Power Knee Mainstream - Clinical Investigation Protocol

Clinical trial (Beta) of Power Knee Mainstream - Dynamic

Power Knee

CONFIDENTIAL DOCUMENT

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2 Summary

Device(s) being tested:	POWER KNEE MAINSTREAM – Dynamic, a pre-market device comparing to users' current microprocessor-controlled knee (MPK). For simplification the device under evaluation in this Clinical Investigation will be referred to as "investigational device" throughout this document.	
Instruments and equipment:	6MWT, Borg scale, Amputee mobility predictor (AMPro), Plus-M (12 item), PEQ, PMQ, L-test, video, data logging by Össur Logic, in house questionnaire for amputee and CPO.	
Subjects recruited:	Inclusion criteria:	Exclusion criteria:
15-18 amputee subjects Up to 5 CPO subjects	50Kg< body weight < 116Kg	50Kg> body weight > 116Kg
	K3-K4 amputees with unilateral transfemoral amputation or Knee disarticulation	Bilateral amputees
	Allows for 37mm knee center height to dome of pyramid alignment	Users with socket problems
	Currently using a MPK or Power Knee	Users with co-morbidities in the contra-lateral limb, which affect their functional mobility
	Older than 18 years old	Younger than 18 years old
	No socket issues/changes in the last 6 weeks and no socket changes expected during the duration of the study period.	Users with stump pain
	Comfortable and stable socket fit	Users with cognitive impairment
	Willing and able to participate in the study and follow the protocol	Users not involved in other clinical tests and/or receiving treatment that the testing might affect.
Procedures:	This is a prospective two group cross-over study, within subject comparison. 3 study visits are planned for amputee subjects, with approximately 2-3 weeks between visits, and an optional fourth visit 8-12 weeks after the third visit. During the first visit subjects will be check for inclusion/exclusion, consented and randomly	

	assigned into two groups and Group 1 (transitioning to the investigational device) will perform functional tests (6MWT, L-test, Borg scale, AMPro) and answer questionnaires on the performance of their current prosthesis to provide baseline information. The Group 1 subjects will be fitted and trained on the investigational device and a recommended prosthetic foot which they will use as their prescribed prosthesis for 2-3 weeks until the second visit, the other half will stay on their prescribed prosthesis until the second visit. During the second visit the subjects of Group 1 will perform the same functional tests as in the first visit (6MWT, L-test, Borg scale, AMPro) on the investigational device and answer questionnaires on the performance of the investigational device, and then return to their prescribed prosthesis. The Group 2 will perform the same tests/questionnaires on their prescribed prosthesis and then be fitted and trained on the investigational device and use it as their usual prosthesis for 2-3 weeks. During the third visit all subject will repeat the tests and questionnaires on the prosthesis they are fitted with (Group1 on the prescribed and Group 2 on the investigational device). Subjects will have the option to use the investigational device for an additional 8-12 weeks, those who choose that will be fitted with the investigational device or will stay on it, depending in which they are in at this point. They will be booked for the fourth visit; they will be contacted via telephone 4-5 weeks later and asked to provide feedback on their experience with the device so far. Those that choose not to keep using the investigational device will be returned to their prescribed prosthesis. During the fourth visit subjects will answer the same questionnaires and perform the same functional tests as the other visits. Data will be collected from the knee on activity. They will then be fitted back to their prescribed prosthesis. End of study. CPO subjects will answer a questionnaire on the ease of setup of the investigational device and provide feedback on the ease of setup of gait functions. See Table 1 below.

