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CLINICAL INVESTIGATION PLAN

"AMBISPECTIVE STUDY EVALUATING THE CLINICAL OUTCOMES OF SAGITTA EVL-R REVISION STEM"

"2022-10_SAGITTA-EVL-R "

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Name of the Promoter: **SERF** Address: 85 Avenue de Bruyères, 69150 Décines-Charpieu- FRANCE Phone: +33 (0)4.72.05.60.10

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Stakeholders
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PROTOCOL SIGNATURE PAGE
"Ambispective Study Evaluating the Clinical Outcomes of SAGITTA EVL R Revision Stem"

Protocol Number: "2022-10"
"Version 1.2" of "21/12/2022"

Legal representative of the Promoter	**Signature**
Name: Lydie BONNEVAY Title: Clinical Project Manager	Date: Visa:
Name: Jean-Charles MONCENIS Title: Regulatory and Clinical Affairs Manager	Date: Visa:

Principal Investigator	**Signature**
I have read all the pages of the protocol of study N° "2022-10" dated 21/12/2022 and all its annexes and validate its content. I confirm that it contains all the information necessary to conduct the study. I undertake to conduct the study in accordance with the protocol and the terms and conditions set out therein.	
Name: DUJARDIN Franck Centre: Rouen University Hospital – Charles Nicolle Hospital	Date: 22/12/2022 Visa: 

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LIST OF ABBREVIATIONS

ANSM	National Agency for the Safety of Medicines and Health Products
BOW	Clinical Research Associate
PCBs	Good Clinical Practice
CNIL	National Commission "Information Technology and Freedoms"
CPP	Committee for the Protection of Persons
CRF	Case Report Form
Eff.In	Adverse effect
EI	Adverse event
EIG	Serious Adverse Event
EII	Unexpected adverse reaction
EIGD	Serious adverse reaction to the medical device
EIGID	Unexpected serious adverse reaction from the medical device
IC	Clinical Investigation
MR	Reference Methodology
WOODPECKER	Clinical Investigation Plan
PTH	Total Hip Replacement

1. GENERAL SYNOPSIS OF THE CLINICAL INVESTIGATION

Title	Ambispective study evaluating the clinical outcomes of revision stem SAGITTA EVL R
ID-RCB No. Protocol version Date	2022-A02295-38 V1.2 21/12/2022
Promoter	**SERF** 85 Avenue des Bruyères 69150 Décines-Charpieu FRANCE
Principal investigator	Prof. DUJARDIN Franck
Rationale/Background	This clinical study is being conducted with the aim of collecting data on hip arthroplasty with revision femoral stems from the SAGITTA® EVL-R range of FEMORAL stems manufactured by SERF. In order to reflect current practice, a comprehensive and ongoing series of patients will be included. This study will confirm the performance and safety of the SAGITTA® EVL R range of revision femoral stems within the MDR 2017/745 regulatory framework and in relation to the recommendations of the MEDDEV 2.7.1 guide. Rev 4 (Clinical Evaluation Guide), which provides for the implementation of a systematic procedure for monitoring clinical data in order to verify the claimed performance of medical devices.
Product under investigation	SAGITTA® EVL R revision femoral stems and CLAV distal locking keys. EVL.
Methodology	Post-marketing clinical follow-up study performed according to routine care with additional procedure neither heavy nor invasive, non-interventional ambispective, monocentric, non-comparative, open-label, of an exhaustive and continuous series of patients.
Ethical considerations	The investigation will be conducted in accordance with the investigation protocol, the regulations in force, including the Public Health Code as well as the Medical Devices Regulation 2017/745, the ISO 14155:2020 standard, as well as in accordance with the ethical principles described in the Declaration of Helsinki. The investigation will start as soon as the authorisations from the competent authorities are received in accordance with the typology of the study, category 4.1. As personal data will be collected and analysed during this investigation, SERF complies with the reference methodology MR 001 (declaration 2140288 v 0). The collection of personal data will also be in accordance with GDPR 2016/679. All data and information relating to patients or their participation in this study will be considered confidential and in accordance with applicable laws and regulations will not be made public. The data collected and stored in a pseudonymised format does not allow the identification of a patient through the data collected. Under no circumstances will the names of patients be transmitted or communicated to SERF.

	Patient consent will be collected by the principal investigator or another surgeon in the department during the on-site follow-up visit. As the EUDAMED database is not yet available, this study will be registered on the public database www.clinicaltrials.gov.
Main objective	To evaluate the medium-term postoperative survival rate (minimum 4 years postoperatively) of SAGITTA® EVL R rods placed between 2016 and 2018, all causes of revision combined.
Secondary objective(s)	The secondary objectives of this study are to: - Study the survival rate by components and by etiology (revision and revision with reconstruction) - Study the patient's satisfaction with his hip prosthesis - Confirm the safety of these implants by studying any complications observed - Evaluate performance through the clinical scores of HARRIS and forgotten prosthesis score of the revision femoral stems SAGITTA® EVL R.
Primary outcome	The **survival rate** will be determined according to the Kaplan-Meier curve with the replacement of the femoral implant, all causes combined.
Secondary outcome(s)	The **survival rate by component** as well as the **survival rate by etiology** will be determined according to the Kaplan-Meier all-cause curve. The **safety** of the implants will be evaluated by the occurrence of adverse events related to the medical device. These elements will be sought by the clinical examination of the practitioner and the radiological examination, carried out as part of routine practice. Patient **satisfaction** with their hip replacement will be assessed using a satisfaction questionnaire. Implant **performance** will be assessed through the Harris Clinical Hip Score (HHS) and Forgotten Hip Score (SHO-12).
Description of the study population	Between January 2016 and December 2018, about 120 patients were operated on with a SAGITTA® EVL R revision femoral stem at the Rouen University Hospital – Charles Nicolle Hospital. All patients with a SAGITTA® EVL R revision femoral stem will be seen again at a medium-term postoperative follow-up visit (minimum 4 years postoperatively). During this follow-up, they will be offered to participate in this clinical investigation.
Criteria for Inclusion of Subjects	- Patient of legal age on the date of surgery, - Patient implanted with a SAGITTA® EVL R revision femoral stem as part of its indications between 01/01/2016 and 31/12/2018, - Patient with a health insurance scheme
Criteria for non-inclusion of subjects	- Patient who has not expressed consent to the collection of his/her data and participation in the study, - Patient unable to understand the surgeon's instructions or perform postoperative follow-up.

	- Patient with a contraindication to the use of the SAGITTA® EVL R revision femoral stem - Patient implanted with a SAGITTA® EVL R revision femoral stem outside of their indication
Number of Subjects	As the study is descriptive, there is no calculation of the number of subjects needed according to a hypothesis. All patients operated on at the Rouen University Hospital – Charles Nicolle Hospital and with a SAGITTA® EVL R femoral stem will be included. This represents about 120 patients.
Treatment(s)/procedure(s) related to the study	**Prospective part:** According to the centre's practice, as part of the systematic follow-up of hip replacement replacements, a clinical examination will be carried out with an assessment of any complications and patient satisfaction. Only a quality of life questionnaire (SHO-12) and the HHS score will be required by this HF in addition to the standard care practiced in systematic follow-up in this center. These questionnaires will be completed jointly by the patients and the surgeon (additional procedure that is neither heavy nor invasive). Routine radiological evaluation will be performed. It allows the evaluation of osseointegration and bone reconstruction to document possible complications. The collection of its data will be carried out in a paper case report form (CRF). **Retrospective part:** In accordance with the patient's agreement, retrospective data will be collected using the patient's medical record and will be collected in the CRF. No additional examination to current practice will be carried out as part of this investigation.
Total duration of the study	The prospective portion of the study will last approximately 5 months depending on patient availability. The duration of each patient's participation in this study is limited to this single consultation. Retrospective data collection will be carried out simultaneously. This is a total duration of the study of 5 months.
Study timeline	The prospective part will begin as soon as regulatory approvals are obtained, scheduled for January 2023 and will be completed in May 2023. The retrospective part will be conducted after the patient consent has been collected. Study closure and report writing: July 2023
Statistical analysis	A statistical analysis will be carried out at the end of the study. This analysis will be carried out by SERF. A descriptive analysis will be done based on the data collected during the study. A follow-up of the events that occurred will be carried out, as well as an analysis of the survival rate according to Kaplan Meier.

2. IDENTIFICATION AND DESCRIPTION OF THE DEVICE UNDER INVESTIGATION

A. DESCRIPTION AND INTENDED USE

The devices under investigation in this clinical investigation (CI) are the SAGITTA® EVL R revision rods, the fixation of which can be completed by the use of two CLAV distal locking keys. EVL.
The SAGITTA® EVL R femoral stem range, in combination with the prosthetic heads and two optional distal locking keys, is suitable for most femoral revisions of total hip prosthesis (THP) with bone defect (Paprosky type I to III and SOFCOT stage II to IV) in order to reduce pain and restore mobility of the hip joint.

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C. DEVICE UNDER INVESTIGATION

Revision femoral stems **SAGITTA® EVL R** (Figure 1) are long, uncemented stems. They are made of forged TA6V alloy (ISO 5832-3 compliant). They have a hydroxyapatite coating (compliant with 13779-2) along the entire implantable length of the stem.
The curved distal part takes up the anatomical arch. The cervico-diaphyseal angle is 130°. The 11/13 assembly cone has an average angle of 4°.
The SAGITTA® EVL R rod range consists of 14 rods on the right side and 14 rods on the left side, with 3 different rod lengths for each side (180 mm, 250 mm or 325 mm).
The attachment of the revision rod can be completed with 2 transcortical locking keys made of titanium (Figure 1) TA6V (ISO 5832-3). With a diameter of 4.5 mm, they are available in 9 lengths: 25; 30 ; 35 ; 40 ; 45 ; 50 ; 55 ; 60 and 65 mm.

