CLINICAL PROTOCOL

The Degen study: Post-market clinical follow-up on the PASS LP, PASS Degen and PASS Tulip systems.

Degen Study # 0313

Sponsor/ Monitor

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Investigator Agreement and Signature Page

Study reference

Degen study #0313 (MDT220150313) // ID RCB: 2017-A03398-45 // Clinicaltrials.gov identifier: NCT04670536

Study title

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Protocol version:

V09- 12 March 2024

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I have read the protocol, including all appendices, and I agree that it contains all necessary details for me and my staff to conduct this study as described. I will conduct this study as outlined herein and will make a reasonable effort to complete the study within the time designated.

I agree to comply with the Declaration of Helsinki, the Clinical Investigation Plan, and Good Clinical Practice, as well as local laws, regulations, and standards. I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation and conduct of the clinical investigation without the prior written consent of Medicrea.

I will provide all study personnel under my supervision copies of the protocol and access to all information provided by Medicrea. I will discuss this material with them to ensure that they are fully informed about the products and the study.

Investigator's Signature:	
Investigator's Name:	
Institution:	
Date:	

Glossary:

Term	Definition
ADE	*Adverse Device Effect*
ADH	*Anterior Disc Height*
AE	*Adverse Event*
AIS	*Adolescent Idiopathic Scoliosis*
CA	*Competent Authority*
CEC	*Clinical Event Committee*
CFR	*Code of Federal Regulation*
CIP	*Clinical Investigation Plan*
CL	*cervical lordosis*
CRA	*Clinical Research Associate*
CRF	*Case Report Form*
CT scan	*Computed Tomography scan*
CTA	*Clinical Trial Agreement*
CV	*Curriculum Vitae*
DD	*Device Deficiency*
DDD	*Degenerative Disc Disease*
DoH	*Declaration of Helsinki*
DTL	*Delegated Task List*
EC/ Ethics Board	*Ethics Committee*
eCRF	*Electronic Case Report Form*
EDC	*Electronic Data Capture*
FAL	*Foreseeable Adverse Event List*
FD	*Financial Disclosure*
FDAAA	*Food and Drug Administration Amendments Act*
GCP	*Good Clinical Practice*
ICH	*International Conference of Harmonization*
IFU	*Instructions For Use*
MedDRA	*Medical Dictionary for Regulatory Affairs*
MRI	*Magnetic Resonance Imaging*
NA	*Not Applicable*
NS	*Non specific*
ODI	*Oswestry Disability Index*

Term	Definition
PDH	*Posterior Disc Height*
PHI	*Protected Health Information*
PI	*Principal Investigator*
PMCF	*post-market clinical follow-up*
PSI	*Patient Satisfaction Index*
RA	*Regulatory Authority*
RIPH II	*Reference to French law: "Recherche interventionnelle à risques et contraintes minimes"*
SADE	*Serious Adverse Device Effect*
SAE	*Serious Adverse Event*
SAP	*Statistical Analysis Plan*
SF-12	*(Medical Outcome Study) Short Form Health Survey 12*
UADE	*Unanticipated Adverse Device Effect*
UAE	*Unavoidable Adverse Event*
USADE	*Unanticipated Serious Adverse Device Effect*
VAS	*Visual Analogical scale*

SUMMARY/SYNOPSIS OF THE STUDY

Title

The Degen study: post-market clinical follow-up on the PASS LP, PASS DEGEN, and PASS Tulip systems.

Instrumentation to be studied

Implants and instruments from PASS LP system (including PASS DEGEN ring rods), PASS Tulip systems, and eventually if used by investigators, other MEDICREA's products (interbody cages, sublaminar bands, etc.)

Sponsor (funding source) - Monitor

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Dr Olivier HAMEL – Clinique des cèdres – Cornebarrieu

Objectives

- This post-market clinical follow-up study aims to collect some data about the performance and safety of MEDICREA's products to treat thoraco-lumbar degenerative diseases. This study is supporting the clinical evaluation report.
- This PMCF will also contribute to state about usability of the implants and instruments.
- The primary objective of the study is to assess the fusion rate at the 24-month visit postoperatively.

The secondary objectives are:

- to assess fusion rate at the 1/6 month and 12-month visit
- to describe the evolution of the patients' quality of life before and at each follow-up after the surgery (change of non-validated ODI score, change of back pain score, change of leg pain score, change of non-validated SF -12 score, patient satisfaction),
- to collect data about the surgeons' satisfaction, with these implants and instruments during the surgery and regarding the patients' evolution
- to collect data about the safety of the implants (device or procedure ‑ related adverse events and all SAEs up to 24 months)

-

Method

Multicenter, retro-prospective, non-comparative post-market clinical follow-up study.

Inclusion criteria

Patients at least 18 years old

Patients suffering from a spinal degenerative disease

Patients requiring spinal surgery for less than 4 levels of a spinal degenerative disease

Patients implanted with MEDICREA's products or patients who are candidate to receive MEDICREA's products, including at least PASS LP and/or PASS Degen and/or PASS TULIP Prime implants

Patients affiliated with a national insurance system

Exclusion criteria

Patients unable or unwilling to sign and understand an information note with proof of patient consent

Patients unable to complete a self-administered questionnaire

Patients-presenting contra-indications to an Xray follow-up

Patients of more than 18 years old under a protection procedure

Patients judged as non-compliant by the investigator or not able to come back for follow-up visits for up to 2 years

Number of clinical centers and patients

At least 75 patients will be included in 4 centers:

- 25 patients with PASS LP implants
- 25 patients with PASS Degen implants
- 25 patients with PASS Tulip PRIME implants

A complete list of names, addresses, professional positions and emergency contact details of the clinical investigators and clinical investigation sites will be distributed under a separate cover. Each center will enroll subjects treated with one specific system.

Length of Study

Enrollment period: estimated to be 57 months

Duration of follow-up: 24 months after the surgery

Retrospective or prospective enrollments can begin as soon as approvals have been obtained from the authorities.

Total study duration: 78 months

Evaluation Tools

- Case report form (CRF): epidemiology, indication, operative data, adverse events, serious adverse events…
- Xrays: in both coronal and sagittal planes (standing neutral position) pre- and postoperatively, full spine if available (from C7 to pelvis). CT scan and MRI if available

- Self-administered patient questionnaires: non-validated Oswestry Disability Index (ODI), non-validated SF-12 questionnaire, VAS pain scores (back and legs) and Patient Satisfaction Index (PSI).

Data will be collected before and after the surgery at each follow-up visit done by surgeons according to their routine practice.

The routine practice for postoperative visits is generally 1-6 months, 12 months and 24 months postoperatively.

No additional examinations nor visits are requested by this current protocol. Only existing data and examinations following the surgeon's routine practice will be collected.

Data collection

	Electronic Case report forms	Patient Self-questionnaires	Fusion assessment Imaging*	AE/DD collection
Preoperative	X	X	X	As they occur
Surgery	X			
Immediate Postoperative	X			
1-6 months (+/- 1 month)	X	X	X	
12 months (7 months – 18 months))	X	X	X	
24 months (18 months – 30 months)	X	X	X	

**CT scan, Xrays, and/or MRI will be done according to the centers' standard of care. Images need to be available for investigators to assess fusion, they are no longer collected by the sponsor.*

1. Justification for the clinical investigation

[References: 1to 3]

The human back is an assembly of bones and muscles connected to each other creating a balanced system able to share some load and perform some movements. But with the time, this assembly is worn and some pains can be felt. This is called degenerative pathology. On the other hand, the spine can be deformed or curved (e.g., scoliosis, kyphosis, and/or lordosis): unnatural curvature of the spine. Scoliosis is a sideways curve of the spine in an S or C-shaped. Lordosis corresponds to a significantly inward curve at the lower back. Kyphosis is characterized by an abnormally rounded upper back.

As a consequence of these two kinds of diseases, patients can suffer from back pain, leg pain, neurological symptoms, and/or functional disabilities. When antalgics are not enough or when the disability is too important, surgery can be performed. The aim of the surgery could be to decompress the suffering nerves and to stabilize the spine to avoid abnormal movements in case of degenerative diseases or to restore a natural curve in case of deformity diseases. This stabilization is obtained thanks to a complex of rods, screws, and connectors, sometimes interbody cages, that are fixed to the vertebrae and that promote osteosynthesis of the instrumented segments.

The purpose of this post-market clinical study is to evaluate the long term safety and efficacy of the MEDICREA's systems PASS LP, PASS DEGEN, and PASS Tulip PRIME to treat degenerative diseases.

This study is supporting the clinical evaluation report. From the standard-of-care perspective, the results of The Degen study are expected to contribute to a better understanding of expected safety and clinical outcomes from a short (intra- and peri-operative) to a medium-term follow-up (post-operatively).

