Power Knee Mainstream - Clinical Investigation Instance

[redacted]

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Basic Mobility and Balance Performance of Low Active Transfemoral Prosthesis Users With [redacted] a powered prosthetic knee

Power Knee

CONFIDENTIAL DOCUMENT

Document Sign-off Information			
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See [redacted] for Sponsor and Principal Investigator details.

Sponsor's Statement: I have reviewed and approved this CII in its entirety and within context of the CIM identified above, and agree to sponsor its implementation

Sponsor:	Date of Signature:
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Principal Investigator's Statement: I have reviewed and approved this CII in its entirety and within context of the CIM identified above, and agree to follow carry out its implementation

Principal Investigator:	Date of Signature:
Electronical Approval of Document, front page [redacted]	*Electronical Approval of Document, front page*

[redacted]

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How to Refer to This Document

[0] CII2020111613, [redacted].

• Summary

Title: *Basic mobility and balance performance of low active transfemoral prosthesis users with* [redacted] *(a powered microprocessor-controlled knee prosthesis).*

Prospective case series design.

This Clinical Investigation Case fits within the broader protocol detailed in [redacted] previously approved by **Vísindasiðanefnd** with approval number **VSN-19-083 [1]**.

Device(s) being tested:	Investigational device: [redacted] – a pre-market device Comparator device: Subjects prescribed prosthetic knee – CE marked product
Subjects recruited:	6 subjects 6 CPO subjects
Inclusion criteria:	50Kg< body weight < 116Kg Cognitive ability to understand all instructions and questionnaires in the study; K1-K2 unilateral transfemoral amputees Allows for 37mm knee center height to dome of pyramid alignment Age ≥ 18 years Willing and able to participate in the study and follow the protocol Comfortable and stable socket fit (5 or over on the SFCS)
Exclusion criteria:	Users with cognitive impairment Users aged <18y Bilateral amputees Users with stump pain affecting their functional mobility Users with socket problems Users with co-morbidities in the contra-lateral limb, which significantly affect their functional mobility

Objectives:	The primary objective of this clinical investigation is to evaluate if the safety and performance of the investigational device for low active users is comparable to their prescribed device. Additionally to evaluate the efficacy of the investigational device in the intended population with regards to specific gait functions, usability and technical features. Part of this investigation is done as part of product validation activities
Instruments and equipment:	**Instruments**: TUG test, 2MWT, In house user questionnaire, 4 square step test (FSST), AMPro, Socket fit comfort score, Stroop test, LCI(modified), socket fit comfort score, CPO usability questionnaire. **Equipment**: Microgate timing gates, video camera, IPad, Investigational device + Components, Comparator, 2 cones, Measuring tape, Chair with armrests, Office chair on wheels, Chair without armrests (typical household chair), Barstool, Stopwatch / smartphone, 4 crutches, Video Display, Össur Logic.
Procedures: a	Participants will be consented, and all tests will take place at the Össur Motion lab Grjóthals 1-5, 110 Reykjavik. There are **two** scheduled study events. At the initial visit, the first study event, for each subject a researcher qualified to obtain informed consent will seat the subject and proceed as described in chapter **13.7 Informed consent** in [redacted]. Prior to fitting the subject will be asked to provide feedback on the current prosthesis, by filling in a questionnaire **and perform AMPro, LCI (modified), TUG test, 2MWT and other validation activities (stand to sit, sit to stand, level ground, stair and ramp walking), as applicable**. The users will be fitted within the standard methods of prosthetic fitting, alignment, introduction, training and walking on various terrain. After initial fitting subjects will carry out **validation tasks (stand to sit, sit to stand tasks, level ground walking at different speeds, stair and ramp walking), stroop test (cognitive loading) and FSST** on the investigational device, after which they will answer an in-house questionnaire to provide feedback. The second event will be 1-14 days later, subjects will be fitted with the investigational device and asked to perform the **TUG, 2MWT** and any validation tasks that could not be completed at visit 1 on the investigational device. If for some reason all tasks cannot be completed at visit 1 and 2, a third visit may be added. Subjects will not wear the device home between visits. The total time period required to implement the clinical investigation is expected to be **4 weeks**. Each individual subject is expected to participate in the clinical investigation for **2 weeks Procedures for CPO subjects:** CPO subjects will come for 1 visit. They will carry out the following tasks and provide feedback through a CPO usability questionnaire:

	Build device in prosthetic system Align device in prosthetic system Configure device parameters Check Battery Status Turn ON and Turn OFF Recognize feedback from the device Charging Battery Pack Swap

Changes from Previous Revision

Changes for Revision 1.00

Initial release.

