l'entretien,
  - la désinfection.

- **Informer des conditions de prise en charge par l'Assurance maladie des prestations ou des DM ;**

- **Fournir un devis ;**
  - **cas particulier des VPH : le devis préalable est obligatoirement remis et il comporte :**
  - les détails du véhicule,
  - la part prise en charge par l'Assurance maladie,
  - le reste à charge pour l'assuré.

- **Informer le patient de la tenue d'un dossier concernant sa prise en charge** et de son droit d'accès, de rectification et de suppression des données le concernant ;
  - **cas particulier de la PPC :** informer le patient sur le dispositif mis en place et le transfert régulier de données concernant le suivi de son traitement, de son accès libre à ses données, de la possibilité d'un arrêt de prise en charge par l'AMO en cas de non suivi du traitement et de la possibilité d'avoir un accompagnement au respect du traitement.

- **Informer de l'échange d'informations entre le patient et l'équipe médicale en charge de la personne pour assurer la prestation, selon les termes de l'article L 1110-4 du CSP.**

1/4 Libre consentement du patient

Le Prestataire doit délivrer ses prestations avec le consentement libre et éclairé du patient dûment informé. Ce consentement peut être retiré à tout moment[4] et [9]. D'une manière générale, le Prestataire respecte les choix du patient, de sa famille et de ses proches[4].

NB : Le patient peut désigner une personne de confiance – qui peut être un parent, un proche ou le médecin traitant – qui sera consultée au cas où lui-même serait hors d'état d'exprimer sa volonté et de recevoir l'information nécessaire à cette fin (art. L1111-6 du CSP) ; dans ce contexte, le Prestataire doit écouter la personne de confiance.

1/5 Respect du secret professionnel

Le Prestataire est tenu au respect absolu des informations concernant les patients, il instruit ses collaborateurs de leurs obligations à ce sujet et veille à ce qu'ils s'y conforment[4] et [9].
Il met en place une organisation qui garantit le respect du secret au sein de ses locaux ou de ses systèmes d'information.
Le secret couvre[4] :
  - ce qui a été confié au Prestataire ;
  - ce qui a été vu, lu, entendu, constaté ou compris dans l'exercice de ses fonctions.

Conditions d'exercice dans les relations avec les patients

1/6 Publicité des DM auprès du public

Relève de la publicité toute forme d'information, y compris le démarchage, de prospection ou d'incitation, qui vise à promouvoir la prescription, la délivrance, la vente ou l'utilisation de ces dispositifs[9].

NB : Ne sont pas inclus dans la définition de publicité notamment les catalogues de ventes et listes de prix s'il n'y figure aucune information sur le dispositif médical.

La publicité pour certains DM (arrêté du 24 septembre 2012 modifié) est soumise à autorisation préalable.
Toute publicité faite auprès du public doit comporter les mentions minimales obligatoires prévues par le décret du 9 mai 2012 – sauf exceptions acceptées par l'ANSM – et exclure les mentions prohibées par le même texte. De manière générale, les informations contenues dans chaque publicité sont exactes, à jour, vérifiables et suffisamment complètes pour permettre au grand public de comprendre l'utilisation à laquelle le dispositif médical est destiné[5].
La convention nationale interdit certaines pratiques de publicité et procédés de marketing :

- Toute communication à visée commerciale auprès des patients qui constituerait une incitation à l'achat ou au renouvellement des produits de santé remboursables[1] ;

- La référence au remboursement total ou partiel par l'Assurance maladie ou par un régime complémentaire et au montant de celui-ci sur des documents promotionnels pour les patients[5] ;

NB : Le Prestataire peut toutefois mentionner sur ses documents de communication, et de manière générale son conventionnement avec l'Assurance maladie.

- La rémunération de praticiens ou d'auxiliaires médicaux, l'encouragement à la prescription ou au renouvellement d'une prestation plus coûteuse que celle nécessitée par l'état du patient, la sollicitation des prescriptions par des moyens tels que le prêt ou le financement gratuit de matériels, le versement de remises ou ristournes à un intermédiaire non prestataire.

- La mise à disposition de personnels à une structure hospitalière ;

- La vente itinérante, de démonstration, de démarchage, la vente par correspondance sur support papier, par voie postale ou par catalogue avec envoi direct à domicile sans relation directe avec l'assuré ;

- La proposition d'avantages, de remises ou de facilités de paiement, sauf si la publicité concerne un dispositif médical de classe I ou IIa[5].

Cette interdiction ne fait pas obstacle aux obligations réglementaires du Prestataire :

- Information individualisée des patients à l'occasion de la délivrance de la prestation sur les conditions de prise en charge par les régimes obligatoires de l'Assurance maladie (tarif de location ou prix de vente et tarif de remboursement).

La publicité comparative est autorisée dès lors qu'elle est loyale, véridique et qu'elle n'est pas de nature à induire en erreur le consommateur. Elle doit être limitée à une comparaison objective qui ne peut porter que sur des caractéristiques essentielles, significatives, pertinentes et vérifiables des biens ou services de même nature et disponibles sur le marché (art L 121-8 du Code de la consommation).

1/7 Locaux adaptés aux activités

Les locaux professionnels du Prestataire doivent être conformes aux exigences et aux normes applicables[1] et [4] et doivent répondre aux caractéristiques suivantes :

- **Accessibilité aux personnes à mobilité réduite ;**

- **Local d'accueil des personnes ayant :**
  - une superficie satisfaisante,
  - des conditions de confort et salubrité,
  - une isolation phonique et visuelle assurant la confidentialité,
  - un affichage des horaires d'ouverture avec respect de ceux-ci ;

- **Lieu d'exposition :**
  - pour la présentation des DM d'aides à la vie et de l'activité du Prestataire,
  - pour l'activité VPH (véhicules pour handicapés physiques), avec choix possible entre différents modèles et possibilité d'essais sur place ;

- **Lieu de stockage des DM :**
  - clairement identifié,
  - accès interdit au public,
  - n'entrainant pas d'altération du matériel ;

■ **Cas particulier des VPH : équipement adapté des espaces d'accueil et d'exposition avec :**
- rampe d'accès,
- surface d'évolution minimum de 16 m²,
- accessibilité par ascenseur aux normes si local à l'étage ;

■ **Locaux de désinfection :**
- séparés des lieux de réception du public,
- avec accès indépendant ;

■ **Atelier de réparation :**
- dans un local proche ou dans l'entreprise,
- avec stocks de pièces détachées courantes permettant la remise en état des DM dans les plus brefs délais.

NB : Le cas échéant, les locaux de l'activité du Prestataire doivent être séparés de toute autre activité menée en parallèle et ne relevant pas du domaine de la santé.

1/8 Personnel qualifié et compétent

La loi du 27 juillet 2005 dite « Borloo », le décret et l'arrêté du 19 décembre 2006 et l'arrêté du 23 décembre 2011 qui en sont issus, la convention nationale des prestataires, les BPDO, certaines prestations de la LPP, exigent un **personnel qualifié et compétent** dans l'exercice de la profession : (I) garants de l'application des règles professionnelles et de bonne pratique et (II) intervenants auprès de la personne malade ou présentant une incapacité ou un handicap. Le Prestataire doit mettre en œuvre des actions permettant d'attester cette qualification.

■ **Le Prestataire ne peut délivrer un matériel ou une prestation que s'il en a la connaissance, l'expérience et la pratique régulière[4].**

■ **Le personnel du Prestataire doit être qualifié[1]** pour dispenser des conseils sur le fonctionnement, l'utilisation, l'entretien des DM.

■ **La présence du personnel** doit être effective dans les locaux lors des horaires affichés.

■ **Le Prestataire doit disposer de personnels ayant le diplôme requis, le cas échéant, pour réaliser certaines prestations, notamment :**
- pharmacien dans le cadre des BPDO[3],
- personnels garants de l'application des règles professionnelles et de bonne pratique de délivrance de ces matériels et services[4]

- infirmier dans le cadre de la prestation pompe à insuline et de la nutrition parentérale[2] (pour ce dernier cas sous réserve de la publication de la LPP).

■ **Le Prestataire met à jour ses connaissances professionnelles et se tient informé de l'évolution[4] :**
- des bonnes pratiques,
- de la législation et de la réglementation.