Table 1- Summary/evaluation of the results of the clinical testing

Study number	Nb of patients implanted	Mean age (years)	Indications	Mean follow-up (months)	Resume
#0301	**166** 136 with a follow up > 12 months and 66 with a follow up > 24 months	**15.0 years old**	AIS	NS	**#0301 PMCF investigation**: The post-market clinical follow-up study (PMCF) "0301" was retrospective, monocenter (NICE), and non-randomized. The objective of the PMCF study was to evaluate the 3D correction of the PASS family (ST2R technique) on adolescent idiopathic scoliosis (AIS).
#0301-02	**21**	**13.9 years old**	AIS	38	**#0301-02 PMCF investigation**: A monocenter retrospective study was conducted to evaluate the efficacy and the safety of the PASS instrumentation and ST2R technique in the treatment of severe scoliosis exceeding 70°. PASS MED until 2007 then PASS LP were evaluated. The following tabular summary summarizes the design as well as the results.

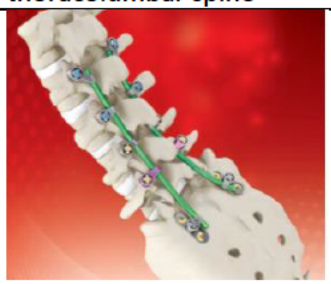
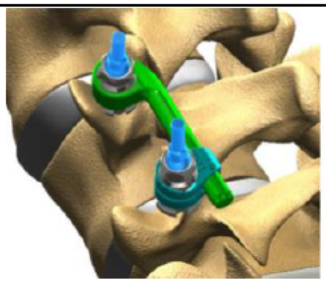
Study number	Nb of patients implanted	Mean age (years)	Indications	Mean follow-up (months)	Resume
#0303	**291**	Not available	Not available	Not available	**#0303 PMCF investigation (Case series):** A case series was conducted by a surgeon in Turkey (Dr A. Sehirlioglu (Gulhane Military Medical Academy Orthopaedics& Traumatology Department, Turkey) to document spinal disorders clinical cases (291 clinical cases) PASS instrumentation tool (implant failure, operative complication, and postoperative infections).
#0305	**83**	**14.5 years old**	AIS	NS	**#0305 PMCF investigation:** The post-market clinical follow-up investigation (PMCF) "0305" was prospective, multicenter. Three centers were involved in the USA (Louisiana, Georgia and Ohio). The purpose of this clinical investigation was to evaluate the clinical, functional, and radiographic outcomes following the reduction of idiopathic scoliosis using the PASS LP® system. The analysis was not done based on the results presented below as no clinical study report is currently available.
#0307	**60**	Not available	Not available	Not available	**#0307 PMCF investigation (Case series):** An observational and monocenter clinical study was conducted by a surgeon in France (Dr J.L. Jouve (La Timone Hospital, Marseille, France) to evaluate the sagittal and coronal correction of idiopathic scoliosis in 60 patients.
#0309	**72** 62 reaching their 6 months follow-up were eligible for analysis	**62.1 years old**	Adult deformity	NS	**#0309 PMCF investigation:** The post-market clinical follow-up investigation (PMCF) "0309" was international, prospective, multicenter. Three centers were involved in France, USA, and UK (Lyon, Denver, and Stanmore). The analysis was not done based on the results presented below as no clinical study report is currently available.
#0314	**63**	**70.0 ± 9.4 years old**	Degenerative diseases	**3.1 ± 0.6 months** for the 59	**#0314 PMCF investigation:** The post-market clinical follow-up study (PMCF) "0314 – PEEK Rods Study" was launched in April

Study number	Nb of patients implanted	Mean age (years)	Indications	Mean follow-up (months)	Resume
				patients followed-up between 1-6 months **19.0 ± 6 months** for the 42 patients followed-up between 12-24 months	2018. This PMCF study is retrospective, observational, multicenter, and non-comparative. This retrospective data collection started in April 2018 and ended in October 2018. One (1) center (one (1) investigator, Dr J.P. Hladky, Les Franciscaines private hospital, Nîmes, France) participated in this clinical study, designed to include patients with thoraco-lumbar degenerative diseases. All adult patients (over 18 years old) suffering from degenerative spine disease, implanted with PEEK rods (which belong to the PASS LP system) distributed by MEDICREA before September 2017 and affiliated with a social security scheme, were included in this study. A minimum of eighty (80) cases was initially expected and finally sixty-three (63) patients were included in this PMCF study, who were operated on with PEEK rods between January 2016 and October 2017. The follow-up was performed 2 years after the surgery in order to collect safety and efficacy (patients' general health and postoperative pain evolutions, radiological assessment over the clinical follow-ups) clinical data on the use of PEEK rods. The results are presented in the table below:
Synthesis					
From an efficacy perspective, analysis of included datasets enables us to reasonably conclude that devices under evaluation (PASS LP and equivalents systems) have good outcomes regarding: - Perioperative outcomes: mean surgery length, mean blood loss - Clinical outcomes: quality of life surveys - Radiological outcomes: spinopelvic parameters From a safety perspective, analysis of included datasets shows that surgeries done with the device under evaluation (PASS LP and equivalents systems) are associated with frequently reported complications, for example, loss of correction/non-union/dural tears/venous injury/revisions/musculoskeletal and connective tissue disorders.					

2. Materials

The **PASS LP® system** is a complete range of products composed of side-loading screws, hooks and rods available in several sizes. To complete this system a rod specifically designed for the degenerative cases was created, the ring rod was included within the **PASS DEGEN system** with shorter screws extensions. The **PASS TULIP system** differs only by the fact that screws allow top-loading of the rod. The purpose of those systems is to stabilize the spine while the fusion of the instrumented segments occurs. The PASS TULIP™ system consists of two sub-systems, the sub-system considered in this study is PASS TULIP™ PRIME.
The system of different sizes and shapes of the implants allows the surgeon to adapt to the pathology and morphology of each of his patients.

Table 2- Material description

Systems	PASS LP® system		PASS TULIP Prime
	Pedicle screw fixation system for the thoracolumbar spine	PASS DEGEN (ring rod)	
Pictures			
Indication	PASS LP™ implants, including PASS DEGEN, are indicated to contribute to correction and surgical stabilization of the thoracic, lumbar and sacral spine only.		PASS TULIP™ implants are medical devices indicated to contribute to correction and surgical stabilization of the thoracic, lumbar and sacral spine only.
Description	The PASS LP system is comprised of: pedicle screws (references beginning [redacted]), sacral plates with sacral screws (references beginning with [redacted] rod-plates (references beginning with [redacted]), crosslinks (reference beginning with [redacted]), connectors (references beginning with	The PASS DEGEN system, a composition kit derived from PASS LP system, is comprised of: left and right ring rods (referenced [redacted], breakaway nut (referenced [redacted]), short angulated connector (referenced [redacted] short initial connector (referenced [redacted]), short post screw	The TULIP PRIME screws (references beginning with [redacted]) are made of Titanium Alloy (Ti-6Al-4V ELI), Cobalt Chrome Alloy (Co-Cr28Mo6) and T40. The TULIP PRIME screws are used in combination with PASS LP system rod.

	[redacted]), breakaway nut (reference [redacted]) and rods (references beginning with [redacted] made of Titanium Alloy (Ti-6AI-4V ELI).	(referenced [redacted]), crosslinks (referenced [redacted], and revision post (referenced [redacted]) made of Titanium alloy (TiAl6V4 ELI).	

In addition, any future approved similar devices or models may be used in the study.

Those products are all CE-marked and all indications assessed in the current PMCF are covered by the instructions for use. These products are used in this study within intended use as described in approved the IFU for which the CE mark has been obtained. Existing approved procedures for the commercial product regarding distribution, shipment, storage, handling, and return of these Devices will be followed.

All these medical devices are manufactured by MEDICREA International, a Medtronic company, 5389 Route de Strasbourg, Vancia, 69140 Rillieux la Pape.

3. Objectives of the study

3.1. Primary objective

- This post-market clinical follow-up study aims to collect some data about the performance of MEDICREA's products to treat thoraco-lumbar degenerative diseases. This study is supporting the clinical evaluation report.
- The primary objective of the study is to assess the fusion rate at the 24-month visit postoperatively.
-

3.2. Secondary objectives

The secondary objectives are:

- to assess the fusion rate at the 1/6 month and 12-month visit
- to describe the evolution of the patients' quality of life before and at each follow-up after the surgery (pain, satisfaction),
- to collect data about the surgeons' satisfaction, with these implants and instruments during the surgery and regarding the patients' evolution
- to collect data about the safety of the implants

This PMCF study will also contribute to assessing the usability of the implants and instruments.

4. Methodology

4.1. Study design

This is a retrospective-prospective, multicenter, non-comparative and observational study (post-market clinical follow-up).

The patients presenting a degenerative disease operated with the PASS LP®/PASS Degen/PASS Tulip system manufactured by MEDICREA® INTERNATIONAL within the enrollment period can be included. The enrollment period will be 57 months. The retrospective part allows enrollment of patients for whom an inform note with certificate of information and consent is signed, and all data already collected are consistent with this protocol.

The standard of care validated by the principal investigators in terms of follow-up is the first follow-up between 1 and 6 months, then 12 months and 24 months. The total study duration is then 78 months (+/-6 months) from the first enrollment to the end of the last follow-up visit of the last patient.

