Power Knee PKA03 - Clinical Investigation Protocol

Investigation on a new Power Knee firmware update on gait and daily life activities, a randomized controlled double-blinded cross-over investigation

Power Knee

CONFIDENTIAL DOCUMENT

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Sponsor's Statement: On behalf of the Sponsor, I have reviewed and approved this CIP in its entirety and agree to sponsor its implementation.

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See List of investigators in **[8]** for investigational site and list of investigators and monitors.

STATEMENT OF INVESTIGATOR COMPLIANCE

This protocol is a prospectively designed study to investigate the performance of the Power Knee Mainstream after a firmware update.

- Implement and conduct this study diligently and in strict compliance with the protocol, good clinical practices (GCP), ISO 14155: 2020 standards, and all applicable laws and regulations.

- Maintain all information supplied by Össur Iceland ehf in confidence and, when this information is submitted to an Ethics Committee (EC), it will be submitted with a designation that the material is confidential.

- Ensure that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions.

This document contains confidential information belonging to the Sponsor (Össur Iceland ehf) and therefore, may not be disclosed to any other person or entity without the prior written permission of the Sponsor unless such disclosure is required by law or regulation.

Investigator Signature

I have read and understand the contents of the clinical protocol including this Statement of Investigator Compliance. I agree to follow and abide by the guidelines set forth in this document.

Principal Investigator Name: Pete Simpson

Principal Investigator Signature	Date

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Tables

1 How to Refer to This Document

[0] CIP2024070123, Clinical Investigation Protocol, [redacted]

2 Summary

Device(s) being tested:	**Device under Evaluation**: POWER KNEE Mainstream with Firmware Update, a modification of a CE-marked device **Comparator**: POWER KNEE Mainstream, currently marketed as "POWER KNEE" For simplification the device under evaluation in this PMCF Investigation will be referred to as "investigational device" throughout this document.	
Instruments and equipment:	**Instruments :** • In-house questionnaire with different activity blocks • 2MWT, 10mWT, 5XSST • Stair Assessment Index **Equipment :** • Investigational device : POWER KNEE Mainstream Firmware Update • POWER KNEE Mainstream, currently marketed as "POWER KNEE" • Pro-Flex Terra feet • Tools for fitting • Detailed protocol • Case report forms (CRFs); in Greenlight Guru – a tablet/computer or printout • Xsens, LASAR Posture, Moticon Insoles, Optogait, Microgate Witty Timing Gate	
Subjects recruited:	Inclusion criteria:	Exclusion criteria:
Phase I: Up to 10 Phase II: Up to 30	50 kg < body weight < 116 kg	Users with pain*
	Lower limb loss, amputation or deficiency	Users with co-morbidities in the contra-lateral limb, which affect their functional mobility (except bilateral amputees)
	Cognitive ability to understand all instructions and questionnaires in the study	Users with osseointegrated prosthesis

	Transfemoral amputees	Users with cognitive impairment
	MPK users who use Power Knee or who tried Power Knee within the last 3 years	Pregnant users***
	Bilateral amputees	
	Hip disarticulation / Knee disarticulation amputees	
	Age ≥ 18 years	
	Moderate to high active subjects	
	Willing and able to participate in the study and follow the protocol	
	Comfortable and stable socket fit**	
	No socket issues/changes in the last 6 weeks	
Procedures:	For **both phases**, subjects will be asked to come for a half-day session. For the phase I, up to 10 subjects will be recruited. For phase II, up to 30 subjects will be recruited. In phase I, the primary objective of this study is to evaluate the efficacy of the investigational device with the firmware update compared to the previous one regarding level-walking, sit-to-stand, and stair ascent activities for moderate to high active prosthetics users within the intended population. This phase can be repeated as many times as needed before validation (phase II). In phase II, the primary objective is to validate the updated firmware. For **both phases**, at the beginning of the visit, a researcher qualified to obtain informed consent will explain the study to the subject and proceed as described in chapter 13.8 Informed consent. The users will be fitted with the Power Knee device in a combination with an Össur foot. If the prescribed foot is an Össur foot, it will be used for the test. If the prescribed foot is not an Össur foot, then Pro-Flex LP will be provided for the test. *Configuration phase:* Both the current marketed firmware and the updated firmware will be optimally configured for each user. This configuration will be carried out by the research engineers (Group 1), who will not participate in the evaluation phase to ensure blinding. *Randomization:* Once optimal configuration is achieved for both firmware versions, users will be randomized into two groups: • Group A will start activities and tests with the current marketed firmware. • Group B will start with the Power Knee Firmware Update.	

	Evaluation phase: For each activity block and according to the randomization, Firmware 1 (either the current marketed firmware or the updated firmware) will be uploaded to the device. Users will then perform the activity block. Following this, Firmware 2 will be uploaded to the device. Users will repeat the same activities and tests performed with Firmware 1. At the conclusion of each activity block, participants will complete a set of questions from the in-house questionnaire to evaluate and compare Firmware 1 and Firmware 2 in relation to the activity block they just performed. This evaluation phase will be done by the other group of research engineers (group 2) who will be blinded. The upload of the firmware will be done by research engineers of the Group 1. *Activity blocks:* The order of the activity blocks is flexible, they can be applied in different sequences, and not all activity blocks need to be complete. • Level-ground walking • 10mWT • Sit-to-stand • 5XSTS • Ramps • Stairs • Squatting • 2-Minute Walk Test • Pro-Flex Terra (For the phase I, they will perform the activity block using the last Firmware of the evaluation part (Firmware 2). For the phase II, they will perform these tasks with the updated firmware.) The activities are video recorded to visually compare the performance of the two firmware. Biomechanical data may be collected. *Debriefing session:* After the testing session, a debriefing session will be organized, and all the research engineers will take part. The blindness will be removed for the users and the research engineers. *End of the visit:* At the end they will be fitted back to their prescribed device. If the user has a Power Knee and if the user agrees, the current marketed version of the firmware will be uploaded to their devices if it was not already. See **Table 1** below for summary of procedures and visits.

* Question on pain affecting their functional ability (yes/no)

** Socket fit: socket comfort score (SCS) over 7

*** Self-reported

Table 1 Summary of procedures and visits for phases I and II

Procedure/Activity		*Recruitment phase*	*Subject visit*
Potential subjects identified, fitting inclusion/exclusion criteria, by LPI or PI from Össur customer database, other clinics, external customers		X	
LPI or PI will call potential subjects and screens by telephone		X	
Subjects will sign ICF			X
Subjects will be fitted with investigational device and prescribed foot			X
Configuration phase: Optimal configuration of both firmware			X
Subjects randomization			X
Evaluation phase:	For each activity block:		X
	Subjects will have the Firmware 1 uploaded on the investigational device Group A: current marketed firmware Group B: updated firmware		
	Subjects will perform the activity block with the Firmware 1		
	Subjects will have the Firmware 2 uploaded on the investigational device Group A: updated firmware Group B: current marketed firmware		
	Subjects will perform the activity block with the Firmware 2		
	Subjects will answer questions to compare Firmware 1 and 2		
Subjects will be fitted back to their prescribed devices			X
Debriefing session			X
(Optional) If the subjects have a Power Knee device and if the users' devices do not have the latest version of the firmware, the research engineers will update the devices with the latest current marketed firmware			X

End of the study		X

3 Changes from Previous Revision

3.1 Changes for Revision 1.00

Initial release.

September 2024

3.2 Changes for Revision 2.00

September 2024

Statement of investigator compliance added

3.3 Changes for Revision 3.00

November 2024

Chapter 2:

- Inclusion/exclusion changed to include complex presentations and users with MPKs who tried Power Knee within the last 3 years
- Number of users for phase II increased from 15 to 30
- Precision of the use of an Össur foot (Pro-Flex LP) if the prescribed foot is not an Össur foot
- Precision of the option of updating the Power Knee firmware for the users' device if the users have a Power Knee
- Equipment: LASAR Posture, Xsens, Moticon Insoles, Optogait, Microgate Witty Timing Gate added
- Table 1: test procedures changed to gather activities in blocks

Chapter 4: MPK added

Chapter 5: Change in the firmware name from PKK3.MMT.03.02.xxx to PKK3.MMV.03.02.xxx.