■ **Cas de la prestation d'insulinothérapie par pompe :**
Les infirmières du Prestataire doivent suivre une formation[2] :
- à l'insulinothérapie ou à l'« environnement médical », formation validée par des experts cliniciens,
- technique sur les pompes à insuline par les fabricants,
- continue, au moins une fois par an, sur les pompes.

■ **Cas de la fourniture des VPH :**
- Le stage auprès du CERAH n'est plus obligatoire pour délivrer des fauteuils roulants, mais reste recommandé par la Fédération dans l'attente d'une nouvelle formation.

À partir du 30 juin 2013, tous les personnels garants de l'application des règles professionnelles et de bonne pratique de délivrance et les personnels intervenant auprès de la personne malade doivent avoir suivi une formation définie par arrêté ou attester d'une expérience professionnelle en qualité d'intervenant ou garant supérieure ou égale à deux ans[4] au 1er janvier 2012, ou si elle a moins de deux ans, d'une formation portant sur au moins deux thèmes spécifiques.

■ **Le Prestataire désigne au sein de sa structure des personnes « garants » du respect :**
- des règles professionnelles,
- des règles de bonnes pratiques de délivrance des prestations.

Il identifie également les personnes « intervenant » auprès de la personne malade ou présentant une incapacité ou un handicap afin de lui délivrer les matériels et les services[4].

■ **Concernant les « garants » :**
- ils sont chargés de **garantir l'application des règles professionnelles et de bonnes pratiques** de délivrance des matériels et des services ;
- ils doivent avoir suivi une des **formations** définies par arrêté ou pouvoir attester d'une expérience professionnelle supérieure ou égale à deux ans en tant que garant ou intervenant, au 1er janvier 2012 ;
- ils ont, le cas échéant, un diplôme de professionnel de santé, les autorisant à exercer en France, régi par la quatrième partie du CSP ;
- **leur diplôme est conforme à l'activité dispensée.** Celui-ci dépend du type de prestation ou de DM mis en œuvre auprès du patient.

Type de prestation ou de DM installé	Diplôme requis pour le « garant »
Oxygénothérapie	Pharmacien
Systèmes actifs pour perfusion	Pharmacien, Infirmier
Matériels pour nutrition entérale	Pharmacien, Infirmier
Appareils de ventilation	Pharmacien, Infirmier, Masseur kinésithérapeute
Appareils de pression positive continue	Pharmacien, Infirmier, Masseur kinésithérapeute
Aérosolthérapie pour pathologies respiratoires chroniques	Pharmacien, Infirmier, Masseur kinésithérapeute

*NB : **Un médecin salarié du Prestataire** peut se substituer à l'un de ces professionnels de santé hors le cas des BPDO, sous réserve :*
- *du respect de la déontologie médicale ;*
- *de ne pas être prescripteur des DM ou services.*

• **Cas particuliers des lits médicaux et accessoires, des supports d'aide à la prévention des escarres, des aides techniques et des VPH :** les garants ne sont pas nécessairement des professionnels de santé.
Ils sont en nombre suffisant et adapté au nombre de personnels intervenants auprès du patient et affectés à la délivrance des DM et services :
- au moins un quart de temps de garant, si le nombre d'intervenants est inférieur ou égal à 12 ;
- au moins un mi-temps de garant, si le nombre d'intervenants est entre 13 et 24 ;
- par extrapolation, au-delà de 24 intervenants, le nombre de garants est calculé au prorata.

1/9 Respect des conditions de mise en œuvre du DM ou service

Le PSAD doit s'assurer, sur la base des éléments à sa disposition, que les DM qu'il délivre sont conformes aux exigences essentielles.

■ **Il concourt au respect des règles de prescription et de prise en charge :**
Une ordonnance prescrivant des produits ou des prestations remboursables ne peut porter sur plus de douze mois[6].
Le matériel ou le service délivré, de même que le délai de mise en œuvre, doivent être adaptés au traitement et au besoin d'autonomie de la personne[1], [2] et [4].
Le Prestataire doit fournir des produits ou prestations tenant compte de la demande de la personne ou de son entourage et de son bien-être.

■ **Les essais des matériels doivent être possibles :**
• chez le Prestataire,
• ou sur le lieu de vie de la personne.

■ **La livraison du matériel doit être effectuée :**
• si nécessaire sur le lieu de vie de la personne,
• par un personnel compétent en mesure de fournir les explications relatives à l'utilisation.

■ **Cas particulier des VPH :**
• Location : délai de livraison sous deux jours ouvrables ;
• Vente : délai tenant compte du besoin de la personne.

■ **Les appareils mis à la disposition du patient doivent être en parfait état et conformes à leur finalité médicale et à leur fonctionnalité technique.**

■ **Le Prestataire doit faire la démonstration du fonctionnement des matériels et s'assurer de leur bonne compréhension.**

■ **Le PSAD forme l'IDE du patient, si nécessaire, à l'utilisation des DM employés[11].**

■ **Cas de l'insulinothérapie[2] :** le Prestataire doit être en mesure de présenter et assurer la formation technique du patient, à la demande du centre initiateur du traitement, de toutes les pompes prescrites par celui-ci.

■ **La mise en service et la vérification du bon fonctionnement du matériel doit être effectuée dans l'environnement dans lequel il doit être utilisé ;**
• même si le DM a été mis en œuvre dans un environnement médicalisé (établissement de santé ou cabinet médical).

■ **Entre deux patients, les DM utilisés pour la location doivent être :**
• nettoyés rigoureusement ;
• désinfectés ;
• techniquement vérifiés ;
• conditionnés et transportés de façon à ne pas être altérés ;
le tout dans les conditions prévues par la notice d'utilisation du matériel.

Cf. Recommandations de la CRAMIF sur les « Conseils pour la récupération, le nettoyage, la désinfection et le stockage des dispositifs médicaux réutilisables ». Site internet : www.cramif.fr puis rechercher « désinfection DM ».

■ **Le Prestataire doit recourir aux procédés de désinfection des DM recommandés par les fabricants ;**
• sinon, il doit pouvoir justifier du mode de désinfection utilisé.

■ **Par ailleurs, pour la revente de certains DM d'occasion (classe IIb et III), le PSAD doit fournir une attestation préalable justifiant la maintenance régulière et le maintien des performances en application de l'arrêté du 30 mars 2012 et du décret du 16 août 2011.**

1/10 Gestion des pannes et réparations en conformité avec la réglementation

Le Prestataire doit assurer le SAV et les réparations concernant un matériel défectueux, dans les délais prévus réglementairement ou dans tous les cas dans des délais raisonnables, selon les besoins de la personne et le type de matériel[1], [2] et [4].

■ **Le Prestataire doit mettre en place un service d'astreinte téléphonique pour les prestations le nécessitant et ce au moins pour les cas et dans les conditions prévus par la LPP :**
- 24h sur 24 ;
- 7 jours/7 ;
- le numéro d'appel ne doit pas être surtaxé dans ce contexte ;
- pour la prestation d'insulinothérapie et pour la prestation de nutrition parentérale à domicile (pour cette dernière sous réserve de la publication de la LPP), l'astreinte doit être réalisée par un intervenant infirmier du Prestataire.

■ **Dans le cas des produits à la location, le Prestataire doit être en mesure d'échanger le matériel défectueux :**
- dans les délais prévus à la LPP ;
- sans aucune facturation supplémentaire.

■ **En cas de nécessité d'assurer la continuité du traitement, due à l'état de la personne, le Prestataire doit fournir un matériel de remplacement :**
- si le matériel est immobilisé plus d'une journée ;
- ayant la même performance que le matériel initial ;
- le plus proche possible, en cas de matériel personnalisé.

■ **Le Prestataire doit respecter les obligations liées à la matériovigilance permettant de garantir la sécurité des patients et de leur entourage[7]. Dans ce cadre, il doit :**
- déclarer les incidents ou risques d'incident résultant de l'utilisation de dispositifs médicaux auprès de l'ANSM ;
- appliquer les directives émanant de l'ANSM concernant les DM qu'il utilise, notamment en cas de rappel.