Table 1 Summary of procedures and visits

Procedure/activity	Recruitment phase: 2-6 weeks prior to baseline	Group 1 visit 1: Baseline	Group 2 visit 1: Baseline	Group 1 visit 2: 2/3w F/U	Group 2 visit 2: 2/3w F/U	Group 1 visit 3: 4/6w F/U	Group 2 visit 3: 4/6w F/U	Visit 4 Optional 8-12w F/U
Potential subjects identified, fitting inclusion/exclusion criteria, by PI from customer database	X							
PI calls potential subjects and pre-screens by telephone	X							
Subject signs ICF, randomization		X	X					
Fitting, Training		X			X			
Subject fills in questionnaires		X		X	X	X	X	X

Subject performs 6MWT w/Borg scale and L-test	X	X	X	X	X	X
PI prints out activity report from investigational device		X			X	X
Subjects that choose to keep using the investigational device are given an appointment in 8-12 weeks from visit 3. Others are fitted with their prescribed prosthesis and end participation.				X	X	
All subjects still active are fitted back to their prescribed prosthesis, end of study.						X
CPO subjects provide feedback on fitting the investigational device	X		X			

3 Changes from Previous Revision

[redacted]

4 Abbreviations

6MWT	Six Minute Walk test
ADE	Adverse Device Effect
AE	Adverse Event
AMPRO	Amputee Mobility Predictor (prosthesis users)
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
CT	Clinical Trial
EC	Ethics Committee (see IEC, IRB, REB and REC)
FU	Follow-Up
ICF	Informed Consent Form
IDMF	Investigational Device Management Form
IEC	Independent Ethics Committee
IFU	Instructions For Use
IRB	Independent/Institutional Review Board
LCI	Local Co-Investigator
LPI	Local Principal Investigator
LRA	Local Research Assistant
PEQ	Prosthesis Evaluation Questionnaire
PI	Principle Investigator
PIS	Participant Information Sheet
PKM	Power Knee Mainstream
REB	Research Ethics Board
REC	Research Ethics Committee
SAE	Serious Adverse Event
SADE	Serious Adverse Device Event
SOP	Standard Operating Procedure
SOTA	State-Of-The-Art
SRA	Sponsor Research Assistant
USADE	Unanticipated Serious Adverse Device Effect

5 Investigational Device

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:	The investigational device is a motor driven microprocessor-controlled prosthetic knee, intended for moderate to high active transfemoral or knee disarticulation amputees. It provides support in locomotion tasks as well as non-cyclical tasks through powered flexion and extension. The investigational device is used with a smart app to adjust and interact with the knee.
Manufacturer of the investigational device:	Össur ehf. Grjothals 1-5 110 Reykjavik Iceland
Name or number of the model/type, including software version and accessories, if any, to permit full identification:	POWER KNEE MAINSTREAM – Dynamic (No product number yet, software version not available yet) Accessories: Lithium Ion Battery pack (no product number yet) Össur Logic is an iOS smart app and it is required to adjust and interact with the knee. It is a standalone software as a medical device, used with other bionic devices as well, the app is documented separately, see **[1].**
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 use as described below. 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:	Unilateral transfemoral / knee disarticulation amputation Bi lateral transfemoral /knee disarticulation amputation **Targeted Medical Indications:** Any medical reasons resulting in amputation at or above the knee level.
Description of the investigational device:	POWER KNEE MAINSTREAM - Dynamic 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 – Dynamic is composed of four devices. Operation of the motorized knee prosthesis relies on a detachable battery pack, which provides system power, and a Prosthesis Configuration Device (software application) 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, the battery pack is provided and an off-the-shelf power supply, allowing conveniently recharging the battery pack when not used in the knee prosthesis. POWER KNEE MAINSTREAM - Dynamic is intended for moderately and highly active amputees (K3 to K4) of moderate/high impact levels, building on established powered knee technology and utilizing the clinical benefits associated with powered prosthetics. The system should not impose any activity limitations and should be designed for ease of use of K3 and K4 users. The device is a non-invasive, single patient, reusable system. 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 - Dynamic is connected to. In other words, the POWER KNEE MAINSTREAM - Dynamic is not in direct physical contact with the amputee. An amputee typically wears prosthesis and thereby utilizes the POWER KNEE MAINSTREAM - Dynamic, 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. 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 Use:** The POWER KNEE MAINSTREAM - Dynamic is intended to fulfil the requirements associated with daily ambulation of individuals showing an average to high activity level. The product targets an amputee population that are trans- femoral unilateral amputees showing good control over their residual limb with respect to the locomotion task range that they intend to address. Based on the user activity level, stump capacity and personal preferences, the product can be configured as a walking-only product or support the complete range of locomotion tasks introduced below. While being optimized for average users, the product can be used by amputees with a body mass ranging from 50kg to 116kg, as long as the maximum assistance and support levels provided by the motorized prosthesis are shown sufficient to sustain the safe product usage. The following paragraphs provide more details on the product intended typical use for the various supported locomotion tasks. **Locomotion Tasks:** POWER KNEE MAINSTREAM - Dynamic provides complete support of the most commonly encountered locomotion tasks in daily living. Moreover, in order to properly address the requirements of a wide range of user activity levels, residual limb control and strength, the product allows the user-specific configuration of the product features, such that optimal performance and safety can be achieved on a user-specific basis. The following paragraphs provide more details on the supported locomotion tasks. Walking: The POWER KNEE MAINSTREAM - Dynamic sustains typical level walking through stance-phase flexion control and swing phase kinematics restoring, while contributing to the overall user forward progression. Automatic cadence adjustment, as well as heel rise control, is provided in order to optimize the product performance with respect to the user needs and personal preferences. Stairs Ascent: The POWER KNEE MAINSTREAM - Dynamic sustains step-over-step stairs ascent for intended users by providing mechanical assistance in the push-off phase and swing phase kinematics in order to favour proper and timely foot placement. For users showing limited residual limb control and strength, it is possible to block this locomotion task. Stairs Descent: The POWER KNEE MAINSTREAM - Dynamic sustains step-over-step stairs descent for intended users by providing mechanical support in the controlled lowering phase of the gait cycle, while again focusing on kinematics and foot placement during the swing phase. Inclined Planes: The POWER KNEE MAINSTREAM - Dynamic can be used on inclined planes ascent and descent for intended users. Again, the product provides assistance and/or support as per configured for each specific task, while proper