Changes for Revision 2.00

Activity level changed to include K1 and K2 users.

Abbreviations

2MWT	Two minute walking test
ADE	Adverse Device Effect
AE	Adverse Event
AMPro	Amputee Mobility Predictor
CIB	(Clinical) Investigator Brochure
CII	Clinical Investigation Instance
CIM	Clinical Investigation Master Protocol
CPO	Certified Prosthetist and Orthotist
DUT	Device Under Test
FMEA	Failure Mode Effect Analysis
FSST	Four Square Step Test
HAD	Hazard Analysis Document
ICF	Informed Consent Form
IDMF	Investigational Device Management Form
IFU	Instructions For Use
IRB	Independent Review Board
LCI	Locomotion Capabilities Index
NA	Not Applicable
PI	Principle Investigator
PSCS	Prosthetic socket fit comfort score
TUG	Timed Up and Go
VSN	Vísindasiðanefnd (Icelandic Research Ethics committee)

• Investigational Device

Exoskeletal prosthetic devices are by their nature non-invasive. They are non-sterile, reusable, single user devices that are part of a prosthetic system consisting of e.g. a liner, socket, lock, adapter, pylon, foot module, foot cover and aesthetic finish. The prosthetic medical device will neither provide any benefits nor has any intended purpose unless being used as a part of such a system.

The device is not intended to be in direct contact with body fluids and only intermittently in contact with the skin.

The device under investigation (the Investigational Device) is a **non-CE-marked** medical device in development, [redacted]

The [redacted] is classified as Class IIa device per rule 9.

[redacted]

[redacted] Knee is a micro-controller controlled battery-operated motorized knee prosthesis. [redacted] is composed of four main devices:

- a motorized knee prosthesis;
- a detachable battery pack;
- a wall-mount, medical-grade, off-the-shelf power supply for charging the battery pack; and
- a configuration software.

Using the on-board motor, the knee generates motion and torque levels coherent with typical human walking gait, including locomotor and non-locomotor locomotion activities. Motor operation is controlled from an array of sensors, combined with advanced gait recognition and control algorithm, which are used to control the behaviour of the knee at all times, through motor actions.

[redacted] prosthetic device also includes a wireless communication channel, allowing for connection with a mobile device where the configuration software is deployed. Configuration software allows for customization of the prosthesis behaviour to the specifics of the end-user gait, such as body weight, segment lengths and personal preferences.

[redacted] is equipped with a battery pack that can both be detached from the device for recharge or charged while connected to the device. Battery pack recharge is performed by the charge circuit integrated to the battery pack and powered using a medical-grade, wall mount, off-the-shelf power supply. Multiple battery packs can be used with the same [redacted] device, allowing to extend the device autonomy.

[redacted] is a non-invasive device. The device does not have applied part and connect to the amputee residual limb through standard interface technologies, such as pin or suction sockets.

[redacted] is a modular prosthetic component. It is meant at being included in a complete transfemoral prosthetic leg. It cannot be used on its own to perform it medical purpose.

[redacted] is designed to be used continuously by the end-user, subject to the typical constraints related to the use of a lower-limb prosthetic device, such as doffing during night time and general maintenance and care.

[redacted] does not incorporate a medicinal substance.

[redacted] does not incorporate viable materials of animal origin.

[redacted] does not incorporate tissues and/or blood derivatives of human origin.

[redacted] is a programmable electrical medical system (pems). Its essential performance is defined as the structural support replacing a lost leg. Loss of this structural support function would not allow the device to fulfill its minimal performance and safety requirements for its intended use. Even if the pems related operations/functions are lost the basic structural support function is not lost and the design allows the user to continue walking safely but with a reduced set of performance and functional features.

At the current developmental stage structural and basic functional tests have been done for the purpose of structural and operational safety of the investigational device. For further development and verifications of the adaptability of the system to the individuals' needs, preferences and performance abilities observational testing involving users of the intended user profile is required and will help to verify the efficacy of the design.