Chapter 6: Study design updated

Chapter 7: Addition of the phrase concerning the fact that the phase I can be repeated as many times as needed. Addition of few hypotheses concerning biomechanical data as exploratory.

Chapter 8:

- Equipment added: LASAR Posture, Xsens, Moticon Insoles, Optogait, Microgate Witty Timing Gate
- For Phase II, number of users increased from 15 to 30
- For phase II: number of investigational devices increased from 5 to 10
- Inclusion/exclusion changed to include complex presentations (hip disarticulation, knee disarticulation and bilateral amputees)
- Inclusion/exclusion changed to include users with passive microprocessor-controlled knees who tried Power Knee within the last 3 years

- Total duration of phase I is therefore one week for every repetition and total duration of phase II is therefore up to three weeks.
- Test procedure updated with the number of users, the possible repetition of phase I and the use of Össur foot for the investigation.
- Data collection updated with the use of LASAR Posture, Xsens, Moticon Insoles, Optogait, Microgate Witty Timing Gate.
- Recruitment strategy updated with the use of investigation sites' database, Össur's customer database, external clinics and customers, word of mouth or customer representative meetings to maximize the reach and efficiency of participant enrollment.
- Table 6 updated according to the new test procedures

Chapter 13:

- Risk of study updated to include users who tried Power Knee.

Annex 17.1:

- Screening form updated to match the inclusion/exclusion criteria

Annex 17.2: questions added and reorganized in activity blocks

Annex 17.5: description of biomechanical data added

4 Abbreviations

ADE	Adverse Device Effect
ADL	Activities of Daily Living
AE	Adverse Event
AR	Adverse Reaction
BL	Baseline
CA	Competent Authority
CEP	Clinical Evaluation Plan
CER	Clinical Evaluation Report
CI	Co-Investigator
CIB	Clinical Investigator´s Brochure
CIP	Clinical Investigation Plan
CIR	Clinical Investigation Report
CRF	Case Report Form
EDS	Electronic Data capture Service
FU	Follow-Up
ICF	Informed Consent Form
IDMF	Investigational Device Management Form
IFU	Instructions For Use
IRB	Independent/Institutional Review Board
KD	Knee Disarticulation
LCI	Local Co-Investigator
LPI	Local Principal Investigator
LRA	Local Research Assistant
MPK	Microprocessor-controlled Knee
PI	Principle Investigator
SAE	Serious Adverse Event
SADE	Serious Adverse Device Event
TF	Transfemoral
USADE	Unanticipated Serious Adverse Device Effect
10mWT	10-meter walk test
2MWT	2-minute walk test
STS	Sit To Stand
5XSST	5 Times Sit To Stand

5 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 under investigation (the Investigational Device) is a **modification of a CE-marked** medical device currently marketed (Power Knee Mainstream). From now on in this document, the investigational device will be referred to as **POWER KNEE Mainstream Firmware Update**. The core component of the system is a motorized knee prosthesis along with other important parts which, are necessary for the device's operation, functionality and safety. More specifically, POWER KNEE Mainstream Firmware Update is composed of four parts. Besides the motorized knee itself one of these is a detachable battery pack providing the system with power and thereby making it operational as a motorized knee prosthesis. Another part is the prosthesis configuration device that allows adjustment of the knee parameters to optimize its performance with respect to the user physiological characteristics, activity level, gait style and personal preferences. Furthermore, with the battery pack comes an off-the-shelf power supply allowing recharging of the battery when not installed in the knee prosthesis.

POWER KNEE Mainstream Firmware Update is based on the concept and technology of the existing POWER KNEE MAINSTREAM which is commercially available, but the firmware has been updated to enhance functions of ADLs such sit to stand, level walking, and stair ascent. Hence some changes in the algorithm have been made:

The description of the modifications for the sit to stand, swing phase, and stair ascent are:

- Sit-to-stand: The change concerns the power delivery from the motor during standing up. The triggering will remain the same, but the motor motion will change.
- Swing phase: During the swing phase, the gains of the motor control changes based on the knee angle relative to the target flexion angle.
- Stair ascent: The stair ascent activity should be more fluid and in synchronization with the user.

See Table 2 for details on the investigational device.

Table 2 Identification and Description of the Investigational Device

Summary description of the investigational device and its intended purpose:	POWER KNEE Mainstream Firmware Update is composed of a motorized knee prosthesis, which forms the core of the system, as well as other devices used to sustain operation on a daily basis. More specifically, POWER KNEE Mainstream Firmware Update is composed of five devices. Operation of the motorized knee prosthesis relies on a detachable battery pack, which provides system power, and a Prosthesis Configuration Device that allow adjustment of the knee parameters to optimize its performance with respect to the user physiological characteristics, activity level, gait style and personal preferences. Furthermore, the battery pack is provided and a charger and an off-the-shelf power supply, allowing conveniently recharging the battery pack when not used in the knee prosthesis. POWER KNEE Mainstream Firmware Update is intended as Power Knee Mainstream, for moderate to high-active users of low to moderate impact levels, building on established powered knee technology and utilizing the clinical benefits associated with powered prosthetics. It is a Class II product and is a further development of a well-established technology. The device is classified as an "External assembled lower limb prosthesis" according to Title 21 §890.3500, bearing the product code ISW (Assembly, Knee/Shank/Ankle/Foot, External). It is 510(k) exempt, except for general requirements. The system is not used in direct contact with the body. It should be noted that the aspect of the prosthesis that is in

	direct physical contact with the amputee is the liner/socket, to which the POWER KNEE Mainstream Firmware Update is connected to. In other words, the POWER KNEE Mainstream Firmware Update is not in direct physical contact with the amputee. An amputee typically wears prosthesis and thereby utilizes the POWER KNEE Mainstream Firmware Update, for up to 18 hours a day over duration of multiple years. The device will be supplied in a hard-plastic case with custom made foam cut-outs to protect the product and all relevant documents and accessories. The devices will be labelled according to regulations concerning non-CE marked investigational devices. 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.
Manufacturer of the investigational device:	Össur Iceland ehf. Grjothals 5 110 Reykjavik Iceland
Name or number of the model/type, including software version and accessories, if any, to permit full identification:	Model: POWER KNEE Mainstream Firmware: [redacted] Different versions might be tested at the different phases.
Traceability during and after the investigation:	Investigation Device Management Form (IDMF) will be used to track the use of each device within the clinical investigation using the device serial number.
Intended purpose of the investigational device in the proposed clinical investigation:	Intended purpose of the investigational device in the proposed clinical investigation is within the intended purpose as described above. See following chapters on the intended purpose of the investigational device in the proposed clinical investigation for details.
The populations and indications for which the investigational device is intended:	**Intended Purpose Statement** The device is intended as part of a prosthetic system that replaces knee function of a missing lower limb. **Indications for Use(s)** Lower limb loss, amputation or deficiency. **Contraindications for Use(s)** No contraindications for use are known for POWER KNEE Mainstream Firmware Update. **Intended Patient Population:** Unilateral transfemoral/ knee disarticulation amputation Unilateral hip-disarticulation or hemi-pelvectomy amputation Bilateral transfemoral that combine unilateral amputation listed above on one side with transfemoral level amputation or any amputation below that level on the contralateral side Limb deficiency with a presentation comparable to the aforementioned that can be fit with a prosthetic knee component **Activity Level**: Moderate to high-active ambulators - Community ambulators