Figure 1 - At the top, a revision femoral stem SAGITTA® EVL R*; at the bottom, a distal locking key CLAV. EVL*

The rod references (
Table ***1***) and keys (Table 2) used in this CI are set out below:

Table 1 – Lengths, sizes, diameters, labels and references of the rods SAGITTA® EVL R

Length	Waist	Ø (mm)	Right Side		Left side	
			Wording	Reference	Wording	Reference
180 mm	2	12	SAGIT. EVL R 2-180 D	RM10450500	SAGIT. EVL R 2-180 G	RM10450520
	3	13	SAGIT. EVL R 3-180 D	RM10450501	SAGIT. EVL R 3-180 G	RM10450521
	4	14	SAGIT. EVL R 4-180 D	RM10450502	SAGIT. EVL R 4-180 G	RM10450522
	5	15	SAGIT. EVL R 5-180 D	RM10450503	SAGIT. EVL R 5-180 G	RM10450523
	6	16	SAGIT. EVL R 6-180 D	RM10450504	SAGIT. EVL R 6-180 G	RM10450524
250 mm	2	12	SAGIT. EVL R 2-250 D	RM10450505	SAGIT. EVL R 2-250 G	RM10450525
	3	13	SAGIT. EVL R 3-250 D	RM10450506	SAGIT. EVL R 3-250 G	RM10450526
	4	14	SAGIT. EVL R 4-250 D	RM10450507	SAGIT. EVL R 4-250 G	RM10450527
	5	15	SAGIT. EVL R 5-250 D	RM10450508	SAGIT. EVL R 5-250 G	RM10450528
	6	16	SAGIT. EVL R 6-250 D	RM10450509	SAGIT. EVL R 6-250 G	RM10450529
325 mm	3	13	SAGIT. EVL R 3-325 D	RM10450510	SAGIT. EVL R 3-325 G	RM10450530
	4	14	SAGIT. EVL R 4-325 D	RM10450511	SAGIT. EVL R 4-325 G	RM10450531
	5	15	SAGIT. EVL R 5-325 D	RM10450512	SAGIT. EVL R 5-325 G	RM10450532
	6	16	SAGIT. EVL R 6-325 D	RM10450513	SAGIT. EVL R 6-325 G	RM10450533

Table 2 - Lengths, diameter, labels and references of the optional CLAV distal locking keys. EVL

Length	Ø	Wording	Reference
25 mm	4.5 mm	CLAV. EVL 25	RM69020020
30 mm		CLAV. EVL 30	RM69020021
35 mm		CLAV. EVL 35	RM69020022
40 mm		CLAV. EVL 40	RM69020023
45 mm		CLAV. EVL 45	RM69020024
50 mm		CLAV. EVL 50	RM69020025
55 mm		CLAV. EVL 55	RM69020026
60 mm		CLAV. EVL 60	RM69020027
65 mm		CLAV. EVL 65	RM69020028

The stems SAGITTA® EVL R as well as the CLAV keys. EVLs are long-term implantable medical devices that are invasive, sterile, non-active and do not contain drugs or biologically active substances (tissues of human or animal origin, or their derivatives), their regulatory description is available in the Table 3.

Table 3 - Regulatory description of products under investigation

Device	Class	Code GMDN	CE marking
SAGITTA EVL R	III	38155 – Press-fit femoral stem prothesis	2003
CLAV. EVL	IIb	46646 – Orthopaedic bone screw, non-bioabsorbable, sterile	2003

Note: for the rest of the CI, under the terms "SAGITTA® EVL R" or "rods" will be included both the SAGITTA® EVL R revision femoral stems and the optional CLAV distal locking keys. EVL, unless specifically specified. The keys can only be used with the rods, so they share the same intended use (target population, indications, etc.) as the latter.

D. TRACEABILITY

The traceability of each implanted device is guaranteed by its batch number and reference number.

E. INTENDED OBJECTIVE OF THE DEVICE IN THE INVESTIGATION

SAGITTA® EVL R rods were used as standard, in accordance with their intended use and within their indications and for their usual target population, see below.

F. POPULATIONS AND INDICATIONS, CONTRAINDICATIONS OF USE FOR WHICH THE DEVICE UNDER INVESTIGATION IS INTENDED

i. INDICATED POPULATION(S) FOR THE DEVICE

Patients intended for treatment with a SAGITTA® EVL R stem are mature skeletal adults with an extremely painful and/or disabled joint, resulting from the failure of a total anterior hip replacement, without gender restriction.
It should be noted that SAGITTA® EVL R rods are suitable for most femoral revision with bone defects (Paprosky type I to III and SOFCOT stage II to IV).
It should be noted that pregnant or breastfeeding women should not be treated with a total hip replacement.

ii. DIRECTIONS

SAGITTA® EVL R rods are intended for use in the revision of the femoral part of a total hip replacement.

iii. CONTRAINDICATIONS

The rods should not be implanted in patients with the following contraindications:
Acute or chronic conditions – local or systemic (heart disease, uncompensated diabetes, regular hemodialysis, decreased immune system defenses, etc.).

G. PREREQUISITES FOR USE

i. EDUCATION AND EXPERIENCE NEEDED

Not applicable, this is an ambispective data collection, as the subjects have already been implanted with the device under investigation.
Only patient follow-up should be carried out by an orthopedic surgeon with knowledge of anatomy, biomechanics and reconstruction surgery of the musculoskeletal system, and previously trained in good clinical practices.
Considering the large number of SAGITTA® EVL R rod insertions performed in the prospective center and the experience of the surgeon who installs the SAGITTA® EVL R rods, no learning curve - including retrospective - is envisaged.

ii. APPLICATION-SPECIFIC PROCEDURES

Not applicable, this is an ambispective data collection, as the subjects have already been implanted with the device under investigation.
Only prospective follow-up of patients will be carried out in accordance with the usual practice of the orthopaedic surgery and traumatology department in question.

3. CI DESIGN RATIONALE

A. EVALUATION OF THE RESULTS OF THE RELEVANT PRECLINICAL EVALUATION PERFORMED TO JUSTIFY THE USE OF THE DEVICE ON HUMAN SUBJECTS

The clinical evaluation of the SAGITTA® EVL R rods and associated locking keys demonstrated their compliance with the essential requirements on safety, acceptability of the benefit/risk balance, clinical performance and acceptability of adverse events.
However, in consideration of the elements evaluated, a post-marketing clinical study is considered necessary in order to:

- Generate postoperative clinical data (state-of-the-art revision rate of 15.2% at 5 years / 20.8% at 10 years).
- To confirm the clinical benefits associated with the use of the rods and their performance.

B. EVALUATION OF CLINICAL DATA RELATED TO THE PROPOSED HF

The purpose of this IC is therefore to collect clinical data concerning the SAGITTA® EVL R rods as well as the CLV keys. EVLs, used for their intended purpose. These data will support and confirm the clinical evaluation of the device as agreed in the post-market surveillance plan implemented by SERF.
This data will complement the data already available regarding the performance and safety of the implant, in order to support compliance with Regulation (EU) 2017/745.

C. CLINICAL DEVELOPMENT STAGE

According to Annex I of ISO 14155:2020, this clinical investigation (CI) is part of the post-market development stage of the device and is therefore qualified as a post-market clinical investigation, observational and with an additional cumbersome or invasive procedure.

4. RISKS AND BENEFITS OF THE DEVICE AND THE CI

A. EXPECTED CLINICAL BENEFITS

The expected clinical benefits or advantages of SAGITTA® EVL R rods are pain reduction and functional recovery of the hip joint.

B. EXPECTED ADVERSE REACTIONS

Known side effects (or complications) related to the use of SAGITTA® EVL R rods or the surgery required for their implantation are identified in the device's instructions for use and listed below:

- Allergy to the various materials that make up the implant and/or surgical equipment, in particular to metal,
- Pseudarthrosis, osteolysis, loosening of the prosthesis,
- Instability, dislocation, insufficient range of motion,
- Deformation, cracking or breakage of a component,
- Bone fracture,
- Collapse, migration, shortening or lengthening of the operated limb,
- Infection, sepsis,
- Delayed healing,
- Local, transient or permanent nerve damage,
- Cardiovascular disorders (hematoma, deep vein thrombosis), pulmonary embolism,
- Urinary tract infection,
- Deep abscess, fistula,
- Deterioration of the femoral and acetabular implant by stem/acetabulum contact during movements of extreme amplitude, mechanical noise may be heard when walking,
- The friction of components with each other can generate wear debris, corrosion or the release of metal particles that can induce a local reaction of the tissues,
- Residual hip pain.

Notes:
Some of these complications can lead to prolonged operating time, revision surgery, or implantation failure/postponement of surgery.
It should be noted that any joint prosthesis is subject to wear and tear that can force the surgeon to operate again.
The surgeon is responsible for complications that may result from an incorrect prescription, a defective operating technique or a lack of asepsis. In no case can these complications be attributed to SERF.