*ANSM. Site internet : www.ansm.sante.fr ; Formulaire de déclaration de matériovigilance Cerfa n°10246*02*

■ **Cas des VPH à l'achat :**
- VPH manuel : délai de dépannage de 3 jours, sauf délais d'acheminement des pièces détachées par le fabricant ;
- VPH électrique : délai tenant compte de l'intérêt de la personne ;
- mise en place d'un VPH manuel de secours sous 24 heures ;
- facturation des réparations selon les forfaits réglementaires.

1/11 Réalisation et suivi de la prestation

■ **Le Prestataire doit assurer une prestation globale auprès du patient, comportant de façon indissociable tous les éléments conduisant à la réalisation de la prestation[1], [2] et [4]** comprenant les aspects :
- techniques ;
- organisationnels ;
- administratifs.

■ **Le Prestataire doit appliquer les conseils d'utilisation et de sécurité donnés par le fabricant du matériel.**

■ **Le suivi d'une prestation comprend** s'il y a lieu :
- **le contrôle régulier de l'observance,** en vue d'alerter le médecin traitant en cas d'anomalie : selon le délai prévu à la LPP ou plus fréquemment si le traitement le nécessite ;
- **le contrôle de la bonne utilisation du matériel ;**
- **le rappel éventuel au patient des informations.**

■ **Le PSAD transmet à l'IDE du patient le ou les protocoles de soins exigés par le médecin ou le service prescripteur[11].**

■ **Le Prestataire doit établir un dossier pour chaque personne prise en charge :**
- le dossier contient tous les éléments concernant le DM, son suivi et le service délivré ;
- les fichiers directement ou indirectement nominatifs doivent être déclarés à la CNIL ;
- le patient a un droit d'accès aux données de son dossier, sur simple demande de sa part.

■ **Des dispositions particulières de la LPP peuvent imposer le respect de précisions et obligations particulières à la charge du PSAD et/ou des patients** (cas de l'insulinothérapie par pompe, de la nutrition entérale, de la PPC notamment).

1/12 Gestion de la reprise du matériel en fin de location

■ **Le Prestataire doit assurer la reprise du matériel en fin de location**[1] :
- Dans les plus **brefs délais** ;
- En **évitant tout risque de contamination** avec d'autres DM lors de son transport dans les véhicules et lors de son stockage.
- Cas de la PPC : Reprise du matériel possible dans le cas de non observance du patient dans des conditions encadrées par la LPP.

■ **Gestion des déchets**

En fin de traitement, le matériel médical non utilisé sera récupéré et traité dans le respect de la règlementation.
Le PSAD s'engage à ne jamais mettre à disposition d'un autre patient un matériel vendu qui aurait déjà été facturé en tant que tel à l'Assurance Maladie.
Le PSAD fournit, le cas échéant, les collecteurs de DASRI aux IDE ou aux patients et indique, au besoin, au patient ou aux IDE, quelles sont les structures les plus proches qui assurent la récupération des déchets.

1/13 Respect des BPDO

La dispensation de l'oxygène à domicile par le Prestataire doit se faire conformément aux Bonnes Pratiques de dispensation à domicile de l'oxygène à usage médical[3] (BPDO actuellement en cours de révision).

■ **L'autorisation de dispenser** de l'oxygène à usage médical est accordée :
- par le directeur général de l'Agence régionale de Santé (ARS);
- après visite de l'inspection de la pharmacie ;
- après avis du Conseil de l'Ordre des pharmaciens.

■ **Pour le Prestataire, un pharmacien engage sa responsabilité** sur l'ensemble des activités liées à la dispensation de l'oxygène.
- Le temps de présence du pharmacien est fonction de l'effectif salarié du Prestataire affecté à la dispensation de l'oxygène.
- Le pharmacien intervient au domicile des patients appareillés en oxygène liquide dans le mois suivant l'initiation du traitement, afin de s'assurer de la conformité de l'installation et de la bonne utilisation du matériel.

■ **Le personnel** affecté à la dispensation de l'oxygène doit être formé et habilité par le pharmacien.

■ **Un système d'assurance de la qualité** doit décrire tous les points concernant la dispensation de l'oxygène.

■ **Des auto-inspections** en évaluent régulièrement l'efficacité.

■ Les **règles de sécurité** liées à la dispensation de l'oxygène doivent être respectées :
- modalités de transfert à partir des réservoirs cryogéniques ;
- maintenance des dispositifs médicaux ;
- conditions de stockage de l'oxygène liquide et gazeux ;
- aménagement des véhicules ;
- traçabilité de l'oxygène et des réservoirs associés.

■ **L'installation de l'oxygène à domicile** doit tenir compte de l'environnement du patient.
Le Prestataire :
- éduque le patient et/ou son entourage concernant les contraintes techniques de l'oxygénothérapie :
  - consignes de sécurité,
  - modalités d'utilisation de l'oxygène,
  - manipulation pratique du matériel,
  - conseils visant à faciliter l'intégration du matériel dans sa vie ;
- organise les dispensations ultérieures ;
- assure une permanence téléphonique.

■ Le Prestataire doit respecter **les obligations liées à la pharmacovigilance** et déclarer à l'ANSM tout effet indésirable susceptible d'être dû à l'oxygène médical.

1/14 Continuité des prestations lors d'un changement de résidence

Le Prestataire doit assurer la gestion de la continuité des prestations en cas de changement temporaire de résidence du patient sur l'ensemble du territoire français métropolitain, pour les cas prévus à la LPP[2].

Dans ce cadre, cette gestion doit se faire **sans surcoût**.

1/15 Assurance en Responsabilité Civile Professionnelle (RCP) obligatoire

Le Prestataire doit être titulaire d'un contrat d'assurance RCP couvrant intégralement son champ d'activités auprès des assurés sociaux[1].

1/16 Reversement du surcoût de consommation d'électricité

Le Prestataire doit **rembourser spontanément au patient,** sans que ce dernier ait à le demander, pour les cas prévus à la LPP, le surcoût de consommation d'électricité lié à l'utilisation de certains DM[2].

1/17 Inscription des patients ventilés à faible autonomie en cas de coupure EDF

Le Prestataire doit spontanément veiller à l'inscription, si nécessaire, auprès des ARS des malades ventilés à faible autonomie, selon les cas prévus à la LPP[2] *(patients trachéotomisés en hypoventilation alvéolaire)*.

1/18 Limitation du reste à charge pour les assurés

Le Prestataire doit veiller à apporter aux bénéficiaires des régimes d'Assurance maladie, une prise en charge financière optimale des prestations et produits remboursables délivrés[2].

- **Il se doit de favoriser** la réduction des écarts entre les prix qu'il pratique et les tarifs de responsabilité servant de base au remboursement.
- **Il se doit de pratiquer** des prix ne dépassant pas le tarif de responsabilité pour les produits et prestations figurant en annexe II de la convention nationale organisant les rapports entre l'Assurance Maladie et les Prestataires.
- **Il se doit de veiller** au renouvellement des droits particuliers en couverture de santé des patients en ALD, invalidité, etc.

1/19 Fourniture de produits pour les patients CMU

Le Prestataire a l'obligation de proposer aux patients bénéficiaires de la CMU (Couverture maladie universelle) **une liste de produits avec des prix de vente limités** réglementairement[2]. Dans ce cadre, le Prestataire doit, vis-à-vis des patients bénéficiaires :

- les informer de l'existence de ces produits ;
- les orienter en première intention sur ces produits ;
- disposer d'un stock permettant de fournir ces produits.

Chapitre 2

Relations avec les professionnels de santé

Le Prestataire doit, dans tous les cas, être à même de déterminer les limites de son exercice, notamment dans le cadre de ses relations avec les professionnels prescripteurs[1].

2/1 Publicité des DM auprès des professionnels de santé

Toute publicité faite auprès des professionnels de santé est soumise aux conditions de publicité et doit comporter les mentions minimales obligatoires prévues par le décret du 9 mai 2012 et notamment :

- La situation du dispositif médical au regard du remboursement par les organismes d'assurance maladie, et le cas échéant, les conditions de prescription et d'utilisation auxquelles a été subordonnée son inscription sur la LPP, pour la destination faisant l'objet de la publicité.
- La publicité ne peut mentionner la position prise à l'égard d'un dispositif médical par une autorité administrative ou une instance consultative d'une manière susceptible d'altérer le sens ou l'objectivité de cette position.