	Impact Level: Low to moderate impact levels. **User weight**: Higher than 50 kg Lower than 116 kg
Description of the investigational device:	See Table 3 below for descriptions of device features and their relation to the investigation.  *Picture 1 : Investigational device* The investigational device is a microprocessor controlled prosthetic knee. It is used for transfemoral and knee disarticulation amputees. It is utilized as part of prosthetic limb system, in other words an amputee requires additional components, such as a foot, to use the POWER KNEE Mainstream Firmware Update in a functioning prosthesis. The POWER KNEE Mainstream Firmware Update requires a certified prosthetist to set-up and fit the device to an amputee. The certified prosthetist uses software called "OssurLOGIC" running on a computer to communicate to the POWER KNEE Mainstream Firmware Update in, such that parameters can be adapted for an amputee. As the POWER KNEE Mainstream Firmware Update in is battery powered (rechargeable lithium ion) a charger is required. The aspect of the prosthesis that is in direct physical contact with the amputee is usually a liner that serves as an interface between the amputee and the rest of the prosthesis. In other words, the device is usually not in direct physical contact with the amputee. As described above, the device is intended to be in contact with intact skin only. The device does not incorporate, as an integral part, a substance or human blood derivative and is manufactured without utilizing tissues of animal origin.
Summary of the necessary training and experience needed to use the investigational device:	Training requirements for subjects and procedures relating to fitting and use of a device will for all general purposes be equivalent to the training and procedures required for using a CE-marked device of a similar type. The device should be supplied and fitted by a certified CPO/CO/CP. For the purpose of this investigation training for subjects will be standardized to assure that all subjects will receive the same training.
Specific medical or surgical procedures involved in the use of the investigational device:	N/A

For further details on the Investigational device, please refer to Power Knee PKA01 Instructions for Use **[4].**

Table 3 Technical and functional features

#	Feature	Description (if not obvious)	Covered by this investigation:
1	Powered knee flexion/extension	Sit to stand support	Yes
2	Controlled yielding	Sit to stand support, safety in ramp and stair ascent	Yes
3	Compliance stance	Support in stance phase in level ground walking	No
4	Actuator torque level	Safety in ramp and stair descent	No
5	Motorized swing phase	Active flexion and extension during walking, enables users to walk further with less exertion.	Yes
6	Natural speed adaptation	No perceived speed limit	Yes
7	Ascent and descent in ramps/stairs		Yes
8	Secure stance phase with locked motor	Perceived safe and stable stance phase	No
9	Flexion hold at different angles	Comfort in standing	No
10	Gait controls	Ease of use of gait functions	No
11	Device setup	For CPO	No
12	Noise level	Acceptable noise level	No

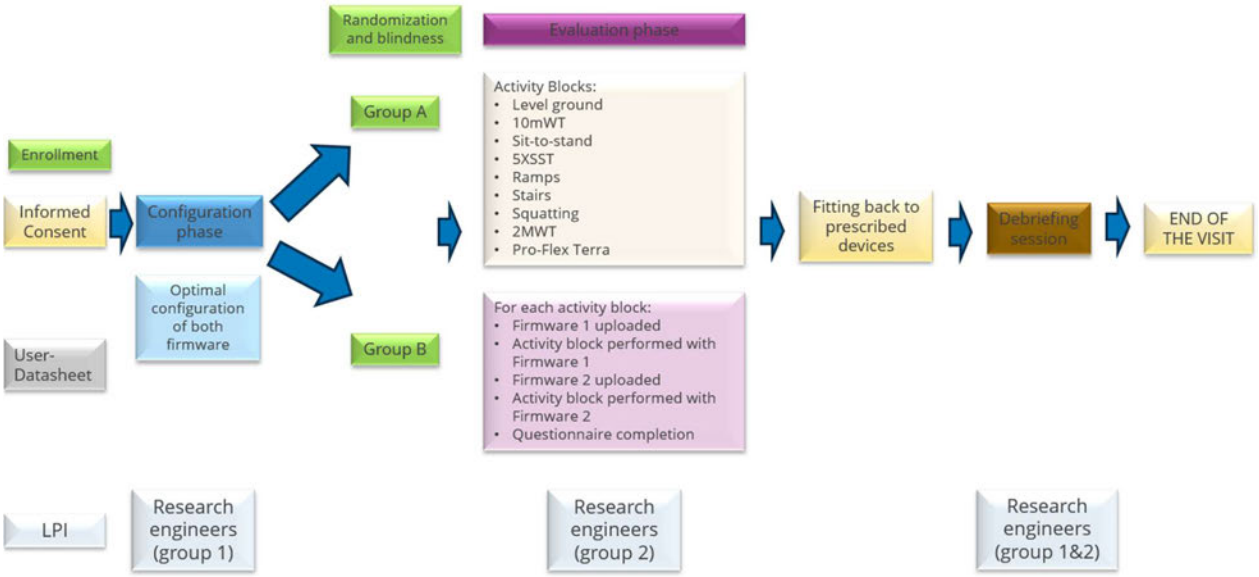
6 Justification for the Design of the Clinical Investigation

The introduction of microprocessor controlled prosthetic knee in 1997 was a major leap in prosthetics in restoring function and increase safety of individuals with a lower limb amputation. Countless studies should the benefits of such devices, e.g. Hafner et al.[1] and Bellmann et al.[2]. However, such devices are still passive with a major shortcoming, which is that they cannot provide positive power to support the user. In other words, they are unable to generate concentric moments to support the user in situations in which such moments are needed. Standing up and step over step stair climbing are two examples where concentric moments are in principal needed, in order to fulfil these tasks. Although recent passive microprocessor controlled prosthetic knees have been introduced that offer modes which facilitate step over step stair climbing, the power needed still has to be generated by the proximal hip joint of the user. Especially in individuals with a transfemoral amputation, who may have reduced all over physical capabilities, such modes cannot be used, due to the physical limitations of the user. This fact is for example substantiated by the inclusion criteria in Bellmann et al., who investigated step by step stair climbing in K-Level 3-4 subjects with a passive microprocessor controlled prosthetic knee. Beside in these rather complex movement patterns, knee power is an also needed for knee flexion in the swing phase while walking. Although the magnitude of the power needed in this state is rather small, providing power has a pronounced clinical impact, since a reduced clearance in swing is associated with a higher risk of falls.

Several studies have provided evidence for the clinical performance of previous versions of the Power knee (PK), which has the same function and intended use, those are detailed in the Literature review device report **[7]**.

Results of studies on previous versions of the Power knee indicate that the Power knee provides support in the sit to stand and stand to sit activity, provides stance phase flexion in level ground walking, support in ascending and descending ramps and stairs and that it does provide active flexion and extension during walking which leads to users being able to walk further and feel less tired. In addition, Pasquina et al.[10] tested the Power Knee as an initial knee prosthesis after combat-related TF amputation or knee disarticulation and found indications that the Power Knee can be helpful as initial prosthesis after TF/KD amputation, participants reached mobility milestones faster than norms identified by expert panel. Shortening the rehabilitation time after amputation has the potential for great savings in healthcare expenditure and large benefits for the patients, e.g. with earlier mobilization and independence. Creylman et al.[11] compared the Power knee and the Rheo knee (passive MPK), their results indicated more symmetric gait with the PK compared to passive MPK. As the literature shows, a powered prosthetic knee which is able to generate concentric moments is of high interest, to better counterbalance the disability of individuals with a lower limb amputation.

Study design for phases I and II



7 Objectives and Hypotheses

The purpose of the investigation is to generate clinical data on the updated device for understanding its full benefits and for collecting performance data.

In phase I, the primary objective of this study is to evaluate the efficacy of the investigation device with the firmware update compared to the previous one regarding level walking, sit-to-stand, and stair ascent activities for moderate to high actives prosthetics users within the intended population for the investigational device.

All the activities will be documented via video documentation and comments will be noted.

A noticeable support of the swing phase in flexion and extension should be visible, plus a similar or an improved capacity at keeping up with the user in comparison to the current firmware. The dynamic of the swing phase while walking will be investigated via the 2MWT and 10mWT and potentially lead to similar or improved performance in comparison to the current firmware.

Concerning the sit-to-stand activities, time to perform the 5 times sit to stand test (5XSST) will be evaluated.

Similar as the previous tasks, stair ascent will be noticeable in the video documentation. In particular the subject will walk upstairs, stop and fully load the prosthetic knee. The time to perform the stair ascent will be documented and the performance will be evaluated with the Stair Assessment Index.

For each activity, the users will be asked to compare both firmware and rate on a worse, equal, better scale, if these tasks felt similar or different with the second firmware (without knowing which firmware is the updated one).

Additionally, feedback on the performance of the Pro-Flex Terra Foot and the POWER KNEE (phase I: with firmware 2, phase II: with updated firmware) will be collected.

The first phase can be repeated as many times as needed.

In phase II, the primary objective is to validate the firmware update.