In addition, situations with an increased risk of failure are also listed:

- Severe muscular, neurological or vascular impairments affecting the affected extremity,
- Destruction, loss or poor bone quality that can affect the stability of the implant (for reasons of fatigue resistance), severe osteoporosis, significant deformities of the joint to be replaced,
- Any associated conditions that could compromise the function or implantation of the prosthesis,
- Systemic or metabolic disorders,
- Intellectual inability of patients to understand the surgeon's instructions,
- Drug addiction, alcohol, tobacco or drug abuse,
- Local bone tumors that may affect the stability of the implant,
- Obesity, overweight, high patient activities, intensive sports practices, patients with balance disorders,
- Bone loss or poor quality likely to affect the stability of the implant (for reasons of fatigue resistance, it is not recommended to use the "Sagitta EVL R" rod when this bone loss is greater than a height of 137 mm with respect to the center head),
- Pregnant or breastfeeding women.

C. ASSOCIATED RESIDUAL RISKS AS IDENTIFIED IN THE RISK ANALYSIS REPORT

The risk management file for SAGITTA® EVL R rods and CLAV locking keys. EVL has been established in accordance with NF EN ISO 14971.

All risks associated with the design, manufacture, transport/storage, use and destruction of the device have been estimated. All residual risks were combined with each other after risk reduction to verify that a new risk was not generated.
Taking into account all the risk control actions put in place, the overall residual risk is considered acceptable.
The residual risks to the patient associated with the implantation of the rod are taken into account in the device's instructions for use, available in Appendix 2.

D. RISKS ASSOCIATED WITH PARTICIPATION IN THE IC

Subjects participating in the clinical investigation benefit from an operating procedure and medical follow-up identical to the procedure and care provided in routine practice. No additional procedures are performed during the implantation of the prostheses or during the follow-up of the subjects.
No specific risks associated with the participation of subjects in HF were identified.

E. POSSIBLE INTERACTIONS WITH CONCOMITANT MEDICAL TREATMENTS

No medical treatment is known to interfere with the expected results of SAGITTA® EVL R revision rod implantation.

F. STUDIES UNDERTAKEN TO CONTROL OR MITIGATE RISKS

Not applicable, no specific risks associated with participation in the HF have been identified. The risks to participants are the same as those encountered with the normal use of a SAGITTA® EVL R revision rod and associated postoperative follow-up.

G. RATIONALE FOR THE BENEFIT/RISK BALANCE

In accordance with the results of the clinical evaluation as well as those resulting from the risk management process applied to SAGITTA® EVL R revision rods, they benefit from minimized and acceptable risks in terms of the associated benefits when used in the context of their indication and in compliance with the instructions for use and recommendations issued by SERF.
The benefit/risk ratio is therefore favourable.

5. CI OBJECTIVES AND ASSUMPTIONS

A. CLAIMS AND PLANNED PERFORMANCE THAT NEED TO BE VERIFIED

The following claims and performances will be considered during the CI:
- The implant survival rate/implant revision rate;
- Reduction of pain;
- Functional recovery of the hip joint

B. EXPECTED RISKS AND ADVERSE EFFECTS THAT NEED TO BE ASSESSED

All the risks and expected adverse effects to be assessed during this CI are listed in the chapter 4.
All the complications observed will be listed in the patient's observation form.
Any effect, event, defect or malfunction that must be reported to the competent authorities will be reported in accordance with the provisions of Chapter 14.

C. MAIN AND SECONDARY OBJECTIVES

i. MAIN OBJECTIVE

The main objective of the HF is to study the survival rate, all causes of revision combined, of SAGITTA® EVL R revision femoral stems inserted between 01/01/2016 and 31/12/2018, in the medium term with a follow-up of at least 4 years postoperatively.

ii. SECONDARY OBJECTIVES

The secondary objectives of this study are to:
- Study survival rates by components and etiology (revision and revision with reconstruction)
- Studying patient satisfaction with their hip prosthesis
- Confirm the safety of these implants by studying any complications observed
- Evaluate performance through the clinical scores of HARRIS (HHS) and forgotten prosthesis score (SHO-12) of femoral stems SAGITTA® EVL R.

The criteria for each of the objectives are presented in Chapter 6.A.iii.

D. PRIMARY AND SECONDARY ASSUMPTIONS TO BE REJECTED OR ACCEPTED BASED ON CI STATISTICAL DATA

Not applicable, the objectives of this CI are descriptive.

E. JUSTIFICATION OF PARAMETERS AND ASSUMPTIONS

Not applicable, the objectives of this CI are descriptive.

6. CLINICAL INVESTIGATION DESIGN

A. GENERAL

i. DESCRIPTION OF THE TYPE OF HF

This is a post-marketing clinical follow-up study performed in routine care with an additional non-heavy and non-invasive Cas 4.1, single-center, non-randomized, observational, non-comparative, ambispective, post-marketing procedure performed under normal conditions of use.

ii. LIMITATIONS OF BIAS

The cohort of subjects included in the study represents a comprehensive and consecutive series of subjects.
The cohort will therefore make it possible to generate data in real-life conditions.
As the inclusions are retro-prospective, this can impact the quality of retrospective data collection.

iii. PRIMARY AND SECONDARY OUTCOMES

The outcomes presented below were chosen in accordance with the HF objectives presented in Chapter 5C.

- Primary outcome:

The medium-term survival rate (minimum 4 years postoperatively) is defined via the Kaplan-Meier analysis, for all patients who still have the stem in place at the follow-up considered. Each inflection point will correspond to revision surgery with removal or change of the stem, all causes of revision combined.

- Secondary outcomes:

Survival rates by components and etiology
The definition is the same as for the primary outcome but with d in subgroups:

- According to the different implant assemblies
- As indicated revision or revision with reconstruction. The CCAM codes related to the intervention will allow this distinction.

Satisfaction
The satisfaction of the subjects will be evaluated through a graduated scale with 5 levels (Likert scale) with the following 5 response options:

- Very satisfied,
- Rather satisfied,
- Neither satisfied nor dissatisfied,
- Rather dissatisfied,
- Very dissatisfied.

Complications
All complications (events, adverse reactions and dysfunctions, serious or not, expected or not; see definitions in the chapter 0) observed since the implantation of the SAGITTA® EVL R rods for each subject will be identified, including those observed outside of the monitoring planned by this ICP.
Complications may also be grouped according to their etiology. In all cases, the causal link with the device under investigation will be studied.

Functional Clinical Scores and Ratings

- *Harris Hip Score*[1]*:*

The Harris score (HHS) is one of the main functional clinical scores used after hip replacement surgery and evaluates 3 "items" relating to the diseased or operated hip:

- Pain (44 points)
- Function (47 points)
- Mobility (9 points)

For a maximum total score of 100 (minimum score:0), the HHS results will be categorized as follows:

[1] Harris WH. Traumatic arthritis of the hip after dislocation and acetabular fractures: treatment by mold arthroplasty. An end-result study using a new method of result evaluation. *J Bone Joint Surg Am.* 1969; 51: 737–55.

	HHS
Excellent	90-100
Good	80-89
Correct	70-79
Bad	< 70

The HHS fill grid is available in **Appendix 5**.

- *Forgotten Hip Score* (FJS-12):[2]

The Forgotten Hip Score (SHO-12) is the French version of the FJS-12 (*Forgotten Joint Score*). The objective of this self-questionnaire is to estimate the degree of neglect of the hip and knee prosthesis through 12 questions.

Each item has 5 levels of response: Never: 0 points
Almost never: 1 point
Rarely: 2 points
Sometimes: 3 points
Often: 4 points

The sum of the items is divided by the number of items and multiplied by 25 to obtain a score out of 100.
The OHSS Fill Grid is available in **Appendix 6**.

Radiographic evaluation:

- *Paprosky's classification*[3] *:*

This classification makes it possible to define the preoperative bone defect.

	Definition	Proximal Metaphysis	Diaphysis
I	Minimal proximal metaphyseal bone loss	Intact	Intact
II	Moderate-to-severe proximal metaphyseal bone loss	Absent	Intact
III			
A	Severe proximal metaphyseal bone loss with diaphysis intact for some distance	Absent	≥4 cm of isthmus
B	Severe proximal metaphyseal bone loss with diaphysis intact for some distance	Absent	< 4 cm of isthmus
IV	Complete loss of metaphsyeal and diaphyseal bone	Absent	Absent

[2] Behrend H, Giesinger K, Giesinger JM, Kuster MS. The "forgotten joint" as the ultimate goal in joint arthroplasty: validation of a new patient-reported outcome measure. J Arthroplasty. 2012 Mar; 27(3):430-436.e1. DOI: 10.1016/J.ARTH.2011.06.035. Epub 2011 Oct 13. PMID: 22000572.

[3] Della Valle C.J., Paprosky W.G. Classification and an algorithmic approach to the reconstruction of femoral deficiency in revision total hip arthroplasty *J Bone Joint Surg Am* 2003 ; 85 (Suppl. 4): 1-6

- *Preoperative fractures will be evaluated by the Vancouver Stadium[4]:*

This classification of periprosthetic hip fractures proposed by Duncan and Masri is the most widely used classification system. It takes into account the site of the fracture, the condition of the femoral implant and the quality of the surrounding femoral bone material.