	kinematics and foot placement represent the focus of the swing phase. Non-cyclical Tasks: The POWER KNEE MAINSTREAM - Dynamic provides either support, assistance, or remains passive for tasks such as standing, sitting, sit-to-stand transfer, stand-to-sit transfer, and kneeling. **Operational Environment** POWER KNEE MAINSTREAM – Dynamic device is intended for use in indoor and outdoor environments, in common daily living environments, like home, office, and public location. POWER KNEE MAINSTREAM – Dynamic device is intended to support typical use in commonly encountered weather conditions, like rain, fog, cold, etc. **Product Configuration** The product is intended to be used with Ossur's standard prosthetic components. It is configured with standard proximal and distal connectors, allowing use with most commonly encountered socket technologies and shank replacement products. Foreseen ankle-foot products to be used with this product are Ossur's Pro-Flex pivot, Pro Flex XC and/or Pro-Flex LP. The device does not incorporate, as an integral part, a substance or human blood derivative referred to in Section 7.4 of Annex I of 93/42/EEC, amended by 2005/50/EEC. It is manufactured without utilizing tissues of animal origin as referred to in Directive 2003/32/EC. Training requirements for subjects and procedures relating to fitting and use of a device will for all general purposes be similar to the training and procedures required for using a CE- marked device of a similar type. POWER KNEE MAINSTREAM - Dynamic is a microprocessor controlled prosthetic knee. It is used exclusively for exo- prosthetic fitting of 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 - Dynamic in a functioning prosthesis. The POWER KNEE MAINSTREAM - Dynamic 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 - Dynamic, such that parameters can be optimized for an amputee. As the POWER KNEE MAINSTREAM - Dynamic is battery powered (rechargeable lithium ion) a charger is required. The device is classified as ***ASSEMBLY, KNEE/SHANK/ANKLE/FOOT, EXTERNAL*** according to Title 21 §***890.3500***, bearing the product code ***ISW***: "***External assembled lower limb prosthesis.***". It is 510(k) and GPM exempt, except for general requirements.