Les PSAD assurant la distribution de DM et des prestations du Titre I de la LPP et réalisant un chiffre d'affaires hors taxes égal ou supérieur à 11 millions d'euros doivent s'acquitter de la contribution sur les dépenses de promotion des DM calculée notamment sur les dépenses engagées pour la promotion, la présentation et la vente des produits et prestations: frais des congrès et des manifestations, rémunérations, frais de publication, achat d'espaces publicitaires....

2/2 Respect des règles de bonnes pratiques dans la mise en œuvre et le suivi du traitement

Le Prestataire doit établir avec l'équipe pluridisciplinaire en charge de la personne une coopération dans l'intérêt de cette dernière et de son entourage[4].

Conformité à la prescription :

Le Prestataire doit se conformer à la prescription médicale et à la préconisation de matériel émise par l'équipe pluridisciplinaire[9] :

- lorsque l'ordonnance ne comporte pas les informations nécessaires à son exécution et à sa prise en charge le Prestataire en informe le prescripteur et sollicite des précisions permettant la délivrance. Le Prestataire mentionne expressément sur l'ordonnance ces précisions, l'accord du prescripteur et sa date, appose sa signature et envoie copie de l'ordonnance modifié au prescripteur pour validation[6] ;
- il doit informer le prescripteur sur le matériel délivré au patient en vue de son suivi.
- il apporte à l'IDE du patient, si nécessaire, sa connaissance qualitative des matériels disponibles et adaptés au traitement, en l'absence d'une obligation dictée par le médecin prescripteur[11].

CODE DE BONNES PRATIQUES DES PSAD

Cas particulier d'un traitement par PPC[1] :

• le Prestataire doit obtenir avant toute mise en oeuvre du traitement les informations sur le réglage des pressions auprès du prescripteur :

- typologie de machine,
- pression constante,
- ou pilotée,
- niveau(x) de pression,
- fourchette minimale, maximale le cas échéant ;
- le Prestataire doit procéder à ces réglages conformément à la prescription médicale.

Contrôle régulier de l'observance :

Si le dispositif médical le nécessite, le Prestataire doit assurer le contrôle régulier de l'observance du traitement, en vue d'alerter le médecin en cas d'anomalie.

2/3 Respect des règles concernant les prescriptions

Rédaction d'aides à la prescription (initiale ou renouvellement).

Le Prestataire peut rédiger des aides à la prescription :

- ayant pour objet de détailler le produit ou la prestation ;
- mentionnant leurs conditions de prise en charge, leurs tarifs et le prix réglementé le cas échéant.

(Ces aides à la prescription sont considérés comme des documents publicitaires ; ils doivent en respecter la forme).

2/4 Respect de l'image d'un professionnel de santé

Le Prestataire ne doit pas tenir de propos pouvant nuire à un professionnel de santé dans l'exercice de sa profession[4].

Concernant un professionnel de santé, le Prestataire ne doit pas :

- tenir des propos critiques ou calomnieux ;
- médire de lui ;
- rapporter des propos pouvant lui nuire.

2/5 Respect strict des interdits dans les relations financières

D'une manière générale, le Prestataire s'interdit toute pratique de nature à compromettre l'indépendance de l'équipe médicale ou paramédicale en charge du patient vis-à-vis de sa liberté de prescription[1], [4] et [9].

Commissions, remises, ristournes ou intérêts[1]

Le Prestataire n'a pas le droit de verser des commissions, remises ou des ristournes à un tiers dont l'activité n'est pas celle de Prestataire.

NB : Un pharmacien d'officine exerçant l'activité de Prestataire est susceptible de recevoir des commissions s'il sous-traite une partie de ses prestations à un autre Prestataire.

Les professionnels de santé ne peuvent recevoir d'un Prestataire sous quelque forme que ce soit, de façon directe ou indirecte des intérêts ou ristournes proportionnels ou non au nombre des unités prescrites ou vendues[9].

Prestation plus coûteuse[1]

Il est interdit au Prestataire, l'encouragement, gratuit ou en échange d'avantages en nature ou en espèces, de la prescription ou du renouvellement d'une prestation plus coûteuse que celle nécessitée par l'état de l'assuré.

Avantage en nature ou en espèces[9]

Le Prestataire respecte strictement les interdits dans les relations avec les professionnels de santé stipulés par l'article L4113-6 du Code de la Santé publique (et ses textes d'applications, tels qu'éclairés par la circulaire ministérielle et le document d'orientation et d'interprétation cosigné du CNOM, LEEM et SNITEM en date du 21 juin 2007).

• En vertu de l'article L 4113-6 du CSP, issu de la loi n°2011-2012 du 29 décembre 2011, est interdit le fait, pour les professions médicales mentionnées ci après, de recevoir des avantages en nature ou en espèces, sous quelque forme que ce soit, d'une façon directe ou indirecte, procurés par des entreprises assurant des prestations, produisant ou commercialisant les produits pris en charge par les régimes obligatoires de sécurité sociale et donc les PSAD.

• **Les professionnels de santé concernés sont les :**
- **professions médicales (médecin, chirurgien dentiste, sage femme)**
- **pharmaciens**
- **infirmiers**
- **masseurs-kinésithérapeutes**
- **pédicures-podologues**
- **orthophonistes et orthoptistes.**

Les dispositions de l'article L 4113-6 s'appliquent également aux étudiants se destinant aux professions visées dans la 4e partie du CSP, à savoir :
- professions médicales (médecin, chirurgien dentiste, sage femme)
- professions de la pharmacie (pharmacien, préparateur en pharmacie)
- auxiliaires médicaux (infirmier, masseur kinésithérapeute, pédicure podologue, ergothérapeute, psychomotricien, orthophoniste, orthoptiste, manipulateur électroradiologie médicale, audio prothésiste, opticien lunetier, prothésiste, orthésiste, diététicien)
- aides-soignants
- auxiliaires de puériculture
- ambulanciers.

Ces dispositions s'appliquent enfin aux associations représentant les intérêts des membres des professions de santé concernées et/ou des étudiants se destinant auxdites professions.

Ces interdictions ne jouent pas dès lors que la convention liant l'étudiant ou le professionnel à l'entreprise a pour objet des activités de recherche ou d'évaluation scientifique, la participation aux manifestations de promotion ou à caractère exclusivement professionnel et scientifique, ou des relations normales de travail.

• En pratique, le Prestataire n'a pas le droit de proposer à un de ces professionnels de santé, notamment :
- une invitation à caractère de loisir, culturel ou sportif, même dans le cadre d'une manifestation professionnelle.

Il ne peut offrir aucune visite touristique, aucune activité ou initiation sportive, aucune place de spectacle ou de manifestation sportive ;

- une invitation à un repas de pure convivialité sans contexte professionnel ;
- une invitation à un repas dans un restaurant coûteux, même avec un objet professionnel ;
- la prise en charge dans le cadre des congrès ou séminaires d'une soirée de gala d'un montant élevé ;
- un financement d'un repas dit de « service » dans un restaurant, même sans activité de loisirs, ayant comme objet la pure convivialité entre membres d'un service hospitalier ou d'un groupe de professionnels de santé ;
- une prise en charge de frais extra-professionnels dans une manifestation professionnelle ;
- une prise en charge de frais d'un accompagnant dans le cadre d'une manifestation professionnelle ;
- un tarif préférentiel dans quelque domaine que ce soit qui permette au professionnel de santé de payer moins cher que le prix du marché habituel.

• **La remise de cadeau est interdite, sauf cas tolérés par l'Ordre des médecins** (objets de faible valeur, moins de 30 euros HT/an par professionnel de santé ; uniquement en rapport avec l'exercice professionnel ; exemples : petits accessoires de bureau de type agenda, pendulette, stylo, post-it).

■ Rémunération des professionnels de santé

Le Prestataire n'a pas le droit de rémunérer ou d'indemniser des praticiens ou auxiliaires médicaux :

- sous quelque forme que ce soit ;
- exerçant en établissements de soins ou ayant une activité libérale.
- **sauf dans les cas**
  - **d'activités de conseil, de coordination ou de formation,… (relations normales de travail) ;**
  - **d'activités de recherche ou évaluation scientifique** telles que prévues à l'article L4113-6 CSP.