- **type A**: fractures involve the trochanteric area
  - **A(G)**: greater trochanter
  - **A(L)**: lesser trochanter
- **type B**: around the stem or just below it
  - **B1**: stem stable
  - **B2**: stem loose
  - **B3**: stem loose, bone stock inadequate
- **type C**: well below the stem

- *Osseointegration of the stem will be assessed by the Engh score [5] (see Appendix 7)*

Measured on postoperative X-rays, it is divided into 2 subparts: fixation and stability.
The final score can be classified into 4 categories:

- <-10°: unstable
- -10 to <0°: suboptimal but unstable
- 0 to +10°: suspected bone growth
- > +10°: osseointegration

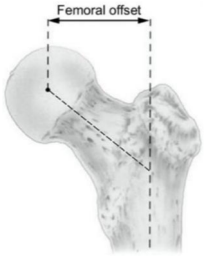
- *Bone reconstruction will be measured by the cortico-medullary index [6]*

This index represents the fineness of the cortex and allows us to evaluate bone quality.

$$\frac{Epaisseur\ os\ cortical}{Diamètre\ extérieur\ du\ fémur} \times 100$$

- *Femoral offset*

The femoral offset is the distance between the diaphyseal axis and the center of the femoral head.



[4]4 Glick, Y. Vancouver classification of periprosthetic hip fractures. Article reference, Radiopaedia.org. (accessed on 18 Oct 2022) https://doi.org/10.53347/rID-52713

5 Engh C.A., Massin P., Suthers K.E. Roentgenographic assessment of the biologic fixation of porous-surfaced femoral components Clini Orthop Relat Res 1990; 257 : 107-127

6 Barnett E., Nordin B.E. The radiological diagnosis of osteoporosis: a new approach Clin Radiol 1960 ; 11 : 166-174

iv. METHODS AND TIMING OF EVALUATION, RECORDING AND ANALYSIS OF VARIABLES

The table below presents the different stages and moments of patient follow-up, and the acquisition of related data.

Study Outline	Retrospective			Prospective part	
	Pre-operative data	Implantation	Immediate post-operative follow-up	Inclusion in the study	Medium-term monitoring
Topic Information				X	
Verification of inclusion criteria				X	
Demographics: Age, height, weight, sex	X				
Medical and surgical history	X				
Implantation of the prosthesis Operative report: Date of operation, type of anesthesia, approach, type of implant and assembly performed, coding of the surgical act (CCAM code)		X			
Radiological examination	X				X
Functional score assessment Modified HHS – SHO-12	X (except SHO-12)				X
Satisfaction					X
Adverse event collection		X	X	X	X

Complications and serious adverse events will be collected independently of the retrospective and prospective parts but over the entire period since the intervention.

v. EQUIPMENT TO BE USED TO EVALUATE CI VARIABLES AND PROVISIONS FOR MAINTENANCE AND CALIBRATION MONITORING

No specific equipment is required for the evaluation of HF variables. No additional examination is required. The radiological examination is performed prior to the follow-up visit, in local radiology centers as well as for follow-up according to standard operating procedures.
In standard tracking, X-rays are taken before each follow-up.

vi. PROCEDURES FOR REPLACING SUBJECTS, IF APPLICABLE

N/A: This is a retrospective data collection. Subjects leaving the study will not be replaced.

vii. INVESTIGATION SITE(S)

An investigation site has been identified for the conduct of this CI:

Rouen University Hospital
Charles Nicolle Hospital
37 Bd Gambetta
76000 Rouen

viii. END OF CI

HF will be considered complete when the last subject has completed their single follow-up visit.
In case of premature termination of the study, refer to Chapter 16 of this protocol.

B. DEVICE(S) UNDER INVESTIGATION AND COMPARATOR(S)

No comparator is used for this CI.

i. DESCRIPTION OF EXPOSURE TO THE DEVICE(S) UNDER INVESTIGATION OR COMPARATOR(S)

For implantation of a SAGITTA® EVL-R femoral stem in the context of hip arthroplasty, the subject may be exposed a maximum of 2 times (2 hips).
The patient is exposed, throughout the time that the implant remains in place, to the following materials:
Titanium TA6V (ISO 5832-3) for the stem and keys.
Hydroxyapatite (ISO 13779-2 and ISO 13779-6) for stem coating.
The human tissues in contact with these materials are: femur, soft tissues, cartilage, blood vessels, and blood.

ii. LIST OF ANY OTHER MEDICAL DEVICES OR DRUGS TO BE USED DURING HF THAT ARE NOT ALREADY LISTED IN THE INSTRUCTIONS FOR USE

No additional drug or surgical treatment is required as part of this HF.

iii. NUMBER OF DEVICES UNDER INVESTIGATION TO BE USED

One (1) device is implanted per femur.
In the particular case of subjects operated bilaterally, two (2) devices may be implanted in the same subject, at a rate of one (1) per femur.

C. TOPICS

i. INCLUSION CRITERIA

- Patient of legal age on the date of surgery,
- Patient implanted with a SAGITTA® EVL-R revision femoral stem in the context of its indications between 01/01/2016 and 31/12/2018,
- Patient benefiting from a health insurance scheme.

ii. CRITERIA FOR NON-INCLUSION

- Patient who have not expressed consent to the collection of their data and participation in the study,
- Patient unable to understand the surgeon's instructions or perform postoperative follow-up.
- Patient with a contraindication to the use of the SAGITTA® EVL R revision femoral stem
- Patient implanted with a SAGITTA® EVL R revision femoral stem outside of their indication

iii. Criteria for Subject's Exclusion

No exclusion criteria were used in this study.

iv. Criteria and procedures for withdrawing a subject, discontinuing participation or losing sight of a subject

When a subject wishes to discontinue participation (for any reason), the principal investigator will be required to document the subject's exclusion or withdrawal of consent. Whenever possible, the reason for the withdrawal of consent should be recorded, especially in the case of a serious adverse event.
When a subject is excluded or if he withdraws his consent, he continues to be followed normally by his orthopaedic surgeon, as part of his normal post-operative follow-up.
All subjects for whom the principal investigator is unable to get in touch after 3 telephone reminders will be considered as 'Lost to follow-up'.
Because HF is ambispective, it is not possible to replace subjects who are lost to follow-up or excluded.

v. Time of enlistment

Participation in this HF will be offered to patients who meet the inclusion criteria during their postoperative follow-up visit.

vi. Timing of Randomization

The CI design is not applicable and does not include the use of a comparator or comparison arm, so there can be no randomized assignment to any of these arms.

vii. Expected duration of participation of each topic

Considering the inclusion period (01/01/2016 – 31/12/2018), the ambispective nature of HF and the planned postoperative follow-up, the duration of participation for a subject will be a maximum of 1 medium-term follow-up (minimum 4 years postoperatively) for patients implanted between 2016 and 2018.

viii. Number of required topics to be included in the CI

Over the period of implantation under consideration (01/01/2016 – 31/12/2018), 120 patients were implanted with a SAGITTA® EVL-R rod in the investigation center selected for HF and can potentially be included. Only patients who meet the screening criteria and agree to participate (inclusion) will be included and their data collected.

ix. Inclusion period

The implementation period considered for the HF is retrospective and extends from 01/01/2016 to 31/12/2018 for the centre in question.
Inclusion of subjects will occur as patients travel to their follow-up visit. Inclusions will be carried out in 5 months, corresponding to the time needed to reconvene all patients.

x. Total expected duration of CI

The study will begin once all the necessary opinions and authorizations have been obtained.
The total duration of the study depends only on its prospective part, which consists of monitoring the subjects in the medium term, at least 4 years postoperatively. Retrospective collection will be carried out as follow-up visits are made, as soon as the patient's consent is obtained. The total duration of the study will be 5 months for follow-ups, at the date of writing of this protocol.

xi. Relationship between the study population and the target population

Due to the ambispective nature of HF, for which implantation of SAGITTA® EVL R rods has already been performed, implanted patients fit the target population. The selection criteria ensure that only subjects that exactly match the target population will be included in the CI.

xii. VULNERABLE POPULATIONS, PREGNANT AND/OR BREASTFEEDING WOMEN

The target population of SAGITTA® EVL R rods as defined in Chapter 2.F.i does not include any vulnerable populations. In addition, the selection criteria as mentioned in chapters 6.C.i to 6.C.iii make it possible to ensure the non-inclusion of vulnerable patients and respect for the target population.

D. PROCEDURES

i. DESCRIPTION OF ANY HF-RELATED PROCEDURES TO WHICH SUBJECTS ARE SUBJECTED (INCLUDING DEVIATIONS FROM STANDARD CARE)

Only an additional procedure that is neither heavy nor invasive is required when participating in this HF compared to the standard care provided as part of the systematic follow-up during hip replacement revision surgery in the investigation center in question. Namely, a quality of life questionnaire (SHO-12 forgotten hip score) and a functional score (HHS Harris Hip Score) are requested in addition. These can be completed in part by the patient or collected by the investigator.
As far as the retrospective part is concerned, all the necessary data will be collected directly from the patients' medical records, the subjects having already undergone the following visits: preoperative visit, intervention, immediate postoperative follow-up. Depending on the date of the operation, one or more intermediate postoperative follow-ups may have been performed. Data on these interim follow-ups will not be collected. Only relevant data in terms of serious adverse events will be collected for these interim follow-ups.
For the prospective part, which concerns only the medium-term postoperative follow-up (minimum 4 years) taking place after the inclusion of patients in the study, the procedures to which the subjects participating in HF will be subjected are listed and briefly described below. These procedures are the same as those performed as part of the systematic follow-up of a hip replacement in the investigation center in question. At the end of the investigation, the subjects continue to be monitored according to the habits of the center.