[redacted] is a non-invasive, single patient, reusable system. The device is not intended to be in direct contact with body fluids and only intermittently in contact with the skin. Training requirements for subjects and procedures relating to fitting and use of the device will for all general purposes be similar to the training and procedures required for using a CE-marked device of a similar type.

Intended Patient Population

User Population:	Lower-limb Amputees;
Amputation Level:	Trans-femoral and knee disarticulated amputations;
Activity Level:	K1-K2
Impact Level:	Low to moderate impact levels
User Weight:	Lower than 116kg;
Connection System:	Össur pyramidal connection system.

Medical Conditions to be treated

Unilateral transfemoral / knee disarticulation amputation

Targeted Medical Indications

Amputation or lack of a leg at or above the knee level for any medical or congenital reason.

Intended Use

[redacted]

Locomotion tasks

[redacted]

[redacted]

Operational Environment

[redacted]

Product Configuration

The product is intended to be used with Ossur's standard prosthetic components. It will be configured with standard proximal and distal connectors, allowing use with most commonly encountered socket technologies and shank replacement products[redacted]

[redacted]

In the initial training provided by a trained CPO, the user capacity should be assessed, and a decision should be made regarding the user needs and alignment within the scope of the protocol.

For further details and IFU content see [redacted].

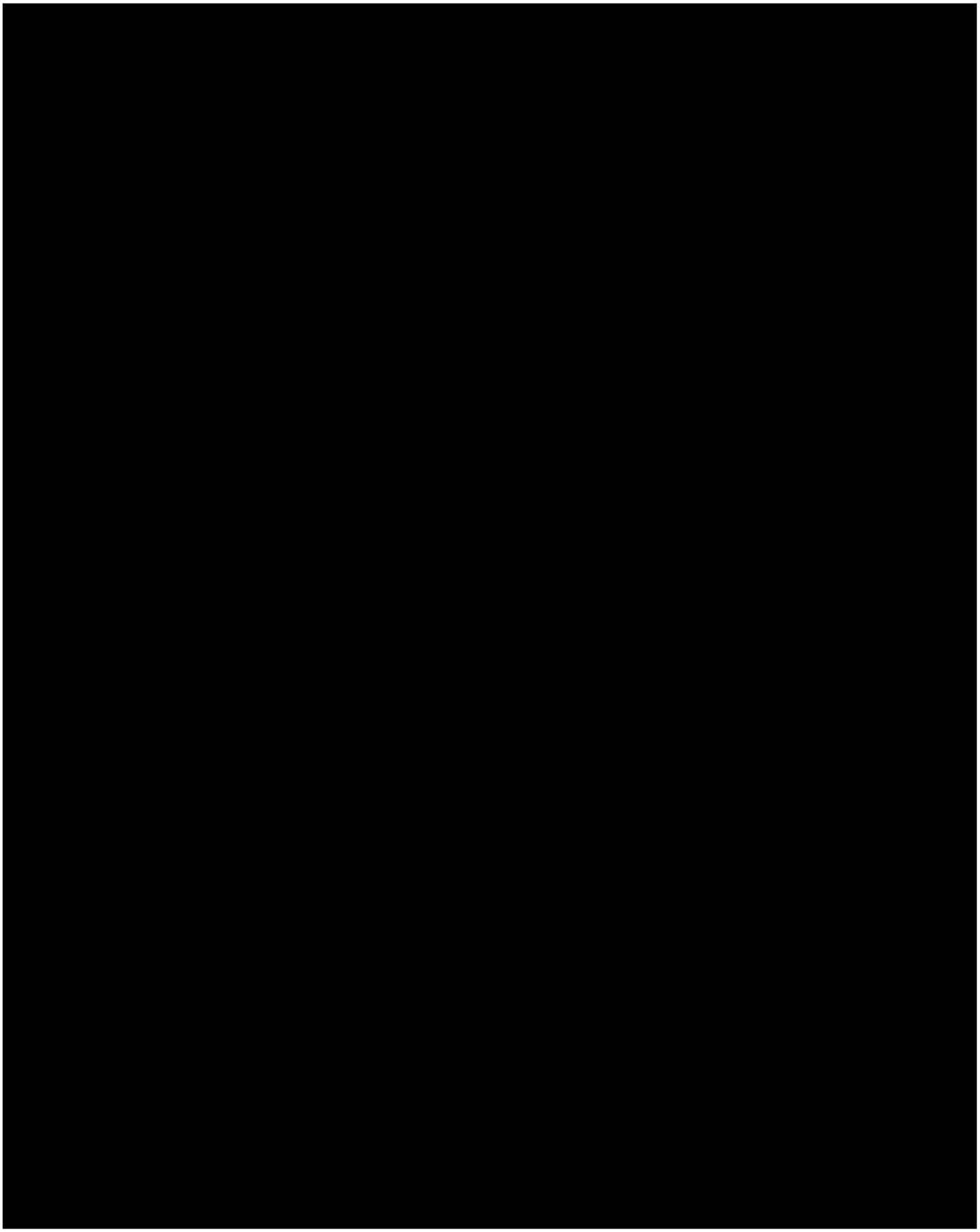

Figure 2 [redacted]

The devices will be labeled according to regulations concerning non-CE marked devices under investigation. R&D engineers will be responsible for identification of devices: on the required label for each device will be a serial number, same format as those used for CE marked Össur devices of a similar type.

Table 1 Technical and functional features

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]		[redacted]
[redacted]	[redacted]		[redacted]
[redacted]	[redacted]		[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]		[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]		[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]		[redacted]
[redacted]	[redacted]		[redacted]

Investigation Device Management Form (IDMF) will be used to track the use of each device within the clinical investigation using the device serial number.

See following chapters on the intended purpose of the device under investigation in the proposed clinical investigation and specific medical or surgical procedures involved in the use of the device.

- Objectives and Hypotheses

[redacted]

The hypothesis and endpoints are specified in Table 2.

For all hypothesis:
$\mu_0 is\ mean\ outcome\ on\ current\ device;$