■ Mise à disposition de personnels, services ou matériel[1]

Le Prestataire ne peut mettre au profit d'une structure hospitalière publique ou privée du personnel qu'il salarie. Par ailleurs, le Prestataire ne peut employer de personnels mis à disposition par une telle structure.

Le Prestataire ne peut mettre de personnel à la disposition d'un prescripteur, même à titre onéreux[1].

Le Prestataire ne peut mettre à disposition d'un professionnel de santé tout service et/ou matériel, notamment de diagnostic[1] :

- à titre gratuit ;
- ou à un prix manifestement sous évalué.

Cas du diagnostic du syndrome d'apnées du sommeil par polygraphie (PG) ou par polysomnographie (PSG) :

- le Prestataire n'a pas le droit de participer à la mise en œuvre de ces actes ;
- le Prestataire est autorisé à assurer la location au prescripteur du matériel nécessaire à la réalisation des actes (PG ou PSG), sous réserve :
  - d'établir un contrat avec le prescripteur avec un tarif défini de façon réaliste,
  - de tenir à la disposition des organismes de prise en charge dans le cadre de leur contrôle, une copie du contrat,
  - de facturer de façon effective le médecin,
  - de veiller au bon recouvrement des factures.

2/6 Frais d'hospitalité, rémunération des professions de santé, respect des procédures auprès des ordres professionnels

Le Prestataire est autorisé à prendre en charge des frais d'hospitalité pour les professions de santé susmentionnées ou à les rémunérer dans le cadre de la recherche scientifique, mais en respectant strictement le processus réglementaire auprès des ordres des professions de santé, défini dans le cadre de l'article L4113-6 et des articles R 4113-104 à 109 du CSP (9).

2.6.1 Conditions de prise en charge de frais d'hospitalité

• **Uniquement dans le cadre de manifestions de promotion ou de manifestations à caractère exclusivement professionnel et scientifique.**

• **Sous réserve :**

- d'établir une convention entre l'entreprise et le professionnel de santé :
  - signée des deux parties,
  - avec remise d'un exemplaire à chacune des parties ;
- de soumettre la convention pour avis préalable à l'ordre de la profession concernée ;
- de respecter le formalisme et les délais réglementaires *(cf. texte ci-après)* ;
- que le montant pris en charge soit :
  - raisonnable,
  - limité à l'objectif professionnel et scientifique,
  - non étendu à d'autres personnes que les professionnels de santé directement concernés.

■ **Pour la constitution d'un dossier de demande d'avis pour prise en charge de frais d'hospitalité (articles R 4113-105 et R 4113-106 CSP) :**

- Lettre décrivant le contexte de la prise en charge (objet de la manifestation), les frais et la durée de la prise en charge (préciser si prise en charge totale ou partielle) ;
- projet de convention avec les invités ;
- noms, raison sociale, adresse du siège social de l'entreprise ou de l'entreprise organisatrice ;
- programme scientifique détaillé (thème, durée du programme médical par rapport à la durée totale de la manifestation, lieu de son déroulement) :
  - si inscription payante : bulletin d'inscription officiel avec tarif (absence de prise en charge de toute activité de loisir, sportive ou culturelle, des cotisations aux sociétés savantes, dîner de gala) ;
- la nature et le montant des différentes prestations ou forfait énumérant les prestations :
  - typologie de transport et classe : train 1re classe, avion classe économique, véhicule personnel (indemnités kilométriques, péages et parkings), taxis, transferts,
  - nombre de repas et coût moyen unitaire des repas,
  - nombre de pauses et coût moyen unitaire,
  - nombre de nuitées, catégorie de l'hôtel et montant négocié de la nuitée incluant le petit déjeuner ;
- liste nominative des professionnels de santé dont le concours a été sollicité (nom, prénom, profession, spécialité, adresse professionnelle).

Le projet doit être adressé par l'entreprise en lettre recommandée avec AR ou coursier avec AR à l'ordre concerné.

■ **Délai réglementaire d'envoi des demandes d'avis aux ordres professionnels :**

Au minimum un mois strict avant le début de la manifestation ; le délai court à compter de l'accusé réception par l'ordre concerné.

■ **Montants de prise en charge ou typologie de frais communément admis :**

- Droits d'inscription dans leur intégralité sauf cotisation aux sociétés savantes, dîner de gala et inscription à une formation diplômante ;
- repas coût moyen unitaire : 60 euros ;
- hôtellerie 3* ou 4* avec tarif négocié ;
- frais de transport : train 1ère classe, avion classe économique, véhicule personnel (indemnités kilométriques, péages et parkings), taxi, transferts en car.

NB : Aucun montant n'est officiellement déterminé de façon réglementaire, ces données sont purement indicatives. L'Ordre des médecins examine chaque dossier et donne des avis au cas par cas, au vu du programme scientifique et de l'intérêt de la manifestation. Les conventions d'hospitalité des autres professionnels de santé sont à établir et à adresser aux ordres concernés (chirurgiens dentistes, infirmiers, masseurs-kinésithérapeutes, pédicures-podologues, pharmaciens, sages femmes).

2.6.2 Conditions de rémunération de professionnels de santé

Hors les cas interdits cités au paragraphe 2.5, la rémunération de professionnels de santé par un Prestataire est possible dans certaines situations :

■ **Relations normales de travail : Activités de conseil, d'expertise, de coordination ou de formation, de documentation,… sous réserve de rédiger un contrat :**

- décrivant les engagements des deux parties ;
- respectant les règles déontologiques applicables aux professionnels de santé ;
- signé par les deux parties ;
- transmis par le professionnel de santé à son ordre professionnel dans le mois qui suit sa signature.

■ **Activités de recherche ou évaluation scientifique sous réserve :**

- de l'énoncé explicite d'un objet et dans un réel but de recherche ou scientifique ;
- d'établir une convention entre l'entreprise et le professionnel de santé ;
- de soumettre la convention pour avis préalable à l'ordre concerné ;
- de respecter le formalisme et les délais réglementaires (R 4113-104 à 109) (réception de la demande d'avis auprès de l'ordre deux mois avant la mise en œuvre de la recherche) ;
- que le montant ne soit pas proportionnel aux prestations ou produits prescrits.

Tout Prestataire adhérent s'engage à transmettre à la Fédération, sur simple demande de sa part, une copie des avis ou à défaut des demandes d'avis effectuées auprès des ordres des professions de santé, afin de vérifier leur conformité à la réglementation.

2/7 Respect des procédures concernant les dons aux associations de recherche ou formations de professionnels de santé

Le Prestataire souhaitant faire un don à une association de recherche ou de formation de professionnels de santé, doit respecter le cadre réglementaire :

■ **Principes :**
- l'objet du don doit être désintéressé ;
- le don doit être destiné à un usage collectif et conforme aux statuts de l'association ;
- le don ne doit pas masquer un interdit dans la relation avec les professions de santé.

■ **Procédure :**
- le donateur doit récupérer les statuts de l'association et vérifier que celle-ci est habilitée à recevoir les dons dans le cadre de la recherche et/ou formation des professions de santé ;
- une lettre d'engagement du président de l'association ou une convention entre le donateur et le bénéficiaire doit attester du bon usage du don ;
- un reçu de don doit être établi, daté et signé par le président de l'association et transmis au donateur.

2/8 Déclaration des conventions[8]

■ **Toutes les conventions conclues entre un PSAD et**
- Les professionnels de santé (professions médicales, pharmaciens, auxiliaires médicaux) ;
- Les associations de professionnels de santé ;
- Les étudiants se destinant aux professions de santé ainsi que les associations et groupements les représentant ;
- Les associations d'usagers du système de santé ;
- Les établissements de santé ;
- Les fondations, les sociétés savantes et les sociétés ou organismes de conseil intervenant dans le secteur des produits ou prestations mentionnés au premier alinéa ;
- Les entreprises éditrices de presse, les éditeurs de services de radio ou de télévision et les éditeurs de services de communication au public en ligne ;
- Les éditeurs de logiciels d'aide à la prescription et à la délivrance ;
- Les personnes morales assurant la formation initiale des professionnels de santé mentionnés au 1° ou participant à cette formation ;

doivent être rendues publiques, de même que tous les avantages consentis aux mêmes personnes.