Inclusion of subjects in the CI
Patients scheduled for their usual follow-up visit will be selected (detailed process available in Chapter 13) and at the end of the screening process, the patient will be included if he or she consents to participate in the study.

Follow-up visits
The follow-up visit will take place as follows: the subject meets the investigator for the systematic clinical examination as carried out in the investigation center, with a search for signs indicating the possible presence of a complication in the operated hip and the evaluation of the patient's satisfaction. The pain experienced by the subject will be reported via the HHS score. HHS and SHO-12 functional scores are collected by the investigator via the appropriate questionnaires submitted to the patient (see Appendices 5 and 6 and section 6.A.iii). Bone reconstruction and osseointegration are evaluated on the X-ray performed prior to the follow-up visit to document a complication. If a revision, removal or change of implant is necessary or in the case of the detection of a complication, the investigator records this in the patient's file.

<u>Summary of the Study</u>
1. Identification of eligible participants:
During a medium-term postoperative follow-up consultation (minimum 4 years) in orthopedic surgery (performed as a clinical routine) for patients implanted with a SAGITTA® EVL R revision rod during the period under consideration, they will be offered to participate in the study

2. Information and collection of consent from people agreeing to participate in the medical consultation
3. Acquisition of clinical data during the follow-up visit
4. End of participation for the participant.

ii. Description of activities carried out by the Proponent's representatives (excluding monitoring)

The sponsor's representatives carry out the following tasks prior to the start of the CI (obtaining all necessary authorisations):

- Selection, definition of roles and responsibilities and verification of the necessary experience of the various stakeholders and collection of possible conflicts of interest;
- Documentary preparation of the study and obtaining the necessary authorizations through the required regulatory submissions;
- Registration of the CI on a public database.

During the conduct of the study, the proponent's activities are:

- Documentation of exchanges between stakeholders as well as competent authorities in charge of CI;
- Evaluation of adverse events reported by the investigator and transmission of the required information to the competent authorities in charge of the HF, as well as to other stakeholders;
- Drafting, documentation of any amendments, as well as obtaining the necessary authorizations if applicable;
- Update if necessary the risk analysis of HF according to the complications observed;
- Communication with investigators of HF advancement;
- Collection of questions from investigators, transmission and documentation of answers to investigators.

When the HF is completed (last visit to last follow-up of the last patient), the sponsor is responsible for the following activities:

- Closure of the CI according to the procedures provided;
- Carrying out the analysis of the data generated;
- Issue of the investigation report.

The monitoring activities for which SERF is responsible are discussed in §6.E.

iii. Any known or foreseeable factors that may affect the effects or interpretation of the results

The observational nature of HF and its duration can have several consequences on its outcomes. First, a high number of patients who have been lost to follow-up or died are expected.
However, replacement of patients who have been lost to follow-up or who have died is not considered due to the ambispective nature of the study.
The bias inherent in the retrospective part could also limit the quality of the data collected.
As the study is observational, factors such as age, associated comorbidities or any other confounding factors, will be taken into account during the analysis of the data.

E. Monitoring plan

The monitoring and audit procedures described in the Good Clinical Practices will be respected.
The monitoring plan is consistent with SERF's usual practices for CI monitoring.
It includes at least one opening visit to the IC, one (or more if necessary) monitoring visits and a closing visit. All monitoring activities will be carried out and/or taken care of by SERF.

7. STATISTICAL CONSIDERATIONS

A. DATA ANALYSIS

The data will be analyzed for the population as treated, since the implantation is performed prior to the start of the HF (retrospective part), in accordance with the purely descriptive nature of the objectives.
The final analysis will take place when the prospective part of the HF is completed, i.e., when the last patient has been seen again during the follow-up visit and the various requests made during the monitoring activities have been closed.

B. DATA DESCRIPTION

Demographic **data** of the included population and surgery, as well as endpoints and safety data, will be presented descriptively:

- Discrete qualitative and quantitative data will be summarized by their number, percentages, and percent confidence interval for each modality;
- Continuous quantitative data will be summarized by their mean, standard deviation, mean confidence interval, median, minimum and maximum.

Clinical data will be analyzed before and after surgery at each follow-up visit (functional measures) when available, including in terms of HHS and SHO-12 functional score if available, calculating score changes between preoperative and follow-up states. The confidence interval of the observed differences will make it possible to quantify the improvement or deterioration of the clinical status.
Radiological **data** will be analyzed before and after surgery at the follow-up visit. X-rays will document possible cases of complications (causal link with the bone defect), and provide information in terms of osseointegration/bone reconstruction.
Failure and revision rates will be analyzed by a Kaplan-Meier survival curve, with any revision surgery with removal or change of the SAGITTA EVL-R rod and/or locking keys as the inflection point. If several causes are identified, specific survival rates can be calculated.
The safety data related to the medical device will be presented throughout the duration of the follow-up. The complications observed can be grouped according to the data describing them provided and their etiology.

C. ANALYTICAL PROCEDURES

i. CALCULATION OF CONFIDENCE INTERVALS

All confidence intervals will be calculated at 95%, i.e.: $z_{\frac{\alpha}{2}} = 1.96$

The confidence intervals for discrete qualitative and quantitative variables will be calculated using the following formula:

$$IC_{95} = \left[p - z_{\frac{\alpha}{2}} \times \sqrt{\frac{p \times (1-p)}{n}} \; ; p + z_{\frac{\alpha}{2}} \times \sqrt{\frac{p \times (1-p)}{n}} \right]$$

With:

- IC_{95}, the 95% confidence interval
- p, the proportion observed;
- $z_{\frac{\alpha}{2}} = 1.96$, the value derived from the normal distribution for a risk α 5%;
- n, the sample size.

The confidence intervals for the means of the continuous quantitative variables will be calculated using the following formula:

$$IC_{95} = \left[m - z_{\frac{\alpha}{2}} \times \frac{\sigma}{\sqrt{n}} ; m + z_{\frac{\alpha}{2}} \times \frac{\sigma}{\sqrt{n}}\right]$$

With:

- IC_{95}, the 95% confidence interval
- m, the observed mean;
- σ, the standard deviation observed
- $z_{\frac{\alpha}{2}} = 1.96$, the value derived from the normal distribution for a risk α 5%;
- n, the sample size.

ii. II. CALCULATION OF THE REVISION RATE

Thus, the all-cause revision rate will be calculated as follows:

$$Taux = \frac{n}{N}$$

Where n is the number of patients who underwent revision surgery and N is the total number of patients included in HF.
Specific revision rates will be calculated using the following formula:

$$T_R = \frac{n_i}{N}$$

With:

- nor, the number of patients who required revision surgery for reason i;
- N, the sample size;

The confidence interval of each revision rate thus observed (one for each reason for revision) will also be calculated as mentioned above.

iii. CALCULATION OF THE SURVIVAL RATE

The Kaplan-Meier analysis is based on the calculation of cumulative conditional probabilities. The survival rate will be calculated using the following formula:

$$S_{t(i)} = \prod_{t(i-1)<t(i)} S_{\frac{t(i)}{t(i-1)}} = \prod_{t(i-1)<t(i)} 1 - \frac{D_i}{N_i}$$

With:

- $S_{t(i)}$, the probability of having the implant in place so far;$t_{(i)}$
- $S_{\frac{t(i)}{t(i-1)}}$, the probability of still having the implant in place knowing that the implant was in place at ;$t_{(i+1)}$ $t_{(i)}$
- $D_i = 1 - N_{s(i)}$, the number of subjects who required removal or change of implant, observed at the time;$t_{(i)}$
- $N_{S(i)}$, the number of subjects with their implant still in place at the time observed at the time;$t_{(i)}$
- $N_i = N_{S(i-1)} - D_i - C_i$, the number of subjects at risk of implant removal or change, observed at time;$t_{(i)}$
- C_i, the number of censored subjects (lost to follow-up, deceased, having left the study) observed between time and ;$t_{(i-1)}t_{(i)}$

D. DEGREES OF SIGNIFICANCE AND STRENGTH OF THE CI

The objectives of this CI are descriptive regarding the use of SAGITTA® EVL-R rods; Thus, no statistical test is performed to compare the results with a comparator device.

E. SAMPLE SIZE

According to the available data, 120 SAGITTA® EVL R revision rods were implanted at the Rouen University Hospital – Charles Nicolle Hospital between 01/01/2016 and 31/12/2018. The final sample size will reflect the current practice of the selected investigation center based on the patient base as observed over the inclusion period and meeting the selection criteria.
The total sample size will depend on the number of subjects who do not object to participation and data collection, the number of subjects who have died and have been lost to follow-up.

F. LEARNING CURVE AND DATA CONSIDERATION

No learning curve will be considered due to the retrospective nature (previously implanted subjects), the experience of the surgeon who implanted the patients, and the number of annual rod insertions in the selected investigation centers. All patients who meet the inclusion criteria and do not object to participation and data collection will be included.

G. HF PASS/FAIL CRITERIA

The nature of HF is observational and its objectives are only descriptive, no statistical criterion defines the success or failure of the investigation.

H. INTERIM ANALYSES AND DISCONTINUATION OF CI FROM A STATISTICAL POINT OF VIEW

i. INTERIM ANALYSES

No interim analysis is envisaged because the prospective part of the study is limited to the patient's only and last follow-up visit.

ii. CESSATION OF HF BASED ON STATISTICAL CRITERIA

The nature of HF is observational, ambispective, and since its objectives are only descriptive, there is no statistical criterion that defines its early termination.