$\mu_1 is\ mean\ outcome\ on\ investigational\ device;$
$and\ d\ is\ the\ margin\ of\ non-inferiority$

Table 2 Endpoints, test methods and hypotheses

	Hypothesis	Construct & Test Methods	Endpoints	Acceptance Criteria
A	Performance in TuG on [redacted] is no worse than on the prescribed device (primary outcome)	TuG-Test	Seconds to complete TuG	Not more than 25% increased time in secs: $\mu_1 - \mu_0 < \mu_0 * d$ *d* = 25%
B	Performance in 2MWT is no worse than on the prescribed device	2MWT	Meters covered within 2min	No more than 20% decrease in meter distance: $\mu_1 - \mu_0 > \mu_0 * d$ *d* = 20%
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

[redacted]

[redacted]

Design of the Clinical Investigation

General

The investigation will be a prospective case series design. Amputees are a small proportion of the general population. The population group specified in the inclusion/exclusion criteria is a further subsample of amputees. For practical reasons, i.e. to achieve statistical power, it is therefore more feasible to use within-subject comparison rather than creating study arms to compare. Furthermore as mobile amputees generally have and use a prosthetic device for their daily activities, within-comparison is feasible comparing to the subjects previous device.

Participants will be consented, and all tests will take place at the Össur Motion lab Grjótháls 1-5, 110 Reykjavik

As stated above the primary outcome is performance in the TUG test, see Table 2, and the secondary endpoints are 2MWT performance, speed limit perception, AE reports, support in sit to stand and stand to sit in that respective order of significance. See previous chapter on objectives and hypothesis and Table 2 for rationale.

[redacted]

See chapter **Procedures** and **Table 2** for analysis of variables.

Equipment required for each subject:

- Pen/pencil
- **Printed out/Online** instruments
- IPad
- Investigational device + Components
- Comparator
- 2 cones
- Measuring tape
- Chair with armrests
- Office chair on wheels
- Chair without armrests (typical household chair)
- Barstool
- Stopwatch / smartphone
- Video camera / smartphone
- 4 crutches

- Video Display
- Microgate timing gates
- Össur Logic mobile application

The equipment used does not require specific monitoring, maintenance, or calibration procedures.

• Investigational Device(s) and Comparator(s)

The subjects will only be asked to use the investigational device during measurements at the study site.

Individual exposure will differ between subjects. At least 2 visits are required, though no more than 3, depending on time required at each visit. Each visit will take approximately 4 hours.

Subjects will provide feedback and conduct functional tests on their prescribed prosthesis as well as the investigational device.