Patients will be informed of their enrollment in this clinical study through an information note given by the surgeon and will inform the surgeon (orally or in writing) of their agreement or opposition to collecting their data. In the case a patient agreed, the surgeon will complete a form attesting that he has recorded the patient's agreement.

Postoperative visits will be scheduled with the patient. If the patient does not show up or cancels the visit, he will be contacted by the center's secretary to schedule another meeting. Each center will make its best effort to make the patients come back.

No control group is implemented for this study and, where needed, a comparison with fusion literature will be made. The following measures have been taken to avoid bias:

- A multi-center design is used to help ensure a representative sample of surgeons performing the procedure and to ensure a reasonable enrollment period
- A limited number of patients per site is determined
- Site training will be performed to assure full understanding and engagement to comply with the study design and all protocol requirements

Table 3- Description of patients arm

	PASS LP arm	**PASS DEGEN arm**	**PASS TULIP Prime arm**
Number of patients	25	25	25
Group arm definition	Implanted with PASS LP system (rod/screws/connectors etc…)	Implanted with PASS DEGEN sub-system (rod/screws/connectors etc…)	Implanted with PASS LP rod and PASS TULIP system screws

4.2. Primary endpoint

The primary endpoint is the fusion status of each patient at the 24-month visit postoperative. This fusion assessment will be done through the analysis of the standard of care imaging (CT-scan, X-rays and/or MRI) by the investigator and through the clinical examination of the patient by the investigator.

4.2.1. Rationale for selection of the primary endpoint:

From the surgical point of view, fusion is the main target of performing the procedure.

The criterion for fusion when assessed thru a CT-scan is bony bridging and when assessed thru X-rays the criteria are bony bridging, no motion (<4˚) in Flexion/Extension views (when collected) and integrity of instrumentation (implanted devices).

A patient will be considered as fused if all the instrumented segments are fused. The fusion status will be presented per patient.

In case multiple imaging has been performed, a CT-scan will be considered as the type of the preferred image type, followed, by an X-ray and then MRI. The fusion rate will be compared to the data observed in the literature with similar devices.

Fusion assessment will be done by surgeons.

4.3. Secondary endpoint

The secondary endpoints of this study include:

- Fusion status at the 1/6 month and 12-month visit
- Change of non-validated ODI score from the preoperative visit to all available postoperative timepoints
- Change of back pain score from the preoperative visit to all available postoperative timepoints
- Change of leg pain score from the preoperative visit to all available postoperative timepoints
- Change of non-validated SF-12 score from the preoperative visit to all available postoperative timepoints
- Patient satisfaction at all available postoperative timepoints
- Surgeon satisfaction at all available postoperative timepoints
- Device or procedure ‑ related adverse events and all SAEs up to 24 months

4.3.1. The Rationale for the selection of the secondary endpoints

Non-validated Oswestry Disability Index (ODI):

The rationale for selecting the non-validated Oswestry Disability Index (ODI) is that it is reliable, accurate, and has good responsiveness, in addition, it is translated to several languages and validated.

The Oswestry Disability Index (ODI) is one of the principal instruments for managing outcomes in spine disorders, including lumbar fusion techniques in patients with chronic low-back pain disorders. The ODI is registered with the International Consortium for Health Outcome Measures as a standard outcome measure (References – 4 to 5). It is spine-specific, considered the “gold standard” by several systematic reviews (References – 5 to 7) and recent surgery guidelines (Reference 8). A non-validated translation has been used.

Back and leg pain scales (VAS)

The study requires an assessment of the level of pain in the back and the legs. Although quantification of pain remains a great challenge, patient-completed visual analogue scales (VAS) are the preferred method to quantify the pain or the changes thereof. Thus, VAS is used in our study as well to quantify pain and pain-like symptoms in the back and legs.

The study utilizes VAS to assess the magnitude and the eventual changes in these two pain types.

A visual analogue scale (VAS, 0-10) will be used to evaluate the level of intensity of leg and back pain as perceived by the patient, where 0 is no pain and 10 is the worst pain possible.

Non-validated 12-Item Short Form Survey (SF-12):

SF-12v2® Health Survey is a practical, reliable, and valid measure of physical and mental health. It assesses the same eight health domains as the SF-36v2 with one or two questions per domain: Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, and Mental Health (Reference 9).

The short-form 12-item survey demonstrated good internal consistency reliability, construct validity, and responsiveness in patients with back pain. A non-validated translation has been used.

Patients' satisfaction

Patient satisfaction is used to evaluate patient satisfaction after surgery and during the follow-up period. Satisfaction is measured at four different levels: (1) surgery met my expectations, (2) I did not improve as much as I had hoped but I would undergo the same operation for the same results, (3) Surgery helped but I would not undergo the same operation for the same outcome, and (4) I am the same or worse as compared to before the surgery.

Surgeon's satisfaction questionnaire

Surgeons will be requested to complete questions about device/surgery satisfaction.

Safety:

The study is designed to observe, assess and document events related to clinical safety and performance of the devices according to approved instructions for use. During the follow-up period, the occurrence of device and procedure related AEs and all serious adverse events will be monitored, registered, and analyzed. To safeguard the safety of the clinical study subjects, all SAEs will be collected even those that may not be directly related to the surgery.

4.4. Study calendar

Enrollment period: 57 months

Duration of patient follow-up: 24 months after the surgery

Prospective enrollments can begin as soon as approvals have been obtained from the authorities.

Total study duration: 78 months

Table 4 - Study Calendar

Checks	Case report form	Patient Self-questionnaires*	Fusion assessment Imaging**	AE/DD collection
Preoperative	X	X	X	
Surgery	X			As they occur
Immediate Postoperative	X			
1-6 months (+/- 1 month)	X	X	X	
12 months (7 months – 18 months)	X	X	X	
24 months (18 months – 30 months)	X	X	X	

**non-validated SF-12/VAS/non-validated ODI/patient's satisfaction/surgeon's satisfaction*

***CT scan, Xrays, and/or MRI will be done according to the centers' standard of care. Images need to be available for investigators to assess fusion, they are no longer collected by the sponsor.*

5. Selection of subjects

5.1. Inclusion criteria

- Patients of at least 18 years old
- Patient suffering from a spinal degenerative disease.
- Patient requiring spinal surgery for less than 4 levels for a spinal degenerative disease
- Patient implanted with MEDICREA's products, or patients who are candidate to receive including at least the PASS LP and/or PASS DEGEN and/or PASS TULIP Prime implants
- Patient affiliated to a national insurance system

5.2. Exclusion criteria

- Patient unable or unwilling to sign and understand an information note with proof of patient consent Patient unable to complete a self-administered questionnaire
- Patient-presenting contra-indications to a Xray follow-up
- Patient of more than 18 years old under a protection procedure
- Patient judged as non-compliant by the investigator or not able to come back for follow-up visits up to 2 years

5.3. *Patient enrollment*

Enrollment of the patient must occur prior to performing any study specific activities.

When a patient and the principal investigator or authorized designee, as required, have personally signed and dated the consent (oral consent possible for the patient), the patient is considered enrolled in the study.

6. Variable to be measured and methods of measurement

6.1. Radiographic evaluation

Images are performed at each follow-up, as per center's standard of care. This will allow the analysis of several points:

- The fusion status: The criterion for fusion when assessed through a CT-scan is bony bridging: both extragraft bone bridging and intragraft bone bridging need to be achieved for a treated level to be considered as fused .
- Implant status: using the X-rays, the investigators will check if the material is not broken, dislocated, loosened, misplaced etc.

Standing radiographs should be taken in a free-standing position: feet approximately shoulder width apart, arms at approximately 45° of shoulder flexion, fingertips placed on the mid-clavicle.

X-rays must include at least the upper and lower instrumented vertebrae. X-rays should be calibrated and if possible provide full spine (from C7 to pelvis).

Clinical sites must use imaging equipment (X-ray and/or CT-scan/MRI) that are maintained and calibrated according to the manufacturer's specifications when performing imaging procedures on subjects for this study.

Imagery will not be collected by the sponsor, only used for fusion assessment by the surgeons.

6.2. Clinical evaluation

The data collected during the follow-up are listed below:

- Preoperative data: age at the surgery, gender, height, weight, indication, possible comorbidities, smoking status, preoperative imagery (X-rays and/or CT-SCAN/MRI), quality of life and pain questionnaires (ODI, SF-12, and VAS), previous spinal history, occupation and physical activities, patient medical history, radicular symptoms.

- Surgery data: surgery date, distal and proximal vertebrae instrumented, operating time, blood loss, materials implanted, surgeons' satisfaction, complications.

- Follow-up: date of the visit, , imagery (X-rays and/or CT-SCAN/MRI), quality of life and pain questionnaires (ODI, SF-12, and VAS), analgesic consumption, occupation and physical activities, clinical assessment, radicular symptoms, radiological assessment, surgeon's opinion, complications.

- End of study: date of the visit, patient complete the study according to the protocol or not, if not reason for premature termination, surgeons' signature.