The investigational device will be assessed with regards to its capability to be used with the indicated patient group, providing benefits to the subjects. No risks or anticipated adverse device effects (ADE) are to be assessed. The hypothesis and endpoints are specified in **Table 2**.

No claims are to be evaluated.

The following performance aspects are to be verified (relating to features in table 3 above):

- The investigational device provides perceived support to the user in sit to stand activities (Powered flexion and extension).
- The investigational device provides perceived support to the user in stand to sit activities (Controlled yielding).
- The investigational device provides natural speed adaptation within typical walking cadence, no perceived speed limit (Natural speed adaptation).
- The investigational device provides natural ambulation in stair ascent.

For all hypothesis:

$\mu_0 is\ average\ of\ measurements\ at\ baseline\ with\ the\ comparator\ (Power\ Knee\ with\ current\ marketed\ firmware)$;

$\mu_1\ is\ the\ average\ of\ measurements\ with\ the\ \ investigational\ device\ \ (Power\ Knee\ with\ firmware\ update)$;

$and\ |M_{NI}|\ \ is\ the\ margin\ of\ non-inferiority$

$and\ |M_E|\ \ is\ the\ margin\ of\ equivalence$

$and\ P_r\ \ is\ the\ probability\ of\ a\ rating$

Clarification: Phase I will include up to 10 subjects and will be conducted before the firmware is going through formal validation. Phase II will include up to 30 subjects and will be conducted to validate the firmware.

Table 4 Endpoints, test methods and hypotheses

	Hypothesis	Test Method	Endpoint	Acceptance Criteria for phase I	Acceptance Criteria for phase II	Limitations, comments
A1	**Sit to stand** activity is perceived as better and not worse with the firmware update compared to previous.	Rating: worse, same, better (1-3)	Rating **score** 1-3	In average no more than 22.5% of the subjects should rate the firmware update no worse.	$H_0: P_{worse} = 0{,}333$ $H_1: P_{worse} < 0{,}333$ $\wedge$ $H_0: P_{better} = 0{,}333$ $H_1: P_{better} > 0{,}333$ $\forall\, p < 0{,}05$	
A2	**Stand to sit** activity is perceived as better and not worse with the firmware update compared to previous.	Rating: worse, same, better (1-3)	Rating **score** 1-3	In average no more than 22.5% subjects should rate the firmware update no worse.	$H_0: P_{worse} = 0{,}333$ $H_1: P_{worse} < 0{,}333$ $\wedge$ $H_0: P_{better} = 0{,}333$ $H_1: P_{better} > 0{,}333$ $\forall\, p < 0{,}05$	
B	**Mobility** is no worse with the firmware update compared to previous.	10mWT	Time in seconds	Exploratory	No significant increase in time needed to perform the 10mWT with the firmware upgrade. $H_0: \mu_0 - \mu_1 \geq \lvert M_{NI} \rvert$ $H_1: \mu_0 - \mu_1 < \lvert M_{NI} \rvert$ $M_{NI} = MDC$ $MDC = 0{,}13\ m/s$[13] $p < 0{,}05$	To be able to check if the knee keeps up with the user in a better way. Sensors logging
C	**Mobility** is no worse with the firmware update compared to previous.	2MWT	Distance in meters	Exploratory	No significant reduction in distance walked on 2MWT with the firmware upgrade. $H_0: \mu_0 - \mu_1 \geq \lvert M_{NI} \rvert$ $H_1: \mu_0 - \mu_1 < \lvert M_{NI} \rvert$ $M_{NI} = MDC$ $MDC = 34\ m$[14] $p < 0{,}05$	Sensors logging
D	Users perception of **level-ground walking** is no worse with the firmware update compared to previous.	Rating: worse, same, better (1-3)	Rating **score** 1-3	In average no more than 22.5% of the subjects should rate the firmware update no worse.	$H_0: P_{worse} = 0{,}333$ $H_1: P_{worse} < 0{,}333$ $\wedge$ $H_0: P_{better} = 0{,}333$ $H_1: P_{better} > 0{,}333$	

					$\forall\, p < 0{,}05$	
E	The PK firmware update shows no worse results in **stair ascent** activities compared to previous.	Stair assessment index	Rating **score** 1-13	Exploratory	$H_0: \mu_0 - \mu_1 \geq \lvert M_{NI} \rvert$ $H_1: \mu_1 - \mu_0 < \lvert M_{NI} \rvert$ $M_{NI} = 1$ point $p < 0{,}05$	Sensors logging ICCs of rs = 1.00 (p < 0.001) [12]
F	Users perception of **stair ascent** is no worse with the firmware update compared to previous.	Rating: worse, same, better (1-3)	Rating **score** 1-3	Exploratory	$H_0: P_{worse} = 0{,}333$ $H_1: P_{worse} < 0{,}333$ $\wedge$ $H_0: P_{better} = 0{,}333$ $H_1: P_{better} > 0{,}333$ $\forall\, p < 0{,}05$	
G	Users perception of **exiting from stair ascent mode** is no worse with the firmware update compared to previous.	Rating: worse, same, better (1-3)	Rating **score** 1-3	Exploratory	$H_0: P_{worse} = 0{,}333$ $H_1: P_{worse} < 0{,}333$ $\wedge$ $H_0: P_{better} = 0{,}333$ $H_1: P_{better} > 0{,}333$ $\forall\, p < 0{,}05$	
H	Users perception of **entering stair ascent mode** is no worse with the firmware update compared to previous.	Rating: worse, same, better (1-3)	Rating **score** 1-3	Exploratory	$H_0: P_{worse} = 0{,}333$ $H_1: P_{worse} < 0{,}333$ $\wedge$ $H_0: P_{better} = 0{,}333$ $H_1: P_{better} > 0{,}333$ $\forall\, p < 0{,}05$	
Secondary						
I	**Exiting stair ascent mode** with the firmware update reduces unexpected movements compared to previous.	2 repetitions of Stair ascent	Count of unexpected movements	Exploratory	Significant reduction in unexpected movements when exiting stair ascent: $H_0: \mu_0 - \mu_1 \leq 0$ $H_1: \mu_0 - \mu_1 > 0$ $p < 0{,}05$	
J	Users perception with Power Knee and **Pro-Flex Terra** is no worse	Rating: worse, same,	Rating **score** 1-3	Firmware 2 will be tested: In average no more than 22.5%	Updated firmware will be tested : $H_0: P_{worse} = 0{,}333$	Sensors logging Activities :

	compared to the combination of the Power Knee and the prescribed foot.	better (1-3)		of the subjects should rate the combination no worse.	$H_1: P_{worse} < 0{,}333$ $\wedge$ $H_0: P_{better} = 0{,}333$ $H_1: P_{better} > 0{,}333$ $\forall\, p < 0{,}05$	Walking on level ground (SSWS, slow and fast) Sit to stand and stand to sit Stair ascent and descent Ramp ascent and descent Squatting
Exploratory						
K	Amount of time needed to perform **5XSST**	5 times sit to stand test	Time in seconds			
L	Temporal spatial parameters during **5XSST**	Moticon Insoles Xsens Optogait	Temporal spatial parameters			
M	Temporal spatial parameters during **2MWT**	Moticon Insoles Xsens Optogait	Temporal spatial parameters			
N	Temporal spatial parameters during **10mWT**	Moticon Insoles Xsens Optogait	Temporal spatial parameters			

8 Design of the Clinical Investigation

8.1 General

The test will be a randomized, controlled, double-blinded, cross-over investigation for both phases I and II.

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. The results of the phase I data collection will be used subsequent to first testing, to further improve the tested device, i.e. PKM. 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.

All investigational activities will be conducted at prosthetic out-patient clinics.

As stated above the primary endpoint is the general usability of the Power Knee Firmware Update in ADLs, which are specifically explained in the secondary endpoints are (see **Table 4)** in that respective order of significance. See previous chapter on objectives and hypothesis and **Table 4** for rationale.

Drop-outs and withdrawals may be replaced if deemed necessary to fulfil the methodological standards of the study.

Instruments for data collection will include the following:

2MWT: 2-minute walk test

10mWT: 10-meter walk test

5XSST: 5 times sit-to-stand test

Specific questionnaire: In-house generated questionnaire on specific features in the investigation device.