I. ACCOUNTING FOR BIASES

i. STATISTICAL BIAS

The statistical biases usually limited by the use of a comparator arm with a randomized distribution for each arm and double-blind conduct cannot be implemented for this HF due to its ambispective non-interventional non-comparative and therefore non-randomized, open-label nature.
However, the subjects included in this study will constitute an ongoing and exhaustive series.

ii. CONFOUNDING FACTORS

Medical and surgical history, as well as intercurrent pathologies, or any other factor such as age, weight, etc. and that may impact clinical outcomes will also be considered during multivariate analysis.

iii. SPECIFYING SUBGROUPS FOR ANALYSIS

Subjects can optionally be classified by assembly for analysis.
In addition, an analysis according to etiology (revision, revision with reconstruction) is envisaged. For this purpose, the CCAM codes related to the surgical procedure will be recovered.

iv. CHECKING AND ADJUSTING ERROR PROBABILITIES

The purpose of this clinical investigation is to describe current practice, with descriptive objectives for the use of SAGITTA EVL-R rods; Thus, no statistical tests or adjustments to these tests are performed.

J. HANDLING MISSING, UNUSED OR ERRONEOUS DATA, INCLUDING ABANDONMENTS AND WITHDRAWALS

i. DATA INCLUSION METHODOLOGY

The simple imputation replacement method can be used if necessary: replace the missing data with a plausible value (mean/median of the variable for the follow-up under consideration, for example) if less than 10% of the data are missing..

ii. EXPLORATORY AND SENSITIVITY ANALYSES

The purpose of this clinical investigation is to describe current practice, the objectives being descriptive concerning the use of SAGITTA® EVL-R rods; Thus, an exploratory analysis and/or sensitivity analysis may be carried out but will not be mandatory.

K. PROCEDURES FOR REPORTING ANY DEVIATIONS FROM THE ORIGINAL STATISTICAL PLAN

All deviations observed and/or achieved from the statistical plan mentioned above will be presented, justified and their impact analyzed, in the study report.

L. IN THE CASE OF MULTICENTRE INVESTIGATIONS, MINIMUM AND MAXIMUM NUMBER OF SUBJECTS TO BE INCLUDED FOR EACH CENTRE

Not applicable, CI is monocentric.

8. DATA MANAGEMENT

A. DATA ENTRY AND COLLECTION METHODS

The data will be collected from the patient records in the paper CRF directly by the investigator. The CRF data will then be entered into a database by a representative of the sponsor.
In accordance with applicable laws and regulations, data confidentiality will be ensured by appropriate security means:
• Patients will be identified in the CRF and the clinical database by a numerical identifier combining the number of the center and the number of the patient. Only the centres will keep a confidential list of included patients that will link the patient's ID to their identity.
• No personal data will be collected.

B. PROCEDURES FOR EXAMINING DATA, CLEANING UP DATABASES, AND ISSUING AND RESOLVING DATA QUERIES

The data will be collected from the CRFs into the study database directly in the investigator center during a monitoring visit. At a minimum, the date of collection of the CRF or the request and the identification number of the subject will be reported. A form collecting the CRFs entered will be signed by the monitor and countersigned by the investigator to attest to the integrity of the data entered.
Data entry may result in requests for clarification called "queries", to which the investigator will respond by confirming or modifying the data concerned. These requests for clarification are annexed to the CRF at the investigator and the sponsor.

C. PROCEDURES FOR VERIFYING, VALIDATING AND SECURING ELECTRONIC CLINICAL DATA SYSTEMS

i. GENERAL

In order to ensure the verification, validation and security of the electronic systems generating, or managing the clinical data entered into the above-mentioned database, SERF has put in place the following elements:

- Update monitoring system;
- Host proxy system;
- Individual workstations equipped with anti-virus software with automatic updates;
- Locking, password access and encryption of mobile workstation partitions;
- Triple level of backups: real-time synchronization of virtual machines, backup to a production server and daily encryption and transfer to a backup hosting site;
- Secure erasure of SERF disks prior to disposal by physical destruction;
- Network protected by a security box (VPN).

ii. SPECIFIC

Backups are encrypted by private keys, and access to the study's production server is protected by NTFS rights.
Clinical data is hosted on the same server as the rest of the SERF information system, but accessible only by the sponsor's clinical department staff and hierarchy.
Access to the clinical data entry system is through username/password authentication. Passwords are controlled for complexity and should be changed regularly. 5 unsuccessful attempts block access to the account.
Any connection to the system and any changes in clinical data are recorded for the duration of the study.

D. MAINTAINING CONFIDENTIALITY AND RESPECTING THE PRIVACY OF SUBJECTS

The confidentiality of the subjects will be ensured by pseudonymization using a patient number (with 3 incremented digits) assigned to the person who is willing to participate in the research and communicated on all the documents necessary for the research; or by erasing by appropriate means nominative data on copies of source documents, intended for research documentation.

E. DATA RETENTION

The investigator should maintain all study documents in accordance with Good Clinical Practice and regulations. The records will be kept until SERF authorizes their destruction. If the investigator declines this responsibility, the retention of records will be assigned to an individual who accepts this responsibility. In the event of a transfer of responsibility or place of storage, the sponsor must be informed in writing.

Data archiving after the completion of the study will be performed in accordance with SERF procedures for archiving clinical data from an investigation. The database that gave rise to the statistical analysis will also be locked and archived by the person responsible for the analysis (paper or computer).

F. RETENTION PERIOD

In accordance with Annex XV Chapter 3.3 of Regulation (EU) 2017/745 on medical devices, which sets out the retention period by the sponsor and the investigator of the documents and data, the data retention period shall be 15 years after the end of the investigation.

G. OTHER ASPECTS OF CLINICAL QUALITY ASSURANCE

In accordance with the General Data Protection Regulation, an impact assessment of the study will be carried out by SERF; The study will also be registered in a specific register.
In addition, as part of the implementation of its quality management system, an internal SERF auditor may be required to carry out an audit of the investigating centre. This audit will ensure compliance with the procedures envisaged by this protocol during the conduct of the investigation.
The health authorities may also be required to carry out audit activities of the investigating centre.

9. AMENDMENTS TO THE CLINICAL INVESTIGATION PLAN

All amendments to the protocol will be made known to all investigators involved in the research. Amendments will be notified to the competent authorities and the Ethics Committee in accordance with the regulations in force.
Investigators sign each amendment prior to implementation and after approval by any authority that previously approved the protocol. Finally, the investigators undertake to respect the content.
Any amendment that modifies the coverage of the subjects or the benefits, risks and constraints of research will be the subject of a new information letter and the signing of a non-opposition form, the collection of which follows the same procedure as that mentioned in the chapter 13.

10. DEVIATIONS FROM THE CLINICAL INVESTIGATION PLAN

A. STATEMENT THAT THE INVESTIGATOR IS NOT AUTHORIZED TO DEVIATE FROM THE ICP

The investigator is not allowed to deviate from the Clinical Investigation Plan, except in the context of protecting the subject's rights, safety, and well-being under emergency conditions. In this case, any deviations must be documented and forwarded to the sponsor as soon as possible.

B. PROCEDURE FOR RECORDING, REPORTING AND GAP ANALYSIS IN RELATION TO THE CIP

This study will be carried out in accordance with the requirements of the protocol. Any deviation from these criteria will be justified and carefully documented. The deviation will be considered a major deviation and considered for the final analysis of the study if it relates to any of the following:

- Information and consent procedure;
- Inclusion/non-inclusion criteria.
- Follow-up visit not carried out;

- Primary outcome.

Major deviations from the protocol will be recorded and will be mentioned in the final report.
In the event of a discrepancy in the subject's information or consent, the investigator must immediately correct the deviation by following the steps outlined in Chapter 13.
In all cases, the investigator should justify the deviation during a monitoring visit, by means of the appropriate documentation.

C. NOTIFICATION REQUIREMENTS AND DEADLINES

Notification of a deviation from the protocol must be communicated to the sponsor as soon as possible via letter, email or any other means of communication containing the justification and documentation relating to the deviation.

D. CORRECTIVE AND PREVENTIVE ACTIONS AND CRITERIA FOR DISQUALIFICATION OF THE PRINCIPAL INVESTIGATOR

At the first major deviation, intentional or unintentional - except for cases of protection of patients' rights, safety and well-being - observed by the sponsor, a reminder of the procedures to be followed will be made to the investigator and/or members of the investigating team.

11. DEVICE ACCOUNTING

Article R1121-3-1 of the Public Health Code only provides for the free supply of devices in cases of interventional research. As the study is carried out after obtaining the CE marking and the device is used for its intended use, the requirements of this chapter do not apply.

A. ACCOUNTING PROCEDURE

Not applicable.

B. PROCEDURES AND INSTRUCTIONS FOR THE RETURN OF POTENTIALLY HAZARDOUS DEVICES

Not applicable.

12. DECLARATION OF CONFORMITY

A. DECLARATION OF HELSINKI

The study will be conducted in accordance with the ethical principles that are set out in the Declaration of Helsinki.

B. Compliance with ISO 14155 NF and national and/or regional regulations

The study will be conducted in accordance with the International Conference on Harmonization for Good Clinical Practice (ICH/GCP) transposed into the ISO 14155:2020 Standard.
It will be carried out in accordance with applicable European, national and local regulatory requirements.
The information of subjects and the processing of data will be carried out in accordance with Regulation 2017/745 on medical devices, the Data Protection Act of 6 January 1978 in its latest version in force and the General Data Protection Regulation (EU) 2016/679 of 27 April 2016.