The comparator device will be whichever prosthetic knee subjects are currently using, MPK or NMPK. Those devices have the same intended use as the investigational device and are indicated for the same condition and population group.

[redacted]

6 subjects are to be enrolled and up to **3** devices will be used, as the investigational devices will be prototype devices and testing will take place on site only, each device may be used for up to 6 subjects. The devices will be reset to manufacturer settings between users. 6 CPO subjects are to be enrolled for usability validation activities.

• Subjects

See **Table 3** for inclusion/exclusion criteria.

Table 3 Inclusion/Exclusion criteria

Inclusion: Only patients with the following characteristics **are eligible** for study entry**:**	**Exclusion**: Patients with the following characteristics **are not eligible** for study entry:
50Kg< body weight < 116Kg	50Kg> body weight > 116Kg
Cognitive ability to understand all instructions and questionnaires in the investigation.	Users with cognitive impairment
Age ≥ 18 years	Users aged <18y
K1-K2 unilateral transfemoral amputees	Bilateral amputees
Allows for 37mm knee center height to dome of pyramid alignment	Users with stump pain

Inclusion: Only patients with the following characteristics **are eligible** for study entry**:**	**Exclusion**: Patients with the following characteristics **are not eligible** for study entry:
Willing and able to participate in the study and follow the protocol	Users with co-morbidities in the contra-lateral limb, which significantly affect their functional mobility
Comfortable and stable socket fit (scoring 5 or higher on PSCS)	Users with socket problems (scoring lower than 5 on PSCS)
No socket issues/changes in the last 6 weeks	

Socket fit will be evaluated using the Prosthetic Socket fit Comfort Score[1], those scoring lower than 5 during screening will be excluded due to not having a stable enough socket fit.

The Prosthetic Socket fit Comfort Score (PSCS) is administered by asking the patient the following question: "If 0 represents the most uncomfortable socket fit you can imagine and 10 represents the most comfortable socket fit, how would you score the comfort of the socket fit of your artificial limb at the moment? Despite its simplicity, the PSCS has shown correlations between patient reports, clinical findings of the physician (redness, pressure marks, sores etc.), and the prosthetic fit as judged by the prosthetist.

Users that report having chronic stump pain during screening will be excluded. Users that report stump pain on testing days will be rescheduled for another time to avoid the pain affecting the performance.

The total time period required to implement the clinical investigation is expected to be **4 weeks**. Each individual subject is expected to participate in the clinical investigation for **2 weeks,** CPO subjects for **1 day.** The estimated time needed to include this number (enrolment period) is **2 weeks.**

6 subjects and 6 CPO subjects will be enrolled. Number of subjects was determined by a sample size calculation, see **Sample Size Calculation.** Sample size for CPOs was determined by how many subjects are needed to validate the usability requirements for CPOs.

• Procedures

i) Test procedure

There are **two** scheduled study events. At the initial visit, the first study event, for each subject a researcher qualified to obtain informed consent will seat the subject and proceed as described in chapter **13.7 Informed consent** in [redacted].

Prior to fitting the subject will be asked to provide feedback on the current prosthesis, by filling in a questionnaire **and perform AMPro, LCI (modified), TUG test, 2MWT and other validation activities (stand to sit, sit to stand, level ground, stair and ramp walking), as applicable**. The users will be fitted within the standard methods of prosthetic fitting, alignment, introduction, training and walking on various terrain.

After initial fitting subjects will carry out **validation tasks (stand to sit, sit to stand tasks, level ground walking at different speeds, stair and ramp walking), stroop test (cognitive loading) and FSST** on the investigational device, after which they will answer an in-house questionnaire to provide feedback.

The second event will be 1-14 days later, subjects will be fitted with the investigational device and asked to perform the **TUG, 2MWT** and any validation tasks that could not be completed at visit 1 on the investigational device.

If for some reason all tasks cannot be completed at visit 1 and 2, a third visit may be added.

Subjects will not wear the device home between visits.