Video

Data logging by Ossur Logic/ Ossur Toolbox

See chapter **10.2 Sample size calculation**.

Equipment required for each subject:

- Detailed protocol
- Chair with Armrests for 5XSST
- Measuring tape
- Markers and a measure corridor/course of known distance for 2MWT and 10mWT
- Video camera for video documentation
- PC to read out Ossur Logic and Ossur Toolbox results
- Case report forms (CRFs) – Tablet/computer OR printed out case report forms
- Investigational device: POWER KNEE with the Firmware Update
- POWER KNEE with the current marketed firmware
- Pro-Flex Terra feet
- Other components as applicable (pylons and adapters for fitting)
- Tools for fitting
- LASAR Posture equipment for alignment
- Xsens (Annex 17.5.1)
- Moticon Insoles (Annex 17.5.2)

- Optogait (Annex 17.5.3)
- Microgate Witty Timing Gate (Annex 17.5.4)

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

8.2 Investigational Device(s) and Comparator(s)

The subjects will be asked to use the investigational device with the updated firmware as they usually do with their primary prosthesis. The comparator device will be the Power Knee Mainstream with the latest firmware version released. It has the same intended use as the investigational device. Furthermore, they are indicated for the same condition and population group.

The subjects will be using the remaining part of their current prosthetic system with the investigational device, as it was used with the comparator device.

For Phase I, up to 10 subjects are to be enrolled, two per days and up to 3 investigational devices will be used.

For Phase II, up to 30 subjects are to be enrolled, two per days and up to 10 investigational devices will be used.

8.3 Subjects

All subjects will be dispositioned as follows:

Screen Failure: Subject did not pass screening procedures, not called in for clinical visit;

Candidate for enrollment: Passed screening procedures, accepts to come in for clinical visit;

Enrolled: Subject signs informed consent;

Fitted: Subject leaves the clinic on the investigational device;

Discontinued: Candidate for enrollment or Enrolled subject whose participation ended because they withdrew consent, were withdrawn by the Investigator, were lost to follow up, or died;

Table 5 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	Users with pain*
Lower limb loss, amputation or deficiency	Users with co-morbidities in the contralateral limb, which significantly affect their functional mobility (except bilateral amputees)
Cognitive ability to understand all instructions and questionnaires in the study	Users with cognitive impairments
Transfemoral amputees	Pregnant users***
MPK users who use Power Knee or who tried Power Knee within the last 3 years	
Bilateral amputees	
Hip disarticulation / Knee disarticulation amputees	
Age ≥ 18 years	
Moderate to high-active users	
Willing and able to participate in the study and follow the protocol	
Comfortable and stable socket fit**	
No socket issues/changes in the last 6 weeks	

* Question on pain affecting their functional ability (yes/no)

** Socket fit: socket comfort score (SCS) over 7

*** Self-reported

A subject can withdraw from participation at any time, at his/her discretion, and this will not have any consequences for the participant's treatment. In such cases a report stating reasons for discontinuation of the participant shall be prepared by the LPI. No further investigational procedures concerning the subject will be conducted, except for a statement explaining the reason for withdrawal, including but not limited to: interacting or interviewing the subject in order to obtain data on him/her; obtaining additional private information on the subject by either observing the subject or collecting or receiving such information from any source.

The LPI can withdraw the participant from the trial at any time. The reasons shall be documented. There are no pre-specified criteria for discontinuation of participants from the trial. The discontinuation of participants in the trial

will not result in replacement with new participants. If withdrawal is due to problems related to the investigational device the participant will be asked for permission to follow the status/condition outside the clinical investigation. The follow-up will be individualized.

The LPI will initiate the recruitment process by screening potential participants from their customer database. This database includes individuals who have previously engaged with their services and fit the criteria for the study. In addition to the local database, participants may be recruited from Össur's customer dabase, external clinics and customers, word of mouth and/or customer representative meetings. The PI or LPI will establish communication with interested participants and will provide detailed information about the study.

For both phases, the visits to the clinic are expected to take 3-4 hours/subject. Total duration of phase I is therefore one week for every repetition and total duration of phase II is therefore up to three weeks.

The total time period required to implement the clinical investigation is expected to be up to 12 months. Each individual subject is expected to participate in the clinical investigation for the time mentioned above. The estimated time needed to include this number (enrolment period) is 1 month for phase I and 3 months for phase II.

At least 15 subjects are required to finish the protocol for statistical data analysis for phase II, see chapter **10.2 Sample size calculation**.

8.4 Procedures

i) Recruitment

Potential subjects will be identified by using the investigation sites' existing database of patients, or from Össur's customer database. Participants may be also recruited from external clinics and customers, through word of mouth, or during customer representative meetings where Össur representatives engage with users and clinicians. Customer representatives, who have prior experience interacting with and servicing patients, will evaluate if a potential participant is cognitively capable of participating in the study. Based on their assessment, the customer representative will inform the LPI of the potential subject and provide their contact information.

The LPI or PI will establish communication with potential participants and provide information about the investigation.

If a potential participant meets the inclusion and exclusion criteria, the LPI or the PI will contact them via telephone. During this call, the LPI or PI will:

- Verify the participant's interest in the study.
- Provide detailed information about the study and potential risk of participating in the investigation
- Answer questions related to the study.
- Conduct a preliminary screening to assess eligibility.

The LPI or PI will communicate to the study monitor the number of users he has identified that meet the inclusion criteria and are willing to participate.

ii) Test procedure

For **both phases**, at the beginning of the visit, a researcher qualified to obtain informed consent will explain the study to the subject and proceed as described in chapter 13.8 Informed consent.

The users will be fitted with the Power Knee device in a combination with an Össur foot. If the prescribed foot is an Össur foot, it will be used for the test. If the prescribed foot is not an Össur foot, then Pro-Flex LP will be provided for the test.

Configuration phase:

Both the current marketed firmware and the updated firmware will be optimally configured for each user.

This configuration will be carried out by the research engineers (Group 1), who will not participate in the evaluation phase to ensure blinding.

Randomization:

Once optimal configuration is achieved for both firmware versions, users will be randomized into two groups:

- Group A will start activity blocks with the current marketed firmware.
- Group B will start activity blocks with the Power Knee Firmware Update.

Evaluation phase:

For each activity block and according to the randomization, Firmware 1 (either the current marketed firmware or the updated firmware) will be uploaded to the device. Users will then perform the activity block.

Following this, Firmware 2 will be uploaded to the device. Users will repeat the same activities and tests performed with Firmware 1.

At the conclusion of each activity block, participants will complete a set of questions from the in-house questionnaire to evaluate and compare Firmware 1 and Firmware 2 in relation to the activity block they just performed.

This evaluation phase will be done by the other group of research engineers (group 2) who will be blinded. The upload of the firmware will be done by research engineers of the Group 1.

Activity blocks:

The order of the activity blocks is flexible, they can be applied in different sequences, and not all activity blocks need to be complete.

- Level-ground walking
- 10mWT
- Sit-to-stand
- 5XSTS
- Ramps
- Stairs
- Squatting
- 2-Minute Walk Test
- Pro-Flex Terra (For the phase I, they will perform the activity block using the last Firmware of the evaluation part (Firmware 2). For the phase II, they will perform these tasks with the updated firmware.)

Debriefing session:

After the testing session, a debriefing session will be organized, and all the research engineers will take part. The blindness will be removed for the users and the research engineers.

The activities are video recorded to visually compare the performance of the two firmware. Biomechanical data may be collected.

At the end they will be fitted back to their prescribed device. If the user has a Power Knee and if the user agrees, the current marketed version of the firmware will be uploaded to their devices if it was not already.

Phase I

The first phase will be used to assess the parameters defined in Table 4. Tasks performed include ADLs; Level ground, inclined, decline walking stair ascent and descent, squatting, standing up and sitting down to a regular chair. Subjects will perform the 5XSST, 10mWT and 2MWT, see full description of functional tests in Annex 17.4. Subjects will be asked to provide feedback on the tasks tested with in-house questionnaires (see Annex 17.2 and 17.3) and open comments.