■ **Informations à fournir :**
• **Pour les conventions :**
■ **L'identité des parties à chaque convention, soit :**
- **a)** Lorsqu'il s'agit d'un professionnel de santé, le nom, le prénom, la qualité, l'adresse professionnelle et, le cas échéant, la qualification, le titre, la spécialité, le numéro d'inscription à l'ordre ou l'identifiant personnel dans le répertoire partagé des professionnels de santé ;
- **b)** Lorsqu'il s'agit d'un étudiant se destinant à l'une des professions relevant de la quatrième partie du code, le nom, le prénom, l'établissement d'enseignement et, le cas échéant, l'identifiant personnel dans le répertoire partagé des professionnels de santé ;
- **c)** Lorsqu'il s'agit d'une personne morale : la dénomination sociale, l'objet social et l'adresse du siège social ;
- **d)** L'identité de l'entreprise concernée ;

■ **La date de signature de la convention ;**

■ **L'objet de la convention, formulé dans le respect des secrets protégés par la loi, notamment du secret industriel et commercial ;**

■ **Lorsque la convention a pour objet une manifestation mentionnée au troisième alinéa de l'article L. 4113-6, le programme de cette manifestation.**

• Pour les avantages :

■ L'identité de la personne bénéficiaire et de l'entreprise *(cf ci-dessus)* ;

■ Le montant, toutes taxes comprises, arrondi à l'euro le plus proche, la date et la nature de chaque avantage perçu par le bénéficiaire au cours d'un semestre civil ;

■ Le semestre civil au cours duquel les avantages ont été consentis.

■ Modalités de publication :

• Les PSAD envoient au responsable du site internet public les informations concernant les conventions et avantages octroyés, avant le 1er août ou le 1er février de chaque année pour les avantages consentis au cours du semestre civil précédent, ou dans les 15 jours de la signature de la convention ; la communication est faite par tout moyen permettant d'établir sa date.

• Dans l'attente de la mise en place du site internet public, les PSAD communiquent les conventions et avantages à chaque conseil de l'ordre concerné par la profession des bénéficiaires, avant le 1er août ou le 1er février de chaque année pour les avantages consentis au cours du semestre civil précédent, ou dans les 15 jours de la convention ; la communication est faite par tout moyen permettant d'établir sa date.
En outre, les PSAD publient ces informations sur leur site internet, un site commun ou le site de leur organisation professionnelle (dans une rubrique dédiée, identifiable et accessible librement et gratuitement), avant le 1er octobre ou le 1er avril de chaque année, pour les informations concernant le semestre précédent. Tout cela dans le respect des obligations réglementaires concernant la sécurité du site, le délai de conservation des données, l'information des intéressés et la déclaration nécessaire à la CNIL conformément à la loi Informatique et Libertés.

L'obligation de publication ne fait pas disparaître les règles d'interdiction, ni le respect des procédures préalables de communication précisées au 2/6.

Chapitre 3

Relations avec les organismes payeurs(1)

3/1 Engagements à la maîtrise médicalisée

Les PSAD peuvent adhérer à la convention nationale permettant de facturer en tiers payant les caisses d'assurance maladie. Ils doivent formellement manifester leur adhésion individuelle à la convention auprès de la Caisse d'assurance maladie de leur lieu d'implantation.
Le Prestataire doit veiller au sein de sa structure, au respect des règles et à la qualité de facturation de ses prestations, auprès des organismes payeurs, pour leur éviter un surcroît de travail ou un paiement de sommes indues. Dans ce sens, il vérifie, dans la mesure du possible, les droits de couverture santé du patient avant de procéder à une demande de facturation.

■ **Le Prestataire doit, d'une manière générale, dans le cadre de ses activités, veiller à ne pas contribuer à générer des dépenses de santé inutiles.**

■ **Il doit aussi :**
• Participer au suivi de la bonne observance des patients.
• Le cas échéant, transmettre les données relatives à l'observance enregistrées par l'appareil PPC.

■ **Le Prestataire n'a pas le droit de participer à la mise en oeuvre des actes de polygraphie (PG) ou de polysomnographie (PSG) pour le compte des médecins, même à titre payant(1).**

3/2 Respect de la procédure de facturation en tiers payant

Pour pratiquer la facturation en tiers payant, le Prestataire doit avoir adhéré à la convention nationale des prestataires(1).
Le Prestataire doit respecter les processus définis par l'Assurance maladie pour la facturation en tiers payant(1) :
• la facture doit être établie sur le modèle de feuille de soins arrêté par la réglementation;
• le numéro de facture doit figurer à l'emplacement spécifié par l'AM ;
• le Prestataire doit adresser à la caisse d'assurance maladie de l'assuré :
  - la feuille de soins originale de la prestation,
  - le duplicata de la prescription médicale, sauf en cas de renouvellement ;
• les données doivent principalement être adressées par télétransmission selon le protocole d'accord national (dispositif B2).

3/3 Respect des formalités de la DEP

Pour les produits et prestations subordonnés à la procédure d'entente préalable, le Prestataire doit établir la DEP sur l'imprimé national en vigueur, à l'exclusion de tout autre document(1).

3/4 Déclaration des locaux et conformités(1)

Le Prestataire doit déclarer aux organismes d'assurance maladie toute ouverture de local destiné à sa pratique professionnelle.
Le Prestataire doit, pour exercer dans un local, l'inscrire au registre du commerce (si l'entreprise est commerciale).
Chaque local doit avoir été reconnu conforme aux conditions d'installation et d'équipement prévus par la convention.
Le prestataire respecte s'il y a lieu les délais d'autorisation nécessaires.

3/5 Déclaration de changement de situation

■ Le prestataire tient à jour les déclarations de ses sites : il communique tout changement de domiciliation, responsabilités, activités aux CPAM et ARS. Le prestataire met en place des actions correctives demandées par la visite d'inspection de l'ARS.

■ **Le Prestataire doit refaire une demande d'adhésion à la convention des prestataires pour tout changement de situation(1) :**
  • ayant des conséquences sur sa responsabilité dans l'exercice de son activité ;
  • ou entraînant un changement de responsabilité juridique.

■ **Le Prestataire dont le respect des obligations conventionnelles ou réglementaires est mis en cause s'engage à :**
  • Examiner de bonne foi les anomalies qu'on lui reproche.
  • Privilégier des moyens de résolution de conflits alternatifs.
  • Préparer sa défense en se faisant assister le cas échéant par un professionnel, en veillant au bon respect des procédures.
  • Corriger s'il y a lieu les pratiques en cause.
  • Respecter les sanctions définitives qui seraient prononcées le cas échéant.

3/6 Facturation auprès des organismes complémentaires

Afin de faciliter les relations de travail avec les organismes complémentaires, le Prestataire favorise dans la mesure du possible, la mise en œuvre de la facturation en tiers payant auprès de ceux-ci.

3/7 Transmission de données pour analyse des dépenses et évolution des pratiques professionnelles

Les organisations professionnelles ont convenu avec l'Assurance maladie de la nécessité de recueillir par panel des données afférentes à leur secteur d'activité, afin d'alimenter l'échange d'informations à caractère économique avec les caisses d'AM, (du type, reste à charge moyen pour l'assuré, montant annuel des facturations, nombre d'assurés)[9].

Dans ce contexte, tout prestatire adhérent s'engage à transmettre à la Fédération, sur simple demande de sa part, des éléments anonymisés de son activité qui permettent de répondre aux attentes de l'AM.

Les PSAD sont tenus de déclarer par voie électronique à l'ANSM, l'ensemble des produits ou prestations qu'ils commercialisent sur la LPP en précisant pour chaque produit ou prestation le code correspondant à l'inscription du produit ou de la prestation sur la liste. Les PSAD sont tenus par conséquent d'actualiser toute modification affectant le code LPP dans un délai de 3 mois à compter de l'entrée en vigueur du nouveau code auquel est rattaché le produit ou la prestation[10].

Par ailleurs, les organisations professionnelles se sont accordées avec le CEPS sur la nécessité d'améliorer et de partager les informations qu'elles détiennent pour une meilleure connaissance des marchés des produits et prestations mentionnés à l'article L-165-1 du code de la sécurité sociale[10].

À cette fin les organisations signataires doivent se doter d'une capacité de recueil anonymisé des données commerciales dans l'objet de répondre à la demande du CEPS.