In accordance with the regulations, a data controller is the referent:

Nathalie Trétout, the data controller

Email: **rgpd@serf.fr** or n.tretout@menix.fr

C. Approvals/Favourable Opinions Required

The investigation is considered a 4.1 case study according to the French national classifications from the ANSM. Consequently, an application must be submitted to a CPP and the ANSM.
Validation by a CPP and compliance with the MR001 reference methodology are required prior to the start of the study.

D. Additional Requirements

Any additional requirements on the part of the Committee for the Protection of Persons or the ANSM will be respected and implemented before the start of the investigation.

E. Insurance

This study is a non-interventional post-marketing study. As such, the sponsor of the study, SERF, in accordance with the legislation in force, is not obliged to take out specific insurance for research.

F. Investigative funding

The financing plan for the study is drawn up separately from the protocol.

13. PROCESS FOR OBTAINING NON-OPPOSITION

A. General process for obtaining informed consent

Informed consent is mandatory for studies meeting the Reference Methodology MR-001.

Prior to the first inclusion and in compliance with good clinical practices, the study investigator(s) are trained by the sponsor in the patient information process as well as in the collection of informed consent during the study set-up visit.

During a patient's visit planned as part of the systematic follow-up of hip replacements, the investigator offers to participate in HF if he or she meets the selection criteria.

To do this, the investigator provides the information relating to the oral test and gives the information letter (see Appendix 3). The investigator also answers any questions he may have. After the subject has been able to consider all the information and has been given the newsletter, and after the reflection period that has been given to him, he then has the choice to give his consent to his participation in the study and the collection of his data. The patient will be able to give consent from the moment he has received all the information until his next follow-up visit.

If the investigator expresses his or her consent, he or she obtains the consent in the form provided (see Appendix 3), of which he or she keeps the copy that he or she has imperatively dated and signed, in the investigator's binder, *and also gives a copy to the subject*. The patient is then included in the HF and considered as a "subject" participating in the HF. *The patient has time to think about it after the presentation of the study to give his or her agreement or not to his participation.*

A copy of the newsletter is given to the subject.

B. SPECIAL CASES

No special case is envisaged because the study is carried out in routine care.

14. ADVERSE EVENTS, ADVERSE DEVICE REACTIONS, AND DEVICE DEFECTS

The term 'complications' used by the investigators includes the different definitions of event, adverse reaction, expected or not, serious or not, and dysfunction.

A. DEFINITIONS OF ADVERSE EVENTS AND ADVERSE REACTIONS TO THE DEVICE

Adverse event (AE): any adverse event, unintentional illness or injury, or adverse clinical signs, including an abnormal laboratory finding, in participants, users, and others, in the course of a clinical investigation, whether or not related to the device under clinical investigation
Serious Adverse Event (SAE): any adverse event that resulted in:

- Death.
- A serious deterioration in the participant's state of health, which is the cause:
  - a life-threatening illness or injury, or
  - a permanent impairment in anatomical structure or function, or
  - hospitalization or prolongation of the patient's hospitalization, or
  - a medical or surgical procedure to prevent any life-threatening illness or injury or permanent impairment of anatomical structure or function, or
  - of a chronic disease.
- Fetal distress, death of the fetus, congenital physical or mental impairment, or birth defect.

A planned hospitalization due to a pre-existing condition or a procedure required by the clinical investigation plan, without a serious deterioration in health, is not considered a serious adverse event. As a reminder, the definitions applicable in the context of medical device vigilance (corresponding to post-marketing surveillance of medical devices).
Serious incident: any incident that has directly or indirectly caused, likely to have resulted or likely to result in:

- The death of a patient, user, or any other person,
- A serious deterioration, temporary or permanent, in the state of health of a patient, a user or any other person,

A serious threat to public health.
Serious Adverse Device Reaction (SAE): An adverse reaction to the device that results in one of the characteristic consequences of a serious adverse event.
Unexpected serious adverse reaction of the device (EIGID): a serious adverse reaction of the device whose nature, impact, severity and consequences have not been identified in the current risk assessment.

B. DEFINITION OF DEFECTS AND MALFUNCTIONS OF THE DEVICE

Malfunction: Failure of the medical device under investigation to function in accordance with its intended use when used in accordance with the instructions, clinical investigation plan, or investigator's brochure.

Device Defect: Any defect in the identity, quality, durability, reliability, safety, or performance of a device under investigation, including any malfunction, misuse, or defect in the information provided by the manufacturer.

Incident: any malfunction or alteration of the characteristics or performance of a device made available on the market, including an error in use due to ergonomic features, as well as any defect in the information provided by the manufacturer and any undesirable side effects.

Serious incident: any incident that has directly or indirectly caused, likely to have resulted or likely to result in:
- The death of a patient, user, or any other person,
- A serious deterioration, temporary or permanent, in the state of health of a patient, a user or any other person,
- A serious threat to public health.

C. EVENTS, SERIOUS ADVERSE REACTIONS, SERIOUS ADVERSE REACTIONS TO THE DEVICE, SERIOUS UNEXPECTED ADVERSE REACTIONS TO THE DEVICE, PUBLIC HEALTH THREATS

See Chapter B.

D. LIST OF UNDESIRABLE REACTIONS THAT MAY NOT BE REPORTED

Only events that are not causally related (see below) to the device being investigated, comparator, or investigation procedure may not be reported to SERF.
Causality is determined by the definitions below:

Unbound	- No temporal link, - Does not follow a known and biologically improbable DM reaction pattern, - Interruption/reduction and reintroduction does not affect SAE, - Site or organ not affected by the MD or procedure, - Other cause identified, - SAE not related to a misdiagnosis result by the MD in HF.
Possible	Weak link but cannot be totally excluded (includes cases for which causality cannot be assessed or no information could be obtained)
Probable	The link seems relevant and/or no other cause can explain the SAE
Causal link	- Temporal link, - Known side effect for this category of MD or this type of procedure,

	- Known DM reaction pattern, - Site or organ affected by the MD or procedure, - Interruption/reduction and reintroduction affects SAE, - Possible other causes have been excluded, - SAE due to a user error, - SAEs related to a misdiagnosis result by the MD in HF.

In all other cases:

- Any **serious adverse event** (SAE) with a proven or reasonably foreseeable causal link;
- Any **defect or malfunction or incident** of a device that could have resulted in a SAE in the absence of appropriate measures or intervention, or if the circumstances had been less favourable;
- Any **new information** concerning the 2 previous points,

The investigator reports the complication to the sponsor according to the deadlines and procedures provided for below.

E. Reporting Deadlines

Event	**MDR Article**	**Method of notification**	**Time limit for notification to the sponsor**
Unrelated AE	NA	In the case report book	No immediate notification
SAEs with a plausible or proven causal link **to** risk of death/serious illness or injury	Art.80	Declaration form	Immediate notification and within a maximum of 3 **days**
SAEs with a plausible or proven causal relationship **with no** risk of death/serious illness or injury	Art.80	Declaration form	
Follow-up of any previously reported events	Art.80	Declaration form	
Serious incident	Arts 87 to 90	Declaration form	

F. Details of the Adverse Event Reporting Process

For unrelated adverse events (see Chapter 14.D), the investigator enters the complication directly in the report form.
In all other cases (adverse effects), the investigator completes the dedicated form (see Appendix 4) present in the patient's observation form, taking care to transmit all the requested information relating to the complication. The investigator forwards the form to the person in charge of the study at SERF, whose contact details are specified in the chapter I below and within the time limits (see above). The form can be sent either by fax or by email (form scanned legibly).
Any information concerning the evolution (resolution, worsening of the patient's condition, etc.) of a reported event must also be sent to the person in charge of the study at SERF via the complication declaration form.

If, for any reason, an **adverse reaction** (of any kind) is identified during monitoring and has not been reported to SERF, the adverse event reporting form will be completed from the patient's medical record or case report form if the information is included.

SERF will record on the database of each study the adverse events of the patients participating in the study.

G. Details of the Device Defect Reporting Process

This study is an observational study. The reports of defects in the device under study were made by each centre according to their usual procedure.

However, as part of the medium-term follow-up (minimum 4 years postoperative years) of this HF, any defect in the device must be communicated to SERF by the investigator who fills in the dedicated form present in the patient's observation form. The investigator sends the form to the person in charge of the study at SERF, whose contact details are specified in Chapter I. The form can be sent either by fax or by email (form scanned legibly).

H. List of foreseeable adverse events and expected adverse reactions of the device

Known adverse events and reactions related to hip replacement and SAGITTA® EVL R implantation are listed in Chapter 4.
The respective incidences and means of treatment of these complications are known and listed in the clinical evaluation of the device, available upon request.

I. Emergency contact information

All serious or non-serious and/or unexpected adverse events and effects related to the device must be reported via the dedicated form, contained in the CRF, to the person in charge of the investigation within the SERF clinical department:

Lydie BONNEVAY
Fax: **04.72.02.19.18**
Email: **clinical@serf.fr**

J. Information related to the data monitoring committee if established

Not applicable, no data monitoring committee has been established as part of this investigation due to its observational nature.

15. VULNERABLE POPULATION

A. Description of the vulnerable population to be included

No vulnerable populations are planned to be included for this clinical investigation.

B. Description of the screening process to identify and protect vulnerable populations

No vulnerable populations are planned to be included for this clinical investigation.