Phase II

The second phase is to validate the parameters defined in Table 4, this phase will include the same tasks and procedures as phase I with up to 30 amputee subjects.

In both phases, subjects will not be asked to carry out tasks they are not comfortable performing or that are considered too demanding.

iii) Measurements and data collection

Lasar Posture may be used to record prosthetic alignment.

The activities are video recorded to visually compare the performance of the two firmware and biomechanical data may be collected.

Inertial Measurements Units from Xsens[15], may be used for measuring subject kinematics (including positions, angles, velocities and acceleration).

Moticon insoles[16] may be used for measuring wireless pressure and acceleration during walking.

Optogait[17] may be used for optical detection of the subject' movements, capturing space and time parameters for gait.

Microgate Witty Timing Gate[18] may be used to measure speed and time of a subject walking between timing gates.

The activity report will be generated from the Power Knee software application and both from Össur Toolbox and Össur Logic.

Table 6 Visit schedule and procedures

		Recruitment phase: 2-6 weeks prior to baseline	Subject visit: baseline
Potential subjects identified, fitting inclusion/exclusion criteria, by LPI or PI from Össur customer database, other clinics, external customers		X	
LPI or PI will call potential subjects and screens by telephone		X	
Subjects will sign ICF			X
Subjects will be fitted with investigational device and prescribed foot			X
Configuration phase: **Optimal configuration of both firmware**			X
Subjects randomization			X
Evaluation phase	**For each activity block:**		X
	Subjects will have the Firmware 1 uploaded on the investigational device Group A: current marketed firmware Group B: updated firmware		
	Subjects will perform the activity block with the Firmware 1		
	Subjects will have the Firmware 2 uploaded on the investigational device Group A: updated firmware		

	Group B: current marketed firmware		
	Subjects will perform the activity block with the Firmware 2		
	Subjects will answer questions to compare Firmware 1 and 2		
Subjects will be fitted back to their prescribed devices			X
Debriefing session			X
If the subjects agree and if the users' devices do not have the latest version of the firmware, the research engineers will update the devices with the latest current marketed firmware			X
End of the study			X

8.5 Compensation

8.5.1 Subject

For both phases, subjects will be compensated for their travel expenses and spent time at the clinic with a [redacted] voucher at the end of each visit. If subjects come from more than 150 miles from the clinic, Össur will pay for requested mileage and be reimbursed as applicable ([redacted].

8.5.2 Clinic

For the Clinical Testing activity, compensation for the orthopedic clinic will be according to the agreement made.

8.6 Responsibilities

Sponsor Coordinating/Principal Investigator (PI)

- Identify sites
- Train site staff on study procedures
- Collect Data
- Investigate possible vigilance cases/SAEs
- Monitor trial
- Technical support

Monitor

- Train site staff on study procedures
- Monitor trial
- Analyze results
- Write report

Sponsor Research Assistants (SRA)

- Technical support

Local Co-Investigator

- Collect data

Local Principal Investigator (LPI)

- Screen subjects
- Explain trial to participants
- Responsible for obtaining informed consent from test subjects
- Conduct all trial procedures at investigators' site
- Collect data
- Fit users with trial device and back to their current prosthesis
- Manage study documentation

8.7 Study monitoring and Oversight

The study monitor will ensure that all procedures are followed correctly and according to the study protocol. The study monitor will gather and review all study data and inform the LPI of missing data or nonconformities to the study protocol.

The study monitor and LPI will maintain communication on a minimum biweekly basis, via telephone and email. The LPI will provide the study monitor with information of all scheduled study visits. The study monitor will visit each investigational site at least once while a study visit takes place.

9 Investigational Device Accountability

The investigational devices will be provided as needed for the study population. Devices will not be packaged but will be labeled according to **FDA** regulatory requirements.

The **LPI** will keep records documenting the receipt, use and return of the investigational device in the Investigational Device Management Form, including:

- Date of receipt
- ID of each investigational device
- Date of use
- Subject ID
- Date of device return
- Date of return of unused, expired or malfunctioning investigational devices, as applicable

10 Statistical Considerations

10.1 Statistical design and procedures

Phase I

The dataset will be assessed with descriptive statistics only, comparing the means and variance for the two data points: prior-evaluation (current device with current firmware) and post-evaluation (investigational device with investigational firmware). Acceptance criteria for the data, as applicable, is defined in **Table 4 Endpoints, test methods and hypotheses**.

Phase II

The hypotheses (A1, A2, D, F, G, H, J) will be assessed with one sample binomial test. Other hypotheses will be tested using a two-tailed, paired, student's t-test (if the data are deemed to be normal) or using the Wilcoxon signed-rank test (if the data are deemed to be non-normal).

Subgroup analysis will not be performed as no subgroups are defined.

Repeated measures analysis has the advantage of increased power vis-à-vis group allocations and reduction in error variance associated with individual difference, as each subject acts as its own control. This is important for studying amputees as the group is a small proportion of the total population, and with specific inclusion/exclusion criteria the total eligible population becomes very small, making it difficult to find and recruit subjects to attain an acceptable level of power. This limited population pool often results in slightly heterogeneous sample, as the amputees available are few and far between, in every sense. Furthermore, no single amputation procedure and therefore amputated stump is exactly the same, making the experience of each amputee a bit unique. The within-subject design significantly reduces the individual differences when comparing the two conditions.

The drawback of the design is the potential of “carryover effects”, i.e. experience from one condition can affect outcome or performance in the other condition, creating a confounding extraneous variable that varies with the independent variable. Such effects are: practice, positive carryover effect to the latter condition; and fatigue, negative carryover effect to the latter condition

10.2 Sample size calculation

Phase I:

Phase I is of exploratory nature, a convenience sample of 10 subjects are unexpected to complete the procedures.

Phase II:

Power analysis for the estimated required sample size was conducted using G*Power. See protocol below:

Exact – Proportion:	Difference from constant (binomial test, one sample case)		
Analysis:	A priori: Compute required sample size		
Input:	Tail(s)	=	One
	Effect size g	=	0.2834003
	α err prob	=	0.025
	Power (1-β err prob)	=	0.80
	Constant proportion	=	0.6666
Output:	Lower critical N	=	14.0000000
	Upper critical N	=	14.0000000
	Total sample size	=	15
	Actual power	=	0.8290491
	Actual α	=	0.0193871

It is therefore expected that **at least 15 subjects** are required to complete the protocol with a power of **0.80** and significance at **0.025**.

For pass/fail criteria, see Table 4 Endpoints, test methods and hypotheses.

10.3 Additional statistical matters

Any deviations from the statistical plan provided in this protocol will have to be approved by the sponsor and the reasons for the deviation reported in the clinical investigational report. Drop-outs and withdrawn participants will be included in the data analysis for the procedures that they completed. They will be grouped together and compared to the group that finished the protocol. Any statistical differences of the two groups will be reported. If the participants have not provided any data, they will not be included in the data analysis. No particular information will be excluded from the statistical analysis and tests, as described above.

11 Amendments and Deviations from the Protocol (CIP)

11.1 Amendments

Any amendments to this protocol must be first approved by the sponsor and PI, and then be evaluated by the IRB and, where appropriate regulatory authorities, before being implemented.

For non-substantial changes (e.g. minor logistical or administrative changes, change of monitor(s), telephone numbers, renewal of insurance) not affecting the rights, safety and well-being of human subjects or not related to the clinical investigation objectives or endpoints, a simple notification to the IRB and, where appropriate, regulatory authorities can be sufficient.

11.2 Deviations

Investigators are not allowed to deviate from this protocol without a formal approval from the IRB, if the deviation affects subject's rights, safety and wellbeing, or the scientific integrity of the clinical investigation. Any such deviation from the protocol is to be documented in detail and the report sent to the IRB.

Under emergency circumstances, deviations from the protocol to protect the rights, safety and well-being of human subjects may proceed without prior approval of the sponsor and the IRB. Such deviations shall be documented and reported to the sponsor and the IRB as soon as possible.

Investigators can request for an approval from the sponsor for a deviation if the deviation does not affect subject's rights, safety and wellbeing, or the scientific integrity of the clinical investigation.