The data listed here are standard information. The protocol requires no data that are not routinely collected.
Data are collected through eCRFs (electronic Case Report Form)

7. Adverse Events and Device Deficiencies

7.1. Adverse Events (AE)

Adverse Event (AE) definitions are provided in Table 5

All Adverse Events, related to the device and/or the procedure and All SAEs must be reported and collected throughout the study duration, starting at the time of signing the information note with proof of patient consent until study exit considering that this study is a post-market clinical study

Reporting of these events to sponsor will occur on an AE Form. Each event must be reported separately. Documented pre-existing conditions are not considered AEs unless the nature or severity of the condition has worsened.

For AEs that require immediate reporting (see Table 5), the preferred way of transmission of AEs and Device Deficiencies (DDs) is the EDC system, but in case the eCRF cannot be accessed, the investigator should contact study personnel by e-mail. The AE/DD worksheet provided to investigators may be used for completion of available information, preferably signed by investigators and attached to the email. The same CIP reporting timelines apply for all types of reporting as if the eCRF would be available.

Any medication/treatment associated with the treatment of an AE must be reported.

Subject deaths are also required to be reported. Refer to Section 7.6 for Subject Death collection and reporting requirements.

7.2. Device Deficiency (DD)

The DD definition is provided in Table 5. DD information will be collected throughout the study and reported to sponsor. Note that DD that result in an AE to the subject should be captured as an AE only.

DD that did not lead to an AE but could have led to a Serious Adverse Device Effect (SADE) (i.e., if suitable action had not been taken, if intervention had not been made, or if the circumstances had been less fortunate) require immediate reporting (see Table 5).

7.3. Processing Updates and Resolution

For any changes in status of a previously reported adverse event or DD (i.e. change in actions taken, change in outcome, change in relatedness), information needs to be updated on, or added to the original AE or DD form. All AEs must be followed until the AE has been resolved, is unresolved with no further actions planned, the subject dies or exits the study, or until study closure, whichever occurs first.

In the event that a subject is withdrawn from the study prior to study completion, all efforts should be made to continue following the subject until all unresolved system or procedure related AEs, as classified by the investigator, are resolved, unresolved with no further actions planned, whichever occurs first.

At the time of study exit, all collected adverse events that are unresolved must be reviewed and an update to the original AE must be reported.

7.4. Definitions/Classifications

Where the definition indicates "device", it refers to any device used in the study. This might be the device under investigation, or any market released component of the system, and includes but is not restricted to: PASS DEGEN,PASS LP, PASS TULIP Prime systems.

Table 5 - Adverse Event and Device Deficiency Definitions

<table>
<tr><th>ISO Definitions for Clinical Investigations of Medical Devices for Human Subjects</th></tr>
<tr><td>Adverse Event (AE): (ISO14155:2020 section 3.2)

Untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated

NOTE 1: This definition includes events related to the investigational medical device or the comparator.

NOTE 2: This definition includes events related to the procedures involved.

NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices or comparators.</td></tr>
<tr><td>Adverse Device Effect (ADE): (ISO14155:2020 section 3.1)

Adverse event related to the use of an investigational medical device

NOTE 1: 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.

NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

NOTE 3: this includes 'comparator' if the comparator is a medical device.</td></tr>
<tr><td>Device Deficiency (DD): (ISO14155:2020 section 3.19)

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

NOTE 1: Device deficiencies include malfunctions, use errors and inadequacy in the information supplied by the manufacturer including labeling.

NOTE 2: This definition includes device deficiencies related to the investigational medical device or the comparator.</td></tr>
<tr><td>Unavoidable Adverse Event (UAE):

An Adverse Event inherent to a surgical procedure that is expected to occur in all subjects for a projected duration according to the Investigator's opinion, including, but not limited to :

<table>
<tr><td>Event Description</td><td>Timeframe (hours) from the surgical procedure</td></tr>
<tr><td>Anesthesia related nausea/vomiting</td><td>24</td></tr>
<tr><td>Low-grade fever (<100°F or 37.8°C)</td><td>48</td></tr>
</table>
</td></tr>
</table>

Sleep problems (insomnia)	72

In all geographies, UAEs, need not be reported unless the adverse event worsens or is present outside the stated timeframe post-implant.

SERIOUSNESS

Serious Adverse Event (SAE): (ISO14155:2020 section 3.45)

Adverse event that led to any of the following

a) death,
b) serious deterioration in the health of the subject, users or other persons as defined by one or more of the following:
    1) a life-threatening illness or injury, or
    2) a permanent impairment of a body structure or a body function, including chronic disease, or
    3) in-patient or prolonged hospitalization, or
    4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
c) Fetal distress, fetal death or a congenital abnormality or birth defect including physical or mental impairment

NOTE 1: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

Serious Adverse Device Effect (SADE): (ISO14155:2020 section 3.44)

Adverse device effect that has resulted in any of the consequences characteristic of a Serious Adverse Event.

Serious Health Threat: (ISO14155:2020 section 3.46)

Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons

NOTE 1: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.

RELATEDNESS	
Procedure-Related	Index Surgery Related: An Adverse Event that occurs due to any procedure related to the Index Surgery
Device-Related	An adverse event that is directly related to the use of any device(s) in the scope of this clinical study
Instrument-Related	An adverse event that is directly related to the use of any Instrument(s) in the scope of this clinical study

Relationship of Adverse Events	Assessment of causality will be assessed for this study on the following basis: **1. Not related**: The relationship to the device or procedures can be excluded when: • The event is not a known side effect of the product category the device belongs to or of similar devices and procedures; • the event has no temporal relationship with the use of the investigational device or the procedures; • the event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible; • the discontinuation of medical device application or the reduction of the level of activation/exposure when clinically feasible and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event; • the event involves a body site or an organ not expected to be affected by the device or procedure; • the event can be attributed to another cause (e.g., an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors); • the event does not depend on a false result given by the investigational device used for diagnosis, when applicable; • harms to the subject are not clearly due to use error. To establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event. **2Possible:** The relationship with the device is weak but cannot be ruled out completely; alternative causes are also possible (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible. **3Probable:** The relationship with the use of the device seems relevant and/or the event cannot reasonably be

	explained by another cause, but additional information may be obtained.
	
	4Causal relationship: the event is associated with the investigational device or procedures beyond reasonable doubt when:
	• the event is a known side effect of the product category the device belongs to or of similar devices and procedures;
	• the event has a temporal relationship with the investigational device use/application or procedures;
	• the event involves a body-site or organ that
	  ○ the investigational device or procedures are applied to;
	  ○ the investigational device or procedures have an effect on;
	• the event follows a known response pattern to the medical device (if the response pattern is previously known);
	• the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the event (when clinically feasible);
	• other possible causes (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
	• harm to the subject is due to error in use;
	• the event depends on a false result given by the investigational device used for diagnosis, when applicable;
	
	To establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device /procedures and the serious event.

7.5. Reporting of Adverse Events

All Adverse Events, related to the device and/or the surgery and All SAEs must be reported considering that this study is conducted post-market. The investigator is responsible for assessing and reporting all AEs to sponsor. All reportable events must be recorded in the subject's medical record and on the Adverse Event and/or Device Deficiency eCRF and promptly reported to sponsor. Ethical Committee (EC) reporting must be completed in accordance with the policies of the governing EC. Regulatory Authority reporting should be in accordance with applicable local regulations.

It is the responsibility of the investigator to identify the occurrence of adverse events and device deficiencies and to ensure the required information is accurately documented on the eCRF.

Reports of adverse events will include the following information, at a minimum:

- Date of event
- Date site became aware of the event
- Diagnosis or description of the event
- Assessment of the seriousness and relationship to the device and/or surgical procedure
- Treatment provided
- Outcome and date of resolution

7.5.1. Adverse Event and Device Deficiency Classification

All AE and DD will be reviewed by a sponsor representative. AEs will be classified according to the definitions provided.

Upon receipt of AE at sponsor, a sponsor representative will review the AE/DD for completeness and accuracy and when necessary will request clarification and/or additional information from the Investigator. Sponsor will utilize MedDRA for Regulatory Activities, to assign a MedDRA term for each AE based on the information provided by the investigator.

AEs will be classified according to the standard definitions as outlined below:

Table 6- Adverse Event Classification Responsibilities

What is classified?	Who classifies?	Classification Parameters
Relatedness	Investigator	Device (PASS LP, PASS DEGEN, PASS TULIP), Procedure, instruments
	Sponsor	Device, Procedure, instruments
Seriousness	Investigator	SAE, DD with SADE potential
	Sponsor	SAE, DD with SADE potential
Diagnosis	Investigator	Based on presenting signs and symptoms and other supporting data
	Sponsor	MedDRA term assigned based on the data provided by Investigator

7.5.2. Adverse Event and Device Deficiency Reporting Requirements

Regulatory reporting of AEs and DDs will be recorded and reported according to local regulatory requirements. Refer to Table 7 for a list of required investigator and sponsor reporting requirements and timeframes.

It is the responsibility of the Investigator and the sponsor to abide by the AE reporting requirements stipulated by local law and the study site's EC.