Chapitre 4

Relations avec les associations de patients

Dans le cadre de ses relations avec les associations de patients, le Prestataire ne doit pas chercher à influencer les membres adhérents quant au choix de leur Prestataire.

Lorsque le Prestataire fait un don à une association de patients, ce don doit :

- avoir un caractère désintéressé ;
- permettre de soutenir l'association dans ses actions d'information, de prévention ou de défense des patients, en rapport avec ses statuts.

Les Prestataires (comme toutes les entreprises fabriquant et commercialisant des produits mentionnés dans la cinquième partie du CSP) doivent **déclarer chaque année, avant le 30 juin auprès de la HAS,** la liste des associations de patients qu'elles soutiennent et le montant des aides de toute nature qu'elles leur ont procurées l'année précédente (Art. L1114-1 du CSP dernier alinéa).

Site internet : www.has-sante.fr

Chapitre 5

Relations entre prestataires

Le Prestataire doit adopter à l'égard des autres Prestataires une conduite loyale.

Concernant les patients déjà appareillés par un autre Prestataire :

- un Prestataire ne doit pas essayer de contacter des patients dans le but de les inciter à changer de Prestataire ;
- un patient bénéficiant d'une prestation et nécessitant en complément de son traitement une autre prestation doit conserver prioritairement le même Prestataire, hors le cas où celui-ci ne serait pas en mesure d'assurer la prestation.

Concernant les salariés des Prestataires :

- Tout Prestataire s'engage à :
  - ne pas inciter de façon déloyale un salarié d'une autre entreprise à intégrer sa propre structure,
  - vérifier l'absence de clause de non concurrence applicable au contrat de travail d'un salarié qu'il envisage de recruter, et si la clause existe, la respecter le cas échéant en ne recrutant pas la personne.

Les PSAD respectent soigneusement les obligations légales prohibant d'une part toute action de nature à affecter la concurrence (pratiques concertées ou restrictives de concurrence, etc…), d'autre part les pratiques abusives ou déloyales (dénigrement, non respect des prescriptions réglementaires…).

Chapitre 6

Relations avec d'autres organisations professionnelles

Autres organisations professionnelles :

Le Prestataire adhérent s'engage à ne pas transférer des informations internes émanant de la Fédération, sauf autorisation préalable, à d'autres organisations professionnelles dont il est adhérent.
Si le Prestataire adhérent constate, dans ses relations avec des professionnels de santé ou d'autres prestataires, des difficultés liées à l'application des dispositions réglementaires ou conventionnelles en vigueur, il en informe la Fédération pour essayer de trouver une solution, sans préjudice des actions judiciaires qu'il serait amené à conduire en tant que de besoin.

Chapitre 7

Respect de l'environnement, développement durable

Dans l'exercice de ses activités, le Prestataire ne doit pas porter atteinte à l'environnement.

■ Il ne doit adopter aucune conduite nuisible à la qualité de l'air ou des eaux.

■ Il doit définir des procédures de traitement des déchets ou de gestion des rebus, conformes à la réglementation, particulièrement en ce qui concerne :

- les déchets d'activités de soins à risque infectieux (DASRI) ;
- les déchets industriels :
  - le Prestataire respecte notamment le décret n° 2005-829 du 20 juillet 2005 relatif à la composition des équipements électriques et électroniques et l'élimination des déchets issus de ces équipements et les arrêtés correspondants (collecte sélective, traitement sélectif de certains composants dangereux, recyclage…) ;
- les eaux usées.

■ Le prestataire reconnaît et protège les droits des lanceurs d'alerte concernant les produits ou procédés pouvant être à l'origine d'un risque grave pour la santé publique ou l'environnement.
Dans les conditions définies par voie réglementaires, ces alertes sont consignées par écrit et l'auteur de l'alerte est informé de la suite qui lui est réservée.

■ L'auteur de bonne foi de l'alerte ne peut faire l'objet d'aucune mesure disciplinaire ni de mesure discriminatoire directe ou indirecte, de quelque nature que ce soit.

Cinquième partie

Le Comité de Bonnes Pratiques

5/1 Composition, rôle et fonctionnement du Comité de Bonnes Pratiques

Le Comité de bonnes pratiques exerce une mission d'information, de médiation ou de sanction.

Il est composé par :

- Cinq membres du Comité Exécutif de la Fédération.
- Deux prestataires adhérents ne faisant pas partie du Comité Exécutif et dont au moins un exerce la même prestation que le prestataire mis en cause, choisis par le Comité Exécutif.
- Il peut être fait appel à l'assistance de conseillers techniques en fonction des sujets de l'ordre du jour, et qui ne prennent pas part au vote.

■ Le président du Comité de bonnes pratiques est élu par ses membres pour chaque dossier à examiner. Le Secrétariat est assuré par les permanents de la Fédération.

■ Les membres du Comité de bonnes pratiques vérifient pour chaque cas qu'ils ne sont pas en situation de conflit d'intérêts.

■ Le Comité de bonnes pratiques se réunit en tant que de besoin, sur convocation de son secrétariat. La convocation précise l'objet de la réunion et joint la lettre de saisine.

■ Les décisions ou avis du Comité de bonnes pratiques sont pris à la majorité simple des membres présents ou représentés, celle du Président étant prépondérante en cas de partage.

5/2 Saisine du Comité de bonnes pratiques

- Tout prestataire adhérent à un syndicat membre de la Fédération ;
- ou tout patient pris en charge par un prestataire adhérent à un syndicat membre de la Fédération ;
- ou tout professionnel de santé en relation avec un prestataire adhérent ;

peut saisir par écrit le Comité de bonnes pratiques pour toute question, problème ou litige concernant un prestataire adhérent et ayant un rapport avec le respect du Code des Bonnes Pratiques.
La personne le saisissant précise la mission (information, médiation ou sanction) qu'elle demande au Comité de bonnes pratiques de remplir.

5/3 Mission d'information

Tout PSAD adhérent peut demander au Comité de bonnes pratiques son interprétation sur une ou plusieurs dispositions du Code de Bonnes Pratiques en précisant la ou les dispositons concernées et les éléments factuels justifiant sa question.

La saisine intervient par lettre RAR adressée au président du Comité de bonnes pratiques. Les éléments figurant dans cette lettre sont tenus confidentiels.

Le secrétariat examine les éléments communiqués et le cas échéant demande des éclaircissements ou informations complémentaires par écrit ou par oral, avant toute transmission aux membres du Comité. Le Comité rédige son avis avec l'assistance du secrétariat. Le Comité de bonnes pratiques répond de la manière qu'il juge appropriée. Les avis rendus dans ce cadre ne peuvent être communiqués à quiconque par le pretataire à l'origine de la demande.

5/4 Mission de médiation

■ Les personnes visées au 5/2 peuvent former une demande de médiation au Comité de bonnes pratiques pour toute diffuculté ou litige se rapportant à l'application ou l'interprétation du Code de Bonnes Pratiques et impliquant un prestatiare adhérent à un syndicat membre de la Fédération.

■ La médiation n'est pas obligatoire et suppose l'accord des deux parties ; pendant le temps de la médiation, les parties s'interdisent de recourir aux juridictions judiciaires.

■ La saisine du Comité de bonnes pratiques se fait par lettre RAR, en précisant les dispositions du Code de Bonnes Pratiques qui sont concernées et les faits justifiant la saisine. Le Président du Comité notifie dans un délai de 15 jours la saisine à l'autre partie intéressée et lui demande si elle accepte la médiation ; il avise sans délai la partie saisissante de la réponse reçue.

■ Le Comité de bonnes pratiques peut également être saisi de manière conjointe.

■ Le Comité de bonnes pratiques convoque par LRAR les deux parties à une réunion et entend leurs explications respectives. Si un accord ne peut être immédiatement trouvé, le président désigne deux membres du Comité éxécutif de la Fédération chargés de trouver une solution avec les parties. Les membres désignés et les parties définissent les dates de réunions et le délai dans lequel ils souhaitent parvenir à un accord. Les membres désignés rendent compte au Comité de bonnes pratiques de l'issue de la médiation.
En cas d'accord, un procès-verbal de médiation mettant fin au différent est rédigé, signé et remis aux parties. En l'absence d'accord, il est simplement constaté que la médiation n'a pu aboutir ; il ne peut alors être fait état par quiconque des éléments discutés lors de la médiation.