In case of a deviation from this protocol taking place without prior approval from the sponsor, and IRB as applicable, it shall be reported to the sponsor within 24 hours of LPI knowledge of the deviation. The LPI responsible for the deviation is to send a report to the sponsor no later than five days after the deviation was reported. The report shall include:

- Reason for deviation
- When deviation took place
- Circumstances of the event
- Identification of all subjects affected by the deviation, if any
    - Details how each subject is affected, e.g. rights, safety or wellbeing
- Details how this deviation might affect the scientific integrity of the clinical investigation

The sponsor and the IRB will evaluate any deviations that take place without prior approval on a case-by-case basis. If the deviation affects subject's rights, safety and wellbeing, and the scientific integrity of the clinical investigation the LPI shall be disqualified from further participation in the clinical investigation.

12 Statement of Compliance

The clinical investigation is sponsored by Össur Iceland ehf.

It shall be conducted:

- in accordance with the ethical principles that have their origin in the Declaration of Helsinki
- in compliance with the ISO 14155 **[2]** International Standard
- in compliance with any regional or national legislations, as applicable

The clinical investigation shall not commence until the required approval from the IRB, and regulatory authority as applicable, has been obtained. Any additional requirements imposed by the IRB or regulatory authority shall be followed, as applicable.

Subjects are provided with health insurance with expenses covered of [redacted] relating to any adverse health outcomes in relation the clinical investigation. Insurance policy number: [redacted]

13 Ethical Considerations

13.1 Anticipated clinical benefits

A patient using the investigational device may or may not benefit clinically from using the device vis-a-vis using another prosthetic knee commercially available. Compared to not using a prosthetic knee the patient will benefit significantly in terms of mobility and ability to live independently.

Anticipated benefits include, among others: improved step-over-step stair navigation; reduced effort to sit/stand and reduce likelihood of falls. See **chapter 6** for details.

Finally, the benefit for the user during the testing is that he/she helps in developing a new MPK.

13.2 Device related risk

Each device designed and manufactured by Össur is subjected to thorough risk assessment, analysis and control, with failure mode effect analysis and hazard analysis, according to PR-00032 Risk Management process, based on ISO 14971 **[1]** (Risk Management for Medical Devices). All changes performed to the software and/or functions of a device are submitted to multi-level verification and, as applicable, validation processes before being authorized for use in a clinical investigation.

The FMEA and hazard analysis are tools for identifying harms, the sequence of events, their probability, and the potential failures that can cause these harms. Anticipated adverse device effects and residual risks associated with the investigational device, are identified in the Hazard Analysis Documentation HAD2016020971 **[3]** and Power Knee PKA01 Instructions for Use **[4]**.

The design criteria are an important input in the risk analysis but also the experience of existing products of similar function and/or type. The device Power Knee Mainstream is currently marketed by Össur; post-market surveillance data provides data on device related risks as experienced in the real-world application of the device:

Events, Incidents and Injuries

Annual Events

[redacted]

Reported to HA	Cases
No	[redacted]

Events, Incidents and Injuries		
Severity - Classification	Cases	Probability (P)
Moderate	[redacted]	
Fall, sustaining Moderate symptoms, stretching or tearing of soft tissue		
Falling, sustaining bone breakage/fracture		
Falling, sustaining cut, necessitating bandage		
Minor		
Falling, sustaining bruising or scraping		
Sustaining bruising or scraping		
Sustaining muscle and or tendon strain		
Negligible		
Falling without sustaining injury		
Insecurity		

Outcome from Post Market Surveillance (PMS) data has not given reason to update risk management documents. No new harm has been identified from the PMS data and results from analysis do not impact conclusion on final risk assessment.

The following reasonably foreseeable misuses have been identified based on current knowledge about transfemoral prosthetic devices and microprocessors-controlled prosthetic knees.

- Use of product by user exceeding the maximum user weight.
- Use of product by user not meeting the minimum user weight.
- Failure to properly maintain the product and/or maintain the product to the expected level of cleanliness.
- Product contamination by foreign substances or operation of the product in dirty or dusty environments.
- Failure to follow recommended or mandatory service schedule.
- Use of the product over the specified maximum life duration.
- User does not read user manual.
- User cannot read user manual.
- User's clinician is insufficiently trained.
- User receives insufficient training from clinician(s).
- Memory failure (user forgets clinicians' training/advice).
- Nascent Error (user performs well meant "optimization", short-cut or improvisation to unusual circumstances).
- User performs activity which subjects the investigational device to undue mechanical stress (jumping off a wall for example).
- Dropping the investigational device (when removing their prosthesis amputees often lean their prosthesis up against a wall which frequently resulting in the limb falling to the ground).
- User does not charge the prosthetic knee.
- User does not have good control over the residual limb.

For a list of foreseeable adverse events and anticipated adverse device effects, together with their likely incidence, mitigation or treatment see Power Knee PKA01 Instructions for Use **[4]**.

13.3 Risk of Study (To Patient)

During each visit, the local principal investigator, a certified prosthetist and orthotist, and the study monitor will be present to ensure the safety. Potential risks with using the Power Knee Mainstream Firmware Update, are the same as using Power Knee and only Power Knee users or users who tried Power Knee, that have been fully trained on the device and its controls, will be recruited.

The study adds no additional risk. Subjects will use the investigational device as their primary prosthesis in the same manner as they would normally do on their current prosthesis. Thus, they are not required to do anything different from their routine clinical visit for acquiring a new MPK prosthesis and their daily living activities.

13.4 Risk Mitigation

For each device designed by Össur risk mitigation is part of the design process according to ISO 14971 **[1] [3].** Furthermore, for each fitting with the Power Knee Mainstream with the updated firmware, a fully qualified professional will ensure the safety of the user. Only Power Knee Mainstream users, that have been fully trained on the device and its controls, will be recruited.

13.5 Benefit-Risk Rationale

The development of a MPK prosthesis is controlled by a multi-level verification and validation processes before being authorized for field testing and subsequent release. The Design & Verification process execution, coupled with the risk management and control strategy deployed for POWER KNEE Mainstream Firmware Update ensure that the risks associated with use of the device in typical daily living conditions does not exceed risks level associated with the operation of any such device under similar conditions.

The residual risks of the investigation and the investigational device are minimal and are significantly out weighted by the benefits of participating in the investigation.

13.6 IRB Review and Communications

The study protocol (CIP), informed consent form, and other study documentation forms require IRB review and approval. Communication to and from the IRB shall be directed from or to the primary Össur contact, the **Sponsor Co-Investigator/Monitor**. Continuous communication will be maintained between Össur and the IRB, as required. Moreover, communication will be maintained between the **LPIs and PI** and the IRB, as required.

13.7 Vulnerable populations

No vulnerable populations will be enrolled.

13.8 Informed Consent

The Local Principal Investigator (LPI) at each site, or any researcher qualified, will obtain from the subject, written signed informed consent form to his/her inclusion in the study, after explaining the rationale for and the details of the study, the risks and benefits of alternative treatments, and the extent of the subject's involvement. The subject will receive a copy of the informed consent.

The protocol consists of different phases, subjects will consent only for the phase they participate in. Signing the ICF only applies to the current phase. If a subject participates in one phase it does not mean they have to participate in the other phases. Enrollment for each phase is separate.

The subjects will be informed that their participation is voluntary and that they can withdraw from participation at any time, at his/her discretion and this will not have any consequences for the participant’s treatment.

In case the information on the ICF changes, and subjects need to be provided with new information, the LPI will contact each subject by phone and explain the new information as required.

Subjects that for any reason are unable to provide informed consent will not be enrolled in the study.

13.9 Participant confidentiality – Data management

a) Subjects will be assigned a random study identification (ID) number. This ID will be used in all relevant documentation. Confidentiality of all relevant subject feedback and information will be maintained through use of the identifying number only, in all documentation. The study sponsor, Össur, will remain the sole owner of the study data.

Data will be collected and stored either through the Electronic Data Capture (EDS) system Smart-Trial, or via paper based CRFs.