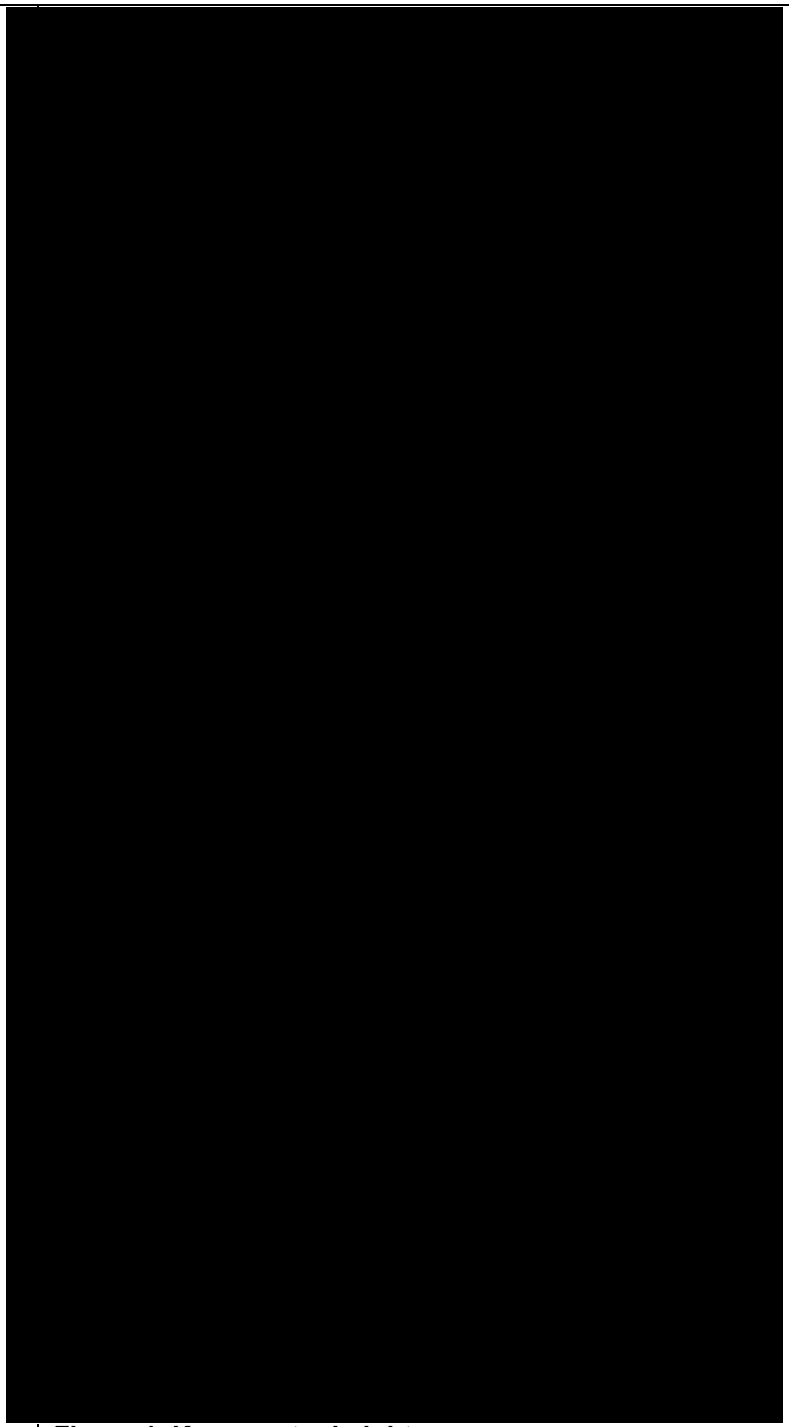

Figure 1, Knee center height

	[redacted] **Figure 2, POWER KNEE MAINSTREAM - Dynamic** 
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 device of a similar type. The device should be supplied and fitted by a certified CPO.
Specific medical or surgical procedures involved in the use of the investigational device:	N/A

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 showed 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 trans-femoral 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 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 **[3]**.

Results of studies on previous versions of the Power knee indicate that the PK 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.[3] 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.[4] 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.

Preclinical testing

Variety of tests and activities have been carried out to verify the safety and performance of the investigational device. Structural test summary is presented in **20 Annex**.

Based on the intended use of the device, as it is not intended to be used directly on skin, the outcome of the risk analysis and that vendors have supplied verification that the device contains no Materials of Concern, biocompatibility testing was not necessitated.