For emergency contact regarding an SAE and/or SADE, contact a study representative immediately (refer to the study contact list provided in the study site's study documents binder/investigator site file or refer to the Sponsor contact information provided on the title page).

Table 7- Reporting Requirements

SAEs	
Investigator shall submit to:	
Sponsor	**All geographies:** Report to the sponsor, without unjustified delay, all serious adverse events.
RA	**All geographies:** Submit to RA per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.
Sponsor shall submit to:	
RA	**All geographies:** Submit to RA per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.
ADEs	
Investigator shall submit to:	
Sponsor	**All geographies:** Submit in a timely manner after the investigator first learns of the effect.
RA	**All geographies:** Submit to RA per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.
Sponsor shall submit to:	
RA	**All geographies:** Submit to RA per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.
SADEs	
Investigator shall submit to:	
Sponsor	**All geographies:** Immediately after the investigator learns of the event or of new information in relation to an already reported event.
RA	**All geographies:** Submit to RA per local reporting requirement
EC	**All geographies:** Submit to EC per local reporting requirement.
Sponsor shall submit to:	
RA	**All geographies:** Submit to RA per local reporting requirement.

EC	**All geographies:** Submit to EC per local reporting requirement.
Investigators	**All geographies:** Submit per local reporting requirement.
All other reportable AEs	
Investigator shall submit to:	
Sponsor	**All geographies:** Submit in a timely manner after the investigator first learns of the event.
RA	**All geographies:** Submit to RA per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.
DDs with SADE potential	
Investigator shall submit to:	
Sponsor	**All other geographies:** Submit or report as required per local reporting requirements.
RA	**All geographies:** Submit to RA per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.
Sponsor shall submit to:	
RA	**All geographies:** Submit to RA per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.
All other Device Deficiencies	
Investigator shall submit to:	
Sponsor	**All geographies:** Submit in a timely manner after the investigator first learns of the deficiency.
RA	**All geographies:** Submit to RA per local reporting requirement.
EC	**All geographies:** Submit to EC per local reporting requirement.

7.6. Subject Death

All subject deaths must be reported by the investigator to sponsor on an AE form (AE with outcome of Fatal) as soon as possible after the investigator first learns of the death. In case of death, there should be one AE with the outcome of Fatal.

In the event of a subject's death, it is recommended that the implanted system be explanted and returned to Sponsor for analysis whenever possible per local process. Local laws and procedures must be followed where applicable. If any system component is returned to sponsor, internal return product reporting systems may be used to gather additional information about the returned device/component.

In summary, the following data will be collected:

- Date of death

- Detailed description of death
- Cause of death

Relatedness to system and/or procedure

Regulatory reporting of Subject Deaths will be completed according to local regulatory requirements.

7.7. Product Complaint Reporting

It is the responsibility of the investigator to report all product complaint(s) associated with a medical device distributed by sponsor, regardless of whether they are related to intended use, misuse or abuse of the product. Reporting must be done immediately and via the regular channels for market-released products. The reporting of product complaints by the clinical team must be done according to post-market vigilance Procedures. Sponsor will notify the RAs (e.g., CA) as applicable for the following incidents immediately upon learning of them and is not limited to AEs and DDs only:

- Any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or instructions for use which led or might have led to the death or serious deterioration in the state of health of a patient, user, or other person.
- Any technical or medical reason resulting in withdrawal of a device from the market by the manufacturer.
- Any serious deterioration in the state of health, including:
  - Life-threatening illness or injury
  - Permanent impairment of a body function or permanent damage to a body structure
  - A condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure

8. Data handling and record keeping

8.1. Information note with proof of patient consent

The process of informed decision-making shall include discussions of the research study with the Investigator, and others as appropriate. Valid Information note with proof of patient consent requires the disclosure of relevant information to a prospective subject about the research; comprehension of the information; and their voluntary agreement.

Patients will be informed of their enrollment in this clinical study through an information note given by the investigator surgeon and will inform the surgeon (by oral or written) of their agreement or opposition to collect their data. In the case a patient agreed, the surgeon will complete a form attesting that he has recorded the patient's agreement.

The formal oral consent of a subject, using the Ethics committee-approved inform note, will be obtained before that subject is submitted to any study procedure. Inform note pages are provided to the patient. The investigator must notify the subject of any significant new findings related to the study that become available during the course of the study which are pertinent to the safety and well-being of the subject.

This inclusion form will disclose the Personal Health Information (PHI) to be collected from subjects in this study, who will have access to that information and the rights of a research subject to revoke their authorization for use of their PHI.

8.2. Source Documents

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents.

Examples of these original documents, and data records include: hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, photographic negatives, microfilm or magnetic media, Xrays, subject files, and records kept at the pharmacy.

The questionnaires are also source documents. Before the MEDTRONIC transition, the questionnaires provided by Medicrea were considered as source documents.

Neurosurgical status (motor and sensitive deficiencies), professional and sportive activities, surgery details (as procedure's duration and blood loss), surgeon's surgery satisfactions, surgeon's opinion and radiological assessment can be recorded directly on the CRF and are considered sources data.

In addition, the AE assessment may be recorded directly in the CRFs.

Sponsor may conduct audits at participating study sites. The purpose of an audit is to verify the performance of the monitoring process and the study conduct, independently of the personnel directly involved in the study. Regulatory authorities may also perform inspections at participating study sites. The investigator and/or institution shall permit Sponsor, ECs and RAs direct access to source data and documents during monitoring, audits and regulatory inspections.

8.3. Data Management

The study data collection initially started via a paper CRF that has been completed and signed by study centers. The paper CRF that had been completed prior to the EDC system go-live will be an electronic CRF as defined in the Data management plan.

Data will be collected using an electronic data management system for studies. CRF data will be stored in a secure, password-protected database which will be backed up nightly. Data will be reviewed using programmed and manual data checks. Data queries will be made available to study sites for resolution. Study management reports may be generated to monitor data quality and study progress. At the end of the study, the data will be frozen and will be retained by Sponsor in accordance with applicable regulations.

All records and other information about subjects participating in this study will be treated as confidential. Data will be transferred and processed by sponsor or a third party designated by sponsor in a key coded form, unless it's impossible to pseudonymize for instance, where the subject's name cannot be removed from the data carrier, such as X-Ray images.

Procedures in the CIP require source documentation. Source documentation will be maintained at the study site. Source documents, which may include worksheets, subject medical records, programmer printouts, and interrogation files, must be created and maintained by the investigational study site team.

The investigator will clearly mark clinical records to indicate that the subject is enrolled in this clinical investigation.

Device data from transmissions will be uploaded to secure servers. Save-to-disk data collected at office visits will be sent to Sponsor. Upon receipt, device data will be maintained with databases and retrieved for analysis and reporting.

8.4. Data Collected - The Electronic Case Report Form (eCRF)

The eCRF contains all the data collected during the course of the study. During the study, investigators must fill clinical data at different times during the treatment of the patient in the Electronic Case Report Form (eCRF). All the demographic and clinical data should be filled in the CRF and the missing data, unreadable data, incorrect data or any deviations from the protocol should be explained.

The eCRF must meet all regulations linked to the clinical study. (**See 11 - Ethics**).

The investigator must ensure that the data reported in the eCRF and all other required study reports are accurate, complete and reported in a timely manner. The data reported on the eCRFs shall be derived from source documents and be consistent with these source documents, and any discrepancies shall be explained in writing At the beginning of the study, data were collected in paper CRFs. All these paper CRFs have been monitored and all collected data will be entered in the eCRFs in the EDC system manually by the sponsor per the Data Entry Guideline.Then the PI or delegated Sub-Investigator is required to approve all data on eCRFs via electronic signature. The sponsor and/or assigned designee will be responsible for the processing and quality control of the data (data management) per the Data Management Plan, which describes the procedures for data review, database cleaning and issue/resolution of data queries. Data will be collected and stored in a validated, password protected database. Data analysis will be conducted utilizing validated software and analysis programs by qualified biostatisticians

Procedures used for data review, database cleaning, and issuing and resolving data:

- Data will be reviewed using programmed and manual data checks.
- Data queries will be made available to centers for resolution.
- Study management reports may be generated to monitor data quality and study progress.

8.5. Patients' questionnaires

The evaluated questionnaires are detailed in the following section (see section 4.3.1. Rationale for selection of the secondary endpoints). Most surgeons commonly use these questionnaires (VAS, ODI, SF-12, PSI) in spinal surgeries. Patients' questionnaires must be filled before the surgery and during each follow-up. These questionnaires must be filled in the waiting room without undue influence by investigator or other study personnel.

The original of the patients' questionnaires should remain archived in the sites. The data will be included in a database by the monitor during the monitoring visit. These questionnaires will be provided to the centers by the sponsor.

8.6. . Data Monitoring Committee and Clinical Events Committee (CEC)

No Data Monitoring Committee nor CEC will be installed for this clinical study as no interventions intended to prolong life or reduce risk of a major adverse health outcome are evaluated, for which favorable or unfavorable study results suggest study termination. Nor are there safety concerns suggesting the need for a Data Monitoring Committee.