A list connecting the ID to the subject´s name will be stored either in the Electronic Data Capture (EDS) system Smart-Trial or in a locked file with the LPI at each site. Only appropriately qualified individuals designated by the Investigator will have access to this information. Access is controlled by password protected accounts. Accounts are enabled with designated permissions only.

b) Physical source data (e.g. signed Informed Consent forms and paper based forms as applicable) will reside in the Local Principal Investigator Site File. This will be physically locked and accessible to the Investigator only.

c) Case report forms in Smart-Trial are developed in accordance with this protocol and are quality checked against the protocol by the study team before use, the same is true in case of paper-based CRFs. In Smart-Trial, validated fields and reference rules are used to control quality of data on entry and where required the order of data collection. In case of paper based CRFs they are reviewed by the investigator and a study monitor to ensure completeness of data.

Data that are missing or collected out of timeframe will be flagged. Smart-Trial contains audit history and data query functionality, in case of paper based CRFs, data queries are raised by the investigator or study monitor. Data queries may be raised ad hoc or at scheduled monitoring visits. Data queries may be reconciled by designated individuals (by account permissions in Smart-Trial) only. Where physical records are used these will be stored as source data in the investigator site file and attached to Smart Trial forms as scans if applicable.

d) The Smart-Trial system is validated as per the Össur QMS Software Validation process PR-00037 **[5]** reported in VAL1825 **[6]**. The validation of the software system consists of review of Smart Trial company validation records. The validation of individual case report forms against the study protocol is performed by the study team and recorded.

e) In case of electronic data collection; SMART-TRIAL (www.smart-trial.com) will be used as the primary Electronic Data Capture tool in this study. SMART-TRIAL is designed and developed in compliance with the PIC/S Guidance, PI-011-3 Good Practices for Computerized Systems in Regulated “GxP” Environments, with software validation based on IEC 62304. SMART-TRIAL is designed to enable the user to comply with Good Clinical Practice (ISO 14155:2020), ICH GCP and other industry requirements, such as FDA 21 CFR Part 11 and HIPAA. All data in SMART-TRIAL is collected, transferred, and stored encrypted in databases, which are hosted on Microsoft Azure ISO certified servers that are managed by SMART-TRIAL within the European Union (Dublin, Ireland). Backups are performed continuously throughout the day and stored within the same server. Given that Smart-Trial does send messaging to patients in research studies, as part of the informed consent process, (as reviewed by the IRB), patients will be asked to consent to communications through these channels. Smart-Trial is adherent to CAN-SPAM and international equivalents. Frames in video recordings will only contain the lower extremities of subjects and any ambulatory assistance provided with their hands. Frames containing the face or other identifiable features of subjects will be deleted immediately, if accidentally captured.

The data of subjects that withdrawn from participation will be deleted unless a specific agreement with these subjects to evaluate their data can be obtained.

g) Photographs and frames in video recordings will only contain as far as possible the lower extremities of subjects and any ambulatory assistance provided with their hands only. Frames containing the face or other identifiable features of subjects will be blurred, cropped or deleted if accidentally captured. The data of subjects that are withdrawn from participation will be retained. Subjects may request that their research data is delinked from their personally identifiable data during the course of the study.

h) In case of EDS, database entry is locked after final patient data is entered. Database is closed and deidentified data exported by the sponsor Co-investigator/Monitor on completion of close-out monitoring activities including resolution of all data queries. Smart Trial audit history is extracted for records of monitoring activities. Exported de-identified data is stored on password protected PC intranet for analysis. In case of paper based data collection, de-identified data is scanned and shared with the sponsor Co-investigator/Monitor after data collection is complete.

Representatives of the sponsor, sponsor co-investigators and monitors, will be present at the study sites. A declaration of confidentiality to be signed by the representatives, ensures necessary data protection. Sponsor representatives will only observe and not interact with subject during the investigational procedures.

i) The data retention period for unlinked clinical data will be a minimum of 5 years in accordance with ISO 14155:2020. Clinical investigation documents, including but not limited to CIP, CIB, CRFs and clinical investigation report(s) should be incorporated into the device technical documentation under the quality management system of the manufacturer.

k) A Clinical Investigation Report (CIR) will be generated by Össur Medical Office. The report will be stored with the device technical file within Össur Quality Management System, along with the unlinked data and all accompanying investigational documents, according to the R&D and Quality documentation procedures. Subjects participating in the study can have access to the results, on demand, when the CIR is internally published.

Study results, data, and documentation will be stored for a minimum of 5 years.

14 Evaluation of Adverse Events and Device Deficiencies

For a list of foreseeable adverse events and anticipated adverse device effects, together with their likely incidence, mitigation or treatment see chapter 13.2 above and in the Power Knee PKA01 Instructions for use **[4]**.

14.1 Definitions of adverse events, effects and deficiencies

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.

An adverse device effect (ADE) is any adverse event related to the use of an investigational medical device, including events resulting from insufficient or inadequate instructions for use, operation, malfunction, etc.

A serious/severe adverse event (SAE) is an AE that:

- Is life-threatening or fatal
- requires or prolongs hospitalization
- results in permanent impairment of a body function
- or results in permanent damage to a body structure.

A serious/severe adverse device effect (SADE) is an adverse device effect that has resulted in any of the consequences characteristic of a SAE.

An anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk management for the device.

An unanticipated adverse device effect (UADE) is a serious adverse effect on health or safety of participants caused by the device if not previously identified in nature, severity, or degree of incidence in the protocol (CIP) or the risk analysis for the device.

A device deficiency (DD) is the inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, use errors, and inadequate labelling.

A use error (UE) is an act or omission of an act that results in a different medical device response than intended by the manufacturer or expected by the user.

See ISO 14155 **[2]** for details.

14.2 Reporting procedures

All device related adverse events will be investigated. Adverse events that are serious, unanticipated and (possibly) device related shall be reported to the sponsor by telephone as soon as possible. The complete adverse event investigation form shall be faxed to the sponsor within 24 hrs. Within ten days the Sponsor will report to the IRB

and FDA. Any serious device related adverse event will lead to the immediate termination of the trial. In this case all participants will be contacted immediately.

As the investigational device will only be used on site under supervision of investigators adverse events will be reported immediately.

Participants will be provided the contact information of the investigator and told to call them in the event of an adverse event that may be connected to previous use of the device.

The investigator shall supply a copy of the complete adverse event investigation form, together with a cover letter to the IRB when events are judged to be serious, unanticipated and (possibly) device related.

Contact in case of serious adverse events and serious adverse device effects:

Pete Simpson mobile: (208)-915-6338; email : psimpson@ossur.com

Any device deficiencies that did not lead to an adverse event but could have led to a medical occurrence

- if either suitable action had not been taken,
- if intervention had not been made, or
- if circumstances had been less fortunate,

shall be reported according to the same procedure as if an ADE had taken place, specified above.

14.3 Suspension or premature termination of the clinical investigation

The sponsor/principal investigator, the IRBs, and the regulatory authorities can decide about investigation continuation. The clinical investigation can be suspended or prematurely terminated if the serious adverse device effects are considered disproportionately large compared to the possible benefits of the intervention. If the investigation is terminated or suspended all participants will be informed and appropriate follow-up will be assured. If sponsor/principal investigator terminates or suspends the investigation the relevant IRBs and regulatory authorities will be provided with a detailed written explanation of the termination or suspension.

The sponsor/principal investigator can upon completion of the analysis of the reason(s) for a suspension decide to lift the suspension, when the necessary corrective actions have been implemented. The investigators, IRBs, and relevant regulatory authorities will be notified and provided with the relevant data supporting the decision.

Breaking of blinding will not be relevant in this trial, since group allocation is visible.

15 Publication Policy

These results are for internal consumption by Össur employees involved with the project, marketing and for regulatory documentation purposes.

Publication will be pursued as agreed by the Sponsor and Investigator.

16 References

Internal Document References:

[1]	EN ISO 14971, Medical devices - Application of risk management to medical devices
[2]	EN ISO 14155, Clinical investigation of medical devices for human subjects - Good clinical practice
[3]	HAD2016020971, Hazard Analysis, [redacted]
[4]	Power Knee PKA01 Instructions for Use
[5]	Software Validation process PR-00037
[6]	Smart-Trial Validation Report VAL1825
[7]	LDR2019020703, Literature Review Device Report, [redacted]
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External Literature References:

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