[redacted]

Table 4 Visit schedule and procedures

	Recruitment phase: 2 weeks prior to visit 1	Subject visit 1:	Subject visit 2:	Subject visit 3: (if needed)
Potential subjects identified, fitting inclusion/exclusion criteria, by CI#1 from customer database	X			
CI#1 calls potential subjects and screens by telephone	X			
Subject signs ICF		X		
Subject fills in background information questionnaire on current prosthesis		X		
Subject completes TUG test on prescribed prosthesis		X		
Subject completes 2MWT on prescribed prosthesis		X		
Subject answers clinical questionnaire on prescribed prosthesis		X		
Subject fitted with investigational device and receives training according to standard treatment		X		
Subject completes product validation tasks on prescribed prosthesis		X		
Subject re-fitted with investigational device			X	(X)
Subject completes TUG test on investigational device			X	
Subject completes 2MWT test on investigational device			X	
Subject completes product validation tasks on investigational device		X	X	(X)

Subject answers clinical questionnaire on investigational device	X	(X)
Subject receives compensation for taking part – end of study	X	(X)

For each subject there is **two** scheduled **visits** to the study site and **questionnaires, tasks and measurements** administrated **two** times during the course of the study. Third visit may be required if all tasks are not completed at visit 1 and 2.

• Statistical Considerations

• Statistical design and procedures

Outcomes will be inspected for normality. If the data are deemed to have a normal distribution the hypothesis will be tested using a two-tailed, paired t-test (Only hypothesis A and B). If data is deemed non-normal that hypothesis will be tested using a Wilcoxon signed rank test. Significance level (alpha) will be set at 0.05.

Other endpoints and acceptance criteria will be assessed with descriptive statistics only, [redacted]

• Sample size calculation

Dite et al.[2] Showed that multiple fallers (TUG 25.0 +/- 6.9) vs nonmultiple fallers (16.2 +/-5.3) can be identified from a TUG test. Under the assumption that a device causing your TUG to worsen would therefore increase your risk of falling we performed a sample size analysis to detect the difference in TUG identified by Dite et al. using G power:

t tests – Means: Difference between two dependent means (matched pairs)

Analysis:	A priori: Compute required sample size	
Input:	Tail(s)	= Two
	Effect size dz	= 1.4067851
	α err prob	= 0.05
	Power (1–β err prob)	= 0.78
Output:	Noncentrality parameter δ	= 3.4459057
	Critical t	= 2.5705818
	Df	= 5
	Total sample size	= 6
	Actual power	= 0.7850930

Results of the sample size calculation showed that a total number of 6 subjects is needed to complete the protocol with a power of 0.79 and significance at 0.05.

• Ethical Considerations

Device related risk

As specified in [redacted], for each new product developed and manufactured by Össur a thorough risk analysis is carried out according to Össur Risk Management process (QM1673), involving hazard analysis and (Failure Mode Effect Analysis) FMEA. The FMEA and hazard analysis help quantifying the criticality and probability of failures and potential harm. The design criteria is an important input in the risk analysis study but also the experience of existing products of similar function. Development and device improvement processes are performed followed the guidelines of Risk Management for Medical Devices (EN ISO 14971). [redacted]

Anticipated adverse device effects and residual risks associated with the investigational device, are identified in the Risk Management Plan [redacted] See excerpt below on foreseeable adverse events and anticipated adverse device effects, together with their likely incidence, mitigation or treatment.

Device related risks were investigated using the general guidelines of ISO14971:2012. The general approach looked separately at the hazard associated with the technology and the hazards associated with the specific combination of product intended use and targeted user population.

[redacted]

Hazard arising from the combination of the prototype intended use and the targeted user population were analyzed in the context of the study herein described. The table below summarizes the most significant

hazards identified during the process, as many of the hazard associated with field use of a powered knee prosthesis are not relevant in the context of a controlled environment study. These entries have been extracted from the complete Hazard Analysis table found in [redacted]

Table 6 – Summary of Hazard Arising from Prototype Use: Unexpected Powered Motion

[redacted]

- References

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

External References:

1	Hanspal RS, Fisher K, Nieveen R. Prosthetic socket fit comfort score. Disabil Rehabil. 2003 Nov 18;25(22):1278-80. doi: 10.1080/09638280310001603983. PMID: 14617445.
2	Dite, Wayne, Helen J. Connor, and Heather C. Curtis. "Clinical Identification of Multiple Fall Risk Early After Unilateral Transtibial Amputation." Archives of Physical Medicine and Rehabilitation 88, no. 1 (January 1, 2007): 109–14. https://doi.org/10.1016/j.apmr.2006.10.015.