9. Statistical Method Analysis

The primary analysis will be performed when all subjects have reached the 24-month visit.

Any deviation or changes from the original statistical plan will be documented.

9.1. General Consideration

Baseline and pre-operative data will include but are not limited to height, weight, age, and preoperative clinical and radiographic measurements. Demographics and other pre-treatment characteristics will be summarized and characterized with appropriate descriptive statistics:

- for continuous variables: number of available data, mean, standard deviation, median, minimum and maximum value (min/max);
- for ordinal variables: number of available data, median, min/max;
- for categorical variables: number of available data, frequency and percentage of each category;
- For the endpoints related to the fusion rate, the point estimate along with the two-sided 95% exact binomial confidence interval will be calculated and presented. For endpoints related to the change of scores, either paired t-test (for normal data) or Wilcoxon signed-rank test will be carried out to test whether the improvement is statistically significant.

For analysis purpose, the analysis window is also defined below:

Table 8 Analysis window defined for each visit for analysis purpose

Study Visit	Analysis Time Window
1-6-month visit (+/-1 month)	From Discharge to Day 213
12-month visit (7 month – 18 months)	Day 214 - 547
24-month visit (+/-6 month)	Day 548 to 914*

*For visits after 914 days post surgery, the information will be summarized in “After 24-month visit”

The statistical software SAS 9.4 or subsequent version will be used to conduct all the analyses.

The analysis for subjects implanted with a PASS LP or a PASS Degen or a PASS Tulip system will be conducted and the results will be presented separately. In addition, the subjects implanted with a PASS LP/PASS Degen system will be grouped together, and the analysis for these subjects will be conducted and the results will be presented as well.

9.2. Sample Size

The sample size is not statistically determined, due to the observational study design, but rather is determined by the sponsor to enroll 25 subjects in each device group (PASS LP or a PASS Degen or a PASS Tulip system).

9.3. Analysis population

9.3.1. Primary Analysis Population

The primary analysis population will include all subjects who are enrolled and implanted with a PASS LP or a PASS Degen or a PASS Tulip system.

9.3.2. *Per-protocol Population*

The per-protocol dataset is a subset of subjects who are included in the primary dataset. Subjects who violate inclusion/exclusion criteria or violate the instructed surgical procedure will be excluded from this dataset.

The per-protocol population will only be used for the analysis of the primary endpoint.

9.4. Efficacy Analysis

9.4.1. Primary Efficacy Endpoint Analysis

The primary endpoint is fusion status at the 24-month visit.

For the primary endpoint fusion at the 24-month visit, all fusion assessments between 548 days to 914 days post-implant will be taken into consideration. For subjects who do not have fusion assessment in this period, however, have demonstrated fusion before 548 days post-surgery, the subject will be considered as having fused at the 24-month visit. For subjects who do not have fusion assessment in this period and have not demonstrated fusion determined before 548 days post-surgery either, the subject's fusion status at the 24-month visit will be considered as missing.

Once the fusion status is determined for each subject, the fusion rate, along with the two-sided 95% exact binomial confidence interval, will be calculated and presented.

In addition, fusion rate base on each treated level will be estimated and presented with the two-sided 95% exact binomial confidence interval.

9.4.2. Secondary Efficacy Endpoint Analysis

1. Fusion status at 1/6-month and the 12-month visit

Similar methods used for the primary endpoint will be used for this secondary endpoint with different time windows for the corresponding visits.

2. Change of non-validated ODI score from the preoperative visit to all post-operative visits
3. Change of back pain score from the preoperative visit to all post-operative visits
4. Change of leg pain score from the preoperative visit to all post-operative visits
5. Change of non-validated SF-12 score from the preoperative visit to all post-operative visits
6. Patient satisfaction at all post-operative visits
7. Surgeon satisfaction at all post-operative visits: a questionnaire will be filled by surgeons during the enrollment period in order to collect his/her opinions with the implants and instrumentations. Those data will allow the sponsor to obtain data on the usability of the products and also to have the surgeon's feed backs.

For secondary endpoint 2-5, when change of scores are approximately normally distributed, the change will be tested using a paired-sample t-test; when the distribution of the data is non-normal, a Wilcoxon signed-rank test may be used in place of the paired t-test. In addition, the scores along with the changes will be presented with descriptive statistics including but not limited to the number of available data, mean, standard deviation, minimum and maximum.

For the secondary endpoints 6 and 7, the number and percentage of subjects in each category will be calculated and presented.

9.5. Safety Analysis

There is no primary safety endpoint, the secondary safety endpoint is all device and/or procedure related AE and all serious adverse event up to the 24-month visit.

9.6. Benefit and risks analysis

This study concerns CE Mark devices. No supplementary procedure other than those applied to the patients implanted with the PASS® LP, PASS Degen and PASS TULIP devices is asked. The fact of participating in it doesn't lead to particular risk for the patient. The participation to this study will bring no direct and immediate benefit to the patient.

This study should only indirectly benefit to future patients for whom we will learn more about procedures.

Risks associated with the participation of the study have been deemed acceptable and the benefits outweigh the risks.

For studies following ISO 14155, the risk analysis process for the "The Degen study, PASS LP/PASS DEGEN/PASS TULIP Prime systems" is being performed in accordance with ISO 14971 and will ensure that the level of risk is acceptable prior to starting the study.

There are no incremental risks introduced to the subject as a result of participation in this study. This clinical investigation has been designed to minimize the possibility for pain, discomfort, fear and other foreseeable risks.

Anticipated adverse effects described in the IFU are described in the following table. Additional precautions, warnings, cautions, and contraindications are included in the device labeling. In addition to the risks associated with surgery of the spine without instrumentation, a number of possible undesirable effects may occur with instrumented surgery (including but not limited to):

Table 9 - Anticipated adverse effects

Anticipated adverse effects	PASS LP and PASS DEGEN	PASS TULIP Prime
1. Detachment, deformation, mobilization, slipping, breakage of one or all of the components	X	X
2. Pain due to the surgery, the fracture, deformation and or migration of an implant.	X	X
3. Fracture of the pedicle during insertion of a pedicle screw.	X	X
4. Fracture of vertebrae	X	X
5. Allergic reaction to the implanted materials and the presence of micro-particles around the implants (metallosis).	X	X
6. Cutaneous problems with the components in areas where the tissue cover is insufficient accompanied by pain and abnormal sensations due to the volume of the device.	X	X
7. Bursitis	X	X
8. Postoperative loss of correction and/or reduction of the spine, partial or total loss of the corrections achieved.	X	X
9. Deep or superficial infection with an inflammatory reaction.	X	X
10. Pseudarthrosis	X	X
11. Neural damage or neural deficit due to surgical trauma.	X	X
12. Leakage of cerebrospinal fluid.	X	X

13. Gastrointestinal disorders, urinary tract disturbances, and/or reproductive disorders including sterility, impotence.	X	X
14. Excessive intraoperative bleeding and/or hematomas.	X	X
15. Growth arrest in fused spinal segments.	X	X
16. Vascular disorders (thrombosis) and/or pulmonary embolism.	X	X
17. Patient's inability to resume normal activities of daily living.	X	X
18. Dural tear.	X	X
19. Disease (deterioration) of the adjacent segments to the assembly.	X	X
20. Death.	X	X

NOTE: Some of the above adverse effects may necessitate surgical revision.

10. Data confidentiality

Patients will be key-coded in the questionnaires and case report forms by a subject number generated by the investigator (a number with 4 figures XXYY for each patient – XX corresponds to the site and YY is a chronologic number given to each new patient included by the site).

Information about study subjects will be kept confidential and managed according to the requirements of the laws about privacy applicable in Europe. Those regulations require an oral or signed subject authorization informing the subject of the following:

- ✓ The personal health information (PHI) to be collected from subjects in this study
- ✓ Who will have access to that information and why
- ✓ Who will use or disclose that information
- ✓ To whom the data may be disclosed and the reasons for this disclosure
- ✓ The rights of a research subject to revoke their authorization for use of their PHI.

If a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

11. Ethics

11.1. Statement(s) of Compliance

This study will be conducted according to the protocol, Clinical trial agreement legal and regulatory procedures and to international standards of Good Clinical Practice for clinical studies. National/local data protection laws and regulations, local applicable regulations, Declaration of Helsinki 2013 and Standards ISO-14155: 2020 will also be followed, with exceptions of:

- Due to the Post market aspect and study type, the following were not performed:
    - ISO 6.4.1 Adverse events: Not all AE will be collected, only AE related to Study device, instruments and/or to the study procedure, and all SAEs. Non-subject AEs will not be collected and USADE unexpectedness assessment is not done as it is a post-market study.
    - ISO 7.9 Investigational device accountability: as devices in this study are commercially available, device accountability will not be performed,
    - ISO 6.3 Randomization, blinding
    - ISO A.5 Pass/fail criteria, statistical hypothesis
    - ISO 10.5 Inform consent in urgent circumstances
    - ISO A.4 Possible interactions with concurrent medical interventions
    - ISO 5.3/5.6.2j/9.2.2e: Statement of the provisions made for subject compensation and indemnification and of insurance to cover liability
    - ISO 5.8: Informed consent
- others elements terminated or done prior to the transition to Medtronic QMS.