C. DESCRIPTION OF THE SPECIFIC PROCESS FOR OBTAINING INFORMED CONSENT

No vulnerable populations are planned to be included for this clinical investigation.

D. DESCRIPTION OF THE SPECIFIC RESPONSIBILITY OF THE ETHICS COMMITTEE

Not applicable.

E. DESCRIPTION OF ANY MEDICAL CARE PROVIDED TO SUBJECTS AFTER HF IS COMPLETED

Refer to Chapter 6.D.

16. PREMATURE TERMINATION OR SUSPENSION OF THE CI

A. CRITERIA AND PROVISIONS FOR PREMATURE TERMINATION OR SUSPENSION OF CLINICAL INVESTIGATION FOR THE ENTIRE INVESTIGATION OR FOR ONE OR MORE SITES

i. FOR THE ENTIRE INVESTIGATION

For reasons of safety of the subjects, in particular in the event of suspension of CE marking for a device, resulting in an unacceptable benefit/risk balance, the investigation will be closed prematurely.

ii. FOR ONE OR MORE CENTRES

- At the initiative of the center or the investigator:
  - Change of the investigating team that does not allow the continuation of the study and the follow-up of the subjects;
  - Force majeure (death of the investigator, climatic incidents, etc.)

In this case, the investigator will forward all relevant documentation to SERF.

- At the initiative of the promoter:
  - Study progress not respected.
  - Major deviations from protocol and/or regulations and good clinical practices.
  - Inability of the investigator to include subjects according to the planned schedule.
  - Lack of patient consent.

B. CRITERIA FOR SETTING UP AND BREAKING THE BLINDING CODE DUE TO SUSPENSION OR EARLY TERMINATION OF IC

Not applicable, the IC is conducted in open-label.

C. SUBJECT TRACKING REQUIREMENT

Any subject with an adverse event should be followed until resolution or stabilization of the event.
In all cases (exclusion of the patient from the investigation, premature termination of HF, withdrawal of consent, etc.), the investigator continues to monitor the subject and provide appropriate medical care for his condition.

17. PUBLICATION POLICY

A. REGISTRATION OF THE STUDY IN A PUBLICLY AVAILABLE DATABASE

This clinical investigation will be registered on the EUDAMED database when it is functional, as well as on the public database (ClinicalTrials.gov).

B. STATEMENT THAT THE RESULTS WILL BE PUBLICLY AVAILABLE

This study may be published. If this is the case, it is envisaged that the preparation of the publication(s) will be carried out by the investigators.
Nevertheless, the results of this study are intended for SERF for the monitoring of its medical devices. In accordance with the legislation in force, it will be possible for the subjects participating in the study to be communicated the results of the investigation to them. The results will be published on the EUDAMED database when it is functional.

C. STATEMENT OF THE CONDITIONS UNDER WHICH CI RESULTS WILL BE PUBLISHED

If there is a publication of the results, all information provided to the investigator by SERF is strictly confidential. The investigator agrees to use the information to perform the investigation but not for any other purpose without the written permission of SERF. It is understood that it is mandatory to provide SERF with all the data obtained during the investigation.
The information obtained from the CI may be used for further development and may be disclosed to health authorities, other investigators and SERF's designated partners as needed.
These publications will be developed and the list of authors will be determined in accordance with the Harvard Guidelines which state that each author must have a substantial and direct intellectual contribution to the work carried out (Authorship Guidelines):

http://www.hms.harvard.edu/fa/guide

With the recommendations of the ICMJE (International Committee of Medical Journal Editors) which indicate that each author must:
1) have made a significant contribution to the conception and design of the study, to the collection of data, or to the analysis, or interpretation of the data,
2) have participated in the writing of the article or in its proofreading, and
3) have given their consent for publication.

The main clinical results, intermediate and final, may be reported at the meetings of the national learned societies and published in the most appropriate international journal. Authors will include the principal investigators, the project methodologist, members of the scientific council, and the local investigators most involved in the project. All investigators will be reported in the list of investigators of the investigation.
In addition, the promoter and the funder(s) of the study will be mentioned in the publications relating to this study.

18. BIBLIOGRAPHY

APPENDIX 1: LIST AND QUALIFICATIONS OF INVESTIGATORS

Name and surname	Function	Department and hospital	Address	Email	Telephone	RPPS Number
Prof. DUJARDIN Franck	Orthopedic Surgeon	Rouen University Hospital Charles Nicolle Hospital	37 boulevard Gambetta 76000 Rouen	franck.dujardin@chu-rouen.fr	0232888007	10 001 915 734

APPENDIX 2: PRODUCT INSTRUCTION LEAFLET UNDER REVIEW

APPENDIX 3: INFORMATION LETTER ON

APPENDIX 4: SRIA-CIDT REPORTING FORM

APPENDIX 5: HARRIS HIP SCORE

PAIN		
No	44	☐
Light, occasional, no limitation of activities	40	☐
Moderate, no effect on daily activities, may occur after unusual activity, use of minor analgesics	30	☐
Moderate, tolerable, some limitations in ordinary activities or at work, taking stronger painkillers	20	☐
Severe pain, severe limitation of activities	10	☐
Totally disabled, permanent pain even in bed	0	☐

LIMP		
No	11	☐
Light	8	☐
Moderate	5	☐
Severe or unable to walk	0	☐

SUPPORT		
None	11	☐
Rod for long walks	7	☐
Cane most of the time	5	☐
A crutch/cane	3	☐
Two rods	2	☐
Two canes or unable to walk	0	☐

MARKET SCOPE		
Unlimited	11	☐
30 minutes	8	☐
10 – 15 minutes	5	☐
In the house	2	☐
From bed to chair	0	☐

ACTIVITIES (shoes, socks)		
With ease	4	☐
With difficulties	2	☐
Total incapacity	0	☐

STAIRS		
Normal, without using the ramp	4	☐
Normal, using the ramp	2	☐
Possible but unorthodox	1	☐
Impossible	0	☐

TRANSPORT PUBLIC		
Able to use transport	1	☐
Unable to use transport	0	☐

SEATED		
Comfortably in a chair for 1 hour	5	☐
On a chair for 30 minutes	3	☐
Unable to sit comfortably in a chair	0	☐

ABSENCE OF VICIOUS ATTITUDES (4 "Yes" = 4 points; Less than 4 "Yes" = 0 points)				
< 30° flessum	Yes	☐	No	☐
< 10° adductum	Yes	☐	No	☐
< 10° internal rotation	Yes	☐	No	☐
Length inequality< 3.2 cm	Yes	☐	No	☐

MOBILITY (* Standard amplitude)	300° - 211°	210° - 161°	160° - 101°	100° - 61°	61° - 30°	30° - 0°
Points	5	4	3	2	1	0
Bending (*140°)	☐	☐	☐	☐	☐	☐
Abduction (*40°)	☐	☐	☐	☐	☐	☐
Supply (*40°)	☐	☐	☐	☐	☐	☐
Belch. External (*40°)	☐	☐	☐	☐	☐	☐
Belch. Internal (*40°)	☐	☐	☐	☐	☐	☐

APPENDIX 6: FORGOTTEN HIP SCORE – SHO12

	1pt	*2pts*	*3pts*	*4pts*	*5pts*
Are you aware of your hip...	Never	Hardly ever	Rarely	Sometimes	Often
1. … in your bed at night?	☐	☐	☐	☐	☐
2. … When you sit in a chair for more than an hour?	☐	☐	☐	☐	☐
3. … When you walk for more than 15 minutes?	☐	☐	☐	☐	☐
4. … when you take a bath or shower?	☐	☐	☐	☐	☐
5. … When you travel by car?	☐	☐	☐	☐	☐
6. … When you climb the steps of a staircase?	☐	☐	☐	☐	☐
7. … When you walk on uneven ground?	☐	☐	☐	☐	☐
8. … When you get up from a low sitting position?	☐	☐	☐	☐	☐
9. … When you stand for a long time?	☐	☐	☐	☐	☐
10.… When you do housework or gardening?	☐	☐	☐	☐	☐
11.… When you are walking or hiking?	☐	☐	☐	☐	☐
12.… when you practice your favorite sport?	☐	☐	☐	☐	☐
12b... during your sexual intercourse?	☐	☐	☐	☐	☐

APPENDIX 7: ENGH SCORE

Fixation			
Appearance of a porous border	☐ Extensive≥ 50% −5 pts	☐ Indeterminate 0 pt	☐ None +5 pts
Bone Bridges	☐ Absence −2.5 pts	☐ Indeterminate 0 pt	☐ Presence +5 pts
Score	……./ 10		
Stability			
Appearance of a smooth border	☐ Extensive≥ 50% −3.5 pts	☐ Indeterminate 0 pt	☐ None +5 pts
Pedestal if distal part not locked	☐ Presence −3.5 pts	☐ Indeterminate 0 pt	☐ Absence +2.5 pts
Calcar modification	☐ Hypertrophy −4 pts	☐ Indeterminate 0 pt	☐ Atrophy +3 pts
Edging	☐ Presence −2.5 pts	☐ Indeterminate 0 pt	☐ Absence +2.5 pts
Migration >5mm	☐ Presence − 5 pts	☐ Indeterminate 0 pt	☐ Absence +3 pts
Appearance of metal particles	☐ Presence − 5 pts	☐ Indeterminate 0 pt	☐ No +1 pt
Score	……./ 17		
Total Score (Fixation + Stability) .. ……../ 27			