5/5 Mission de sanction

Les personnes visées au 5/2 peuvent saisir le Comité de bonnes pratiques d'une demande de sanction contre un PSAD adhérent en cas de non respect des dispositions du Code de Bonnes Pratiques ou de la réglementation, ou si les termes d'une précédente médiation n'ont pas été respectés. Le Comité peut également être saisi par le Conseil d'administration de chaque syndicat membre de la Fédération.

La lettre de saisine adressée en RAR à son Président, doit mentionner le nom de l'entreprise adhérente concernée, les dispositions dont la violation est alléguée, les faits justifiant la saisine et comporter copie des pièces justificatives étayant la mise en cause. Si la saisine est incomplète le Président demande les éléments complémentaires à l'auteur de la plainte et peut décider de la classer s'il ne les recoit pas dans le délai qu'il a fixé.

Lorsque la plainte est complète, le Président désigne un rapporteur chargé de permettre au Comité de bonnes pratiques d'analyser le litige pour lequel il a été saisi. Il s'adresse au PSAD concerné pour lui communiquer la plainte et les pièces justificatives et lui demander de fournir, dans le délai d'un mois, toute explication ou élément qu'il juge nécessaire pour assurer sa défense.

Si ces éléments n'apparaissent pas immédiatement suffisant pour classer la plainte, le Président du Comité convoque le PSAD adhérent pour qu'il communique oralement les éléments de sa défense, dans un délai d'un mois. L'auteur de la plainte est également convoqué et peut présenter ses observations.

■ **Après audition, le Comité rend sa décision, graduée en fonction de la situation et des éléments qui ont été discutés :**

- classement sans suite ;
- avertissement ;
- mise en demeure ;
- exclusion de la Fédération ;
- transmission aux autorités compétentes.

Tous les types de décision ci listées et notamment la sanction de l'exclusion nécessitent que le Comité Exécutif de la Fédération en soit informé et que la décision soit ratifiée par les organes décisionnaires des syndicats membres de la Fédération dans les conditions prévues par leurs statuts.

La décision du Comité de bonnes pratiques est rendue dans un délai maximum de trois mois de la plainte et notifiée à l'auteur de la plainte et au PSAD adhérent. Elle ne préjuge pas d'une éventuelle décision d'une autorité juridictionnelle.

Sixième partie

Acte d'engagement de tout adhérent à un syndicat membre de la Fédération

Chaque adhérent à un syndicat membre de la Fédération ou personne faisant une demande d'adhésion doit remplir deux exemplaires du formulaire page 59 et les signer.

Un exemplaire est conservé par l'adhérent, un autre est transmis au syndicat membre de la Fédération concerné.

Annexes

APPENDIX 3- DECLARATION OF HELSINKI

WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964
and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington DC, USA, October 2002 (Note of Clarification added)
55th WMA General Assembly, Tokyo, Japan, October 2004 (Note of Clarification added)
59th WMA General Assembly, Seoul, Republic of Korea, October 2008
64th WMA General Assembly, Fortaleza, Brazil, October 2013

Preamble

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

The Declaration is intended to be read as a whole and each of its constituent paragraphs should be applied with consideration of all other relevant paragraphs.

2. Consistent with the mandate of the WMA, the Declaration is addressed primarily to physicians. The WMA encourages others who are involved in medical research involving human subjects to adopt these principles.

General Principles

3. The Declaration of Geneva of the WMA binds the physician with the words,

"The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."

4. It is the duty of the physician to promote and safeguard the health, well-being and rights of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

5. Medical progress is based on research that ultimately must include studies involving human subjects.

6. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best proven interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

7. Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights.

8. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

9. It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.

10. Physicians must consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

11. Medical research should be conducted in a manner that minimises possible harm to the environment.

12. Medical research involving human subjects must be conducted only by

individuals with the appropriate ethics and scientific education, training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional.

13. Groups that are underrepresented in medical research should be provided appropriate access to participation in research.

14. Physicians who combine medical research with medical care should involve their patients in research only to the extent that this is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.

15. Appropriate compensation and treatment for subjects who are harmed as a result of participating in research must be ensured.

Risks, Burdens and Benefits

16. In medical practice and in medical research, most interventions involve risks and burdens.

Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects.

17. All medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or groups affected by the condition under investigation.

Measures to minimise the risks must be implemented. The risks must be continuously monitored, assessed and documented by the researcher.

18. Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed.

When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study.

Vulnerable Groups and Individuals

19. Some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm.

All vulnerable groups and individuals should receive specifically considered protection.

20. Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

Scientific Requirements and Research Protocols

21. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.

22. The design and performance of each research study involving human subjects must be clearly described and justified in a research protocol.

The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, potential conflicts of interest, incentives for subjects and information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study.

In clinical trials, the protocol must also describe appropriate arrangements for post-trial provisions.

Research Ethics Committees

23. The research protocol must be submitted for consideration, comment, guidance and approval to the concerned research ethics committee before the study begins. This committee must be transparent in its functioning, must be independent of the researcher, the sponsor and any other undue influence and must be duly qualified. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and

standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration.

The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No amendment to the protocol may be made without consideration and approval by the committee. After the end of the study, the researchers must submit a final report to the committee containing a summary of the study's findings and conclusions.

Privacy and Confidentiality

24. Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information.

Informed Consent

25. Participation by individuals capable of giving informed consent as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees.

26. In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.

After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

All medical research subjects should be given the option of being informed about the general outcome and results of the study.

27. When seeking informed consent for participation in a research study the physician must be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship.

28. For a potential research subject who is incapable of giving informed consent, the physician must seek informed consent from the legally authorised representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject, the research cannot instead be performed with persons capable of providing informed consent, and the research entails only minimal risk and minimal burden.

29. When a potential research subject who is deemed incapable of giving informed consent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorised representative. The potential subject's dissent should be respected.

30. Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research group. In such circumstances the physician must seek informed consent from the legally authorised representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research must be obtained as soon as possible from the subject or a legally authorised representative.

31. The physician must fully inform the patient which aspects of their care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never adversely affect the patient-physician relationship.

32. For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse. There may be exceptional situations where consent would be impossible or impracticable to obtain

for such research. In such situations the research may be done only after consideration and approval of a research ethics committee.

Use of Placebo

33. The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best proven intervention(s), except in the following circumstances:

Where no proven intervention exists, the use of placebo, or no intervention, is acceptable; or

Where for compelling and scientifically sound methodological reasons the use of any intervention less effective than the best proven one, the use of placebo, or no intervention is necessary to determine the efficacy or safety of an intervention

and the patients who receive any intervention less effective than the best proven one, placebo, or no intervention will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention.

Extreme care must be taken to avoid abuse of this option.

Post-Trial Provisions

34. In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process.

Research Registration and Publication and Dissemination of Results

35. Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.

36. Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made

publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

Unproven Interventions in Clinical Practice

37. In the treatment of an individual patient, where proven interventions do not exist or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorised representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information must be recorded and, where appropriate, made publicly available.

APPENDIX 4- HYPERGLYCEMIA AND HYPOGLYCEMIA PROTOCOL INSTRUCTIONS

HYPERGLYCEMIA PROTOCOL:

If a participant's CGM reading is ≥300 mg/dL for over 1 hour, or ≥400 mg/dL at any point, the participant or their caregiver will be instructed to take the following steps:

- Perform a blood ketone measurement with the study ketone meter. Participants will also be encouraged to check ketones if they are clinically concerned.
- Correction insulin may be taken per the participant's usual routine.
- Participants will be instructed to change their pump site and administer correction insulin via insulin syringe or pen for ketones ≥0.6 mmol/L and to additionally notify study staff for ketones ≥3.0 mmol/L.

HYPOGLYCEMIA PROTOCOL:

If a participant receives a CGM hypoglycemia threshold alert or notes that the CGM glucose is below the hypoglycemia threshold alert value,

- A confirmatory fingerstick testing will be performed.
- The participant or their caregiver will be instructed to treat hypoglycemia with ~16 grams of fast-acting oral glucose (corresponding to half of soda can or 3 pieces of sugar n°4).
- A confirmatory fingerstick testing will be performed 20 minutes after fast-acting oral glucose intake, if CGM glucose reading is still < 80 mg/dL.