This study will be publicly registered in accordance with the 2007 Food and Drug Administration Amendments Act (FDAAA) and Declaration of Helsinki on http://clinicaltrials.gov (PL 110 ‑ 85, Section 810(a)) with the following identifier: NCT04670536, and the completion will be published in this same register.

The principles of the DoH have been implemented through the Information note with proof of patient consent process, EC approval, study training, clinical trial registration, risk-benefit assessment, and publication policy.

In addition to the regulatory requirements outlined above, the study will be conducted according to the national and local law(s), regulations, standards, and requirements of the country (s) where the study is being conducted.

11.2. Ethic Committee approval

Protocol, Information note with proof of patient consent and required study documents must be approved by the Ethic committee according to the applicable regulations.

Clinical investigation shall not begin until the required approval/favorable opinion from the Ethics Committee.

Additional requirements imposed by local regulations, the EC and RA shall be followed, if appropriate.

11.3. Insurance

Due to the observational post-market design of the study, a specific clinical study liability insurance is not applicable. All patients included in this study are affiliated to a national insurance system s and covered under applicable laws and regulations.

11.4. Subject Exit, Withdrawal or Discontinuation

Patients may withdraw from the study at any time and for any reason. Stop of data collection for patients in the study may occur in the following cases:

- Withdrawal of consent by patient
- Patient lost-to-follow-up
- Patient death
- Patient did not undergo the instrumented lumbar fusion as defined in this protocol

Premature termination at any stage of the study will not cause any prejudice to the patient and patient will be followed according to their standard of care If the subject wishes to exit from the study (i.e. the subject revokes consent), the study site is required to document the reason for exit on the CRF. In addition, study sites shall follow the regulations set forth by the governing EC. If known, the reason for withdrawal shall be recorded in the CRF.

If a patient is included and then discontinued before the end of the enrollment period, another patient can be included to obtain a consistent population to assess.

No subjects should be withdrawn by investigators unless compelling medical justification is present. It is recommended investigators discuss any withdrawals with the study team prior to withdrawing subjects.

11.4.1. Study Exit

A study exit eCRF is required for all subjects. Prior to exiting a subject from the study, it is recommended to follow the subject until all ongoing system and/or procedure related AEs are resolved or unresolved with no further actions planned. Following exit, subjects will continue to receive standard medical care. All data available through the time of the subject's exit will be used for analysis.

Subjects are urged to remain in the study as long as possible but may be exited from the study for any of the following situations:

- completed
- adverse event
- death
- lost to follow-up
- physician decision
- protocol deviation
- screen failure
- sponsor request
- technical problems

- unsuccessful procedure
- withdrawal by subject
- Other

11.4.2. Study Completed

At the completion of the 24-month follow-up visit, subjects will be exited from the study. The 24-month follow-up visit and exit visit should be combined, and both a 24-month follow-up CRF and an End of study CRF need to be completed.

11.4.3. Lost to Follow-up

Before considering a subject as lost to follow up, the investigator should make every attempt to contact the subject to have the subject return for follow ‑ up to determine their clinical status and the occurrence/resolution of AEs, if any.

A subject is considered to be lost to follow-up if at least two attempts to contact the subject are unsuccessful. The method of attempt (e.g., one letter and one phone record, or two letters) must be documented in the subject's medical record. In addition, regulation set forth by the governing EC must be followed.

11.5. Suspension and Early Termination

11.5.1. Planned Study Closure

Study closure is defined as closure of a clinical study (last patient last visit) that occurs when sponsor and/or regulatory requirements have been satisfied per the Clinical Investigation Plan and/or by a decision by sponsor or regulatory authority, whichever occurs first. The study closure process is complete upon distribution of the Final Report or after final payments, whichever occurs last. For each center, Ethics Board approval renewals are required per local/country regulation until the study closure process is complete at that center.

11.5.2. Early Termination or Suspension

Sponsor reserves the right to suspend or terminate the study at any time. Reasons may include, but are not limited to, the following:

- Insufficient enrollment to complete the study within the expected timeframe
- Identification of unacceptable safety profile; suspicion of an unacceptable risk will result in a suspension, confirmation of an unacceptable risk will result in termination
- Product performance/product supply issues

- EC or governing regulatory authority (if applicable) suspension and/or termination of the study

Sponsor reserves the right to suspend or terminate the study at an individual site. Reasons may include, but are not limited to the following:

- Non compliance with the protocol
- Serious or repeated deviations at the site
- Failure to implement required corrective and preventive actions
- Insufficient enrollment to complete the study within the expected timeframe
- Loss of appropriately trained site personnel

Investigators are required to notify the EC of study suspension/termination. For European sites the Sponsor will notify the EC of study suspension/termination. Subjects will be notified by the investigator of suspension/termination due to unacceptable risk or of termination due to any other cause.

If, for any reason, sponsor suspends or prematurely terminates the investigation at an individual investigation site, sponsor shall inform the responsible regulatory authority as appropriate and ensure that the EC is notified, either by the Principal Investigator or by sponsor. If the suspension or premature termination was in the interest of safety, sponsor shall inform all other Principal Investigators and investigational sites, the EC and where appropriate, the regulatory authorities. The Principal Investigator or authorized designee shall promptly inform the enrolled subjects at his/her investigation site, if appropriate. In case of early investigation site suspension or termination subjects will be followed-up as per standard of care. Approval shall be obtained from the ECs and, where appropriate, regulatory authorities before the clinical investigation resumes.

If subjects have been informed of the suspension, the principal investigator, or authorized designee shall inform them of the reasons for suspension and of its lifting.

11.6. CIP Amendments/ Information note with proof of patient consent

Any revisions or amendments to the CIP or Information note with proof of patient consent document, along with a statement of justification for the changes, will be submitted to all affected RAs and governing ECs, according to applicable regulations. All amendments to the CIP shall be agreed upon between sponsor and the principal investigator(s), or the coordinating investigator. Approval by regulatory agencies and ECs (where applicable) must be obtained prior to implementing a CIP revision at the study site.

No product changes are expected, however in case an update happens an assessment will be done to evaluate if CIP update is needed.

11.7. Protocol Deviation

A study deviation is defined as an event within a study that did not occur according to the CIP or the CTA.

Prior approval by Sponsor is expected in situations where the investigator anticipates, contemplates, or makes a conscious decision to deviate. Prior approval is not required when a deviation is necessary to protect the safety, rights or well-being of a subject in an emergency or in unforeseen situations beyond the investigator's control (e.g.,sponsor is required for such situations.

All study deviations must be reported on the CRF regardless of whether medically justifiable, pre-approved by sponsor, an inadvertent occurrence, or taken to protect the subject in an emergency. Multiple deviations of the same type at the same visit may be reported on one case report form.

Reporting of study deviations should comply with EC policies and/or local laws and must be reported to sponsor as soon as possible upon the study site becoming aware of the deviation. Reporting of deviations must comply with EC policies, local laws, and/or RA requirements. All study deviation will be reported in the final study report.

Sponsor is responsible for analyzing deviations, assessing their significance, and identifying any additional corrective and/or preventive actions (e.g. amend the CIP, conduct additional training, terminate the investigation). Repetitive or serious investigator compliance issues may result in initiation of a corrective action plan with the investigator and study site, and in some cases, may necessitate suspending enrollment until the problem is resolved or ultimately terminating the investigator's participation in the study. Sponsor will provide study site-specific reports to investigators summarizing information on deviations that occurred at the investigational study site on a periodic basis.

11.8. Confidentiality

Investigators and all the persons involved in the study must keep the information confidential, like the subject's personal information and results of the study. The investigator surgeon keeps a confidential identification list of the patients. All the data which will be given to the sponsor will be codify and the name and address of the patient must never be mentioned.

11.9. Records Retention

The hospital will keep its medical records and study related records as defined by local regulation.
Sponsor will retain the study records according to Medtronic corporate policy and record retention schedule.

11.10. Investigator/Investigation Site Selection

All investigators managing the subject's surgery must be qualified practitioners and experienced in the diagnosis and treatment of subjects. All implanting physicians must be experienced and/or trained in the handling of study products.

Study site personnel training will be completed and documented prior to participation in this study. Sponsor contracts with participating institutions/investigators through a Clinical Trial Agreement that defines the scope and responsibilities and associated compensation related to carrying out the obligations under a sponsored clinical study.
An overview of study centers participating in this clinical study is available under a separate cover upon request to the sponsor and in the Investigator Site File.

11.11. Principal Investigator Obligation

Each site will have a Principal Investigator (PI). The PI has overall responsibility for the day-to-day conduct of the trial at the site and for the integrity of the trial data generated by their site. Specifically, the PI is responsible for the following:

- Protecting the rights, safety, and welfare of the subjects in their care
- Obtaining written Information note with proof of patient consent of all subjects prior to any trial-related procedures, and only after Ethics Committee and regulatory approval (if applicable) of the trial
- Obtaining and maintaining Ethics Committee approval
- Conducting the investigation in accordance with the signed agreement, CIP, applicable laws and regulations, and any conditions of approval imposed by an Ethics Committee or regulatory authorities
- Providing accurate financial disclosure to the sponsor, including any relevant changes during the course of the trial and for 1 year after the completion of the trial.
- Approving all case report forms (or authorizing a sub-investigator to do so); approval of the case report form indicates the data represented are accurate and have been reviewed.
- Maintaining accurate, complete, and current records, including:
    - All correspondence with another investigator, the sponsor, the monitor, the Ethics Committee (including required reports), or regulatory agency
    - Records of each consented subject's case history, signed and dated Information note (s) with proof of patient consent (s), CRFs, and source documents
    - The CIP, and documentation of dates of and reasons for each protocol deviation
    - Any records required by a regulatory agency
    - Ensuring that clinical records are clearly marked to indicate that the subject is enrolled in the study.
- Allowing time with the trial monitor and Sponsor trial staff members during Sponsor site visits
- Informing the sponsor if any action is taken by an Ethics Committee or regulatory authority
- Proposes to the sponsor any appropriate modification(s) of the CIP or investigational device or of the use of the investigational device,
- Failure to perform the investigator obligations or to complete corrective and preventive actions identified during monitoring or auditing activities may result in Principal Investigator or site personnel disqualification, and/or lead to suspension or termination of the study at the site.
- The investigator will permit study-related monitoring, audits, and inspections by the sponsor and government regulatory bodies.

Informs the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that can be required.

11.12. Oversight of Study Personnel

The Principal Investigator may delegate study-related tasks to appropriate trained and qualified personnel to ensure alignment between contractual obligations and delegated study responsibilities.

The delegation of study-related tasks will be documented on the Delegation of Authority Log and the Principal Investigator will provide ongoing oversight of all delegated study-related tasks.

The Principal Investigator will ensure training is provided, completed and documented for all staff performing delegated study-specific tasks.

Sponsor will train study site personnel on the clinical investigation plan, on relevant standards and regulations, information note provided to patient and process, on data collection and reporting tools. If new members join the study site team, they will receive training on the applicable study requirements relevant to their role before contributing to the study.

Study center personnel participating in the clinical study will be trained in study activities relevant to their role. Training must be completed and documented prior to that individual conducting any study related activities.

Investigator and/or study coordinator meeting(s) or telephone conference call(s) may be held to discuss the CIP, training, study results, etc. Continued training may occur through interim meetings or telephone conference calls to discuss relevant study issues.

12. Study Monitoring

It is the responsibility of the Sponsor to ensure proper monitoring of this study.

The monitoring visits on site or remote (planned with the investigator) will be performed regularly by a trained CRA (Clinical Research Associate). The investigator will allocate adequate time for such monitoring activities. The Investigator will also ensure that the monitor or other compliance reviewer is given access to all the study-related documents (e.g., patients' medical files and other source data/documentation) and study-related facilities (e.g., pharmacy, radiology, etc.) and has adequate space to conduct the monitoring visit. The CRA will check, among others, the presence of patients' information notes in the patients' medical file, the respect of inclusion criteria, the primary outcome…

All data in the CRF of each patient must be in accordance with the source data (e.g., patient's medical file). The CRA is bound to respect the confidentiality of data he has access to.

The CRA will check also regularly the conformity of the CRF with the protocol and the regulatory requirements in effect and that all CRF are completed with all required information.

12.1. Monitoring Visits

The frequency of monitoring visits may be based upon subject enrollment, study compliance, number of adverse events, number of deviations, observations from previous monitoring visits, and any suspected inconsistency in data that requires investigation. Regulatory documents will be reviewed at each study site. Monitoring for the study, including site initiation visits, interim monitoring visits, and close-out visits, will be done in accordance to the study-specific monitoring plan.

Monitoring visits may be conducted periodically to assess study site progress, the investigator's adherence to the CIP, regulatory compliance including but not limited to EC approval and review of the study, maintenance of records and reports, and review of source documents against subject CRFs in accordance to the study-specific monitoring plan. Monitors review study site regulatory and study compliance by identifying observations of non-compliance and communicating those observations along with recommendations for preventative/corrective actions to study site personnel. Monitors may work with study personnel to determine appropriate corrective action recommendations and to identify trends within the study or at a particular study site.

13. Publication Plan

This study will be submitted to international peer reviewed congresses and journals for presentation and publication chosen in mutual agreement between the sponsor and the main investigator.

Publications will be handled as indicated in the CTA. Publications will adhere to authorship criteria defined by the International Committee of Medical Journal Editors (ICMJE, Uniform requirements for manuscripts submitted to biomedical journals, www.icmje.org). Individual authorship criteria defined by the target journal or conference will be followed when it differs from ICMJE criteria, or the more stringent criteria for authorship will be applied.

Investigators, sponsor personnel or contributors to a manuscript or abstract, must at a minimum meet all of the conditions below to be included as an author:

- Substantial contributions to conception and design of the work, or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

The selected authors will be responsible for drafting the publication. All listed authors must fulfill the authorship conditions stated above to be included as authors, and all contributors who fulfill the conditions must be listed as authors.

All investigators not listed as co-authors will be acknowledged and will be individually listed according to the guidelines of the applicable scientific journal when possible. Any other contributors will be acknowledged by name with their specific contribution indicated.

The order of quotation of the other authors in publications and communications will be established according to their relative contribution among patient's number included in the study, among the quality of the collected data and the time spent in the center if the investigator left before the end of the study.

14. Version History

Version	Summary of changes	Justification of changes	Potential impact of the change on performance, effectiveness, or safety or other endpoints	Identification of the affected study documents	Author(s)/Title
1.0	Not applicable, new document	*NA*	*NA*	*NA*	[redacted]
2.0	Following the French ethics committee (CPP) submission (first round of questions), addition of few precisions/details.	*Complementary informations required by ethic committee following the 1st submission.*	*NA*	*CIP V2.0* *Synopsis V2.0* *CRF V2.0* *Inform consent note V2.0* *Questionnaires V1.0* *Investigator list V1.0*	[redacted]
3.0	Addition of 2 investigators	*Addition of 2 investigators in the study.*	*NA*	*CIP V3.0* *Investigator list V2.0*	[redacted] */Clinical Research Associate*
4.0	Addition of 2 investigators Enrollment period extension	*Addition of 2 investigators in the study and enrollment period extension as number of inclusions was not reached.*	*NA*	*CIP V4.0* *Inform consent note V3.0* *Investigator list V3.0*	[redacted] *Clinical Project Manager*
5.0	Inclusion period extension Addition of new arm: PASS TULIP Genesis Increasment of patient number in existing arm	*Inclusion period extension as number of inclusions was not reached.* *MEDICREA International would like to add the PASS TULIP GENESIS sub-range, whose first references were CE marked as of May*	*NA*	*CIP V5.0* *CRF V3.0*	[redacted] */ Clinical Project Manager*

		2019, as a new study arm. *Increase for the existing arms (PASS LP, PASS DEGEN, PASS TULIP PRIME) in the number of patients in each arm (+5 patients for each arm)*			
6.0	Enrollment period extension Re-specify assessment criteria Justification about number of patient required Update 2 IP practice places.	*Enrollment period extension as number of inclusions was not reached.* *Re-specify assessment criteria following notified body request*	*NA*	*CIP V6.0* *Synopsis V3.0* *Investigator list V4.0*	[redacted] [redacted]*/ Clinical Project Manager*
7.0	Enrollment period extension	*Enrollment period extension as number of inclusions was not reached.*	*NA*	*CIP V7.0*	[redacted] [redacted] *(Clinical Research Specialist)*
8.0	Regarding the justification of changes, many changes have been done. Main changes are listed below: - PASS TULIP Genesis arm cancellation - Adaptation of visit windows/analysis windows - Patient arms analysis definition - Fusion re-definition - ISO 14155:2020 compliance: AE specifications and reporting, Data Management (e.g., audit trail), site team responsibilities, Statistical methods, early termination or suspension, publications plan.	*Following the acquisition of MEDICREA by MEDTRONIC, the study has been transitioned to Medtronic quality management system, to improve the quality of the study, to add some specifications.*	*NA*	*CIP V8.0* *Synopsis V4.0* *CRF V4.0*	[redacted] [redacted] *(Clinical Research Specialist)*

V9.0	- Number of sites - Update of Coordinating Investigator - Specification of the Safety part: UAE's report/ Relatedness report/Rewording - Few ISO14155:2020 updates: clinicaltrial.gov publication; EC/RA information of suspension/early termination; EC/RA approval before investigation resumes; Subjects infomation of suspension; Propose to sponsor CIP/investigational device modification; Subject's information of any new significant findings occurring during the clinical investigation	- *Updates of some typologies and missing point observed during the study FU* - *Following the ISO14155:2020 Gap analysis, some clarifications are provided in this revision*	*NA*	*CIP V9.0 Synopsis V5.0*	[redacted] [redacted] *(Clinical Research Specialist)*

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