Based on the results of these tests, calculations, specifications, and design verification and validation activities it is considered justifiable to use the device in human subjects.

Existing clinical data

No clinical data exists for the investigational device.

[redacted]

The data represented in the PMS report was gathered from Ossur's complaint and service system. Information from field reports (Weekly AM Reports from Ossur Americas) were used to track user and customer feedback over time. **[2]**

7 Objectives and Hypotheses

The primary objective of this study is to evaluate the efficacy of the investigational device in reducing exertion during walking compared to passive MPKs.

Additionally to evaluate the efficacy of the investigational device in the short and long term compared to passive MPKs and previous versions of the Power Knee, during daily living activities i.e. walking on level ground, in stairs and inclines, rising from and sitting down to a chair as well as performance of gait functions and ease of set up for average to highly active transfemoral/knee disarticulation amputees and CPOs.

[redacted]

No risks or anticipated adverse device effects (ADE) are to be assessed. Any side-effects occurring will be documented.

The hypotheses and endpoints are specified in Table 4.

***For all hypothesis*:**
$\mu_1 is\ average\ of\ measurements\ with\ comparator\ at\ 2\ weeks;$
$\mu_2 is\ the\ average\ of\ measurements\ at\ 2\ week\ follow\ up\ (investigational\ device);$
$\mu_3 is\ the\ average\ of\ measurements\ at\ 8-12\ week\ follow\ up\ (investigational\ device);$

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

Table 4 Endpoints, test methods and hypotheses

	Hypothesis	Test Method	Endpoint	Acceptance Criteria
A	Subjects **reduced exertion performing 6MWT** compared to previous prosthesis (primary outcome)	*BORG scale*	*Mean difference in BORG score pre and post 6MWT compared to comparator*	$H_0: \mu_1 \leq \mu_2$ $H_1: \mu_1 > \mu_2$ *p<0.05*
B	Subjects **improved performance in 6MWT** compared to previous prosthesis.	*6MWT (meters)*	*Average distance walked in 6MWT compared to comparator*	$H_0: \mu_1 \geq \mu_2$ $H_1: \mu_1 < \mu_2$ *p<0.05*
C	Subjects report on average no worse **support in sit to stand and stand to sit** than with previous prosthesis.	Self-report*:* *PMQ (Questions 9 and 10)* *Likert scale 0-4*	*Total score of PMQ questions 9 and 10 compared to comparator*	$H_0: \mu_1 \geq \mu_2 + \lvert M_{NI} \rvert$ $H_1: \mu_1 < \mu_2 + \lvert M_{NI} \rvert$ $\lvert M_{NI} \rvert = 1$ *p<0.05*
D	Subjects perceived **safety in hill descent** is no worse than with previous prosthesis.	Self-report: *Modified PEQ 14F (rate your **safety** when walking down a steep hill using the prosthesis)* *Likert Scale 1-10*	*Average score compared to comparator*	$H_0: \mu_1 \geq \mu_2 + \lvert M_{NI} \rvert$ $H_1: \mu_1 < \mu_2 + \lvert M_{NI} \rvert$ $\lvert M_{NI} \rvert = 1$ *p<0.05*
E	Subjects perceived **safety in stair descent** is no worse than with previous prosthesis.	Self-report: *Modified PEQ 13D (rate your **safety** when walking downstairs using the prosthesis)* *Likert Scale 1-10*	*Average score compared to comparator*	$H_0: \mu_1 \geq \mu_2 + \lvert M_{NI} \rvert$ $H_1: \mu_1 < \mu_2 + \lvert M_{NI} \rvert$ $\lvert M_{NI} \rvert = 1$ *p<0.05*
F	Subjects perceive **no speed limitation** while walking with the investigational device.	Self-report(yes/no): *„Are you satisfied with your walking speed using your prosthesis/test prosthesis?"* Support question: *"Do you feel that your walking speed is limited by your prosthesis/test prosthesis?"*	*Proportion of subjects (p) reporting satisfaction with walking speed on investigational device.*	$H_0: p < 80\%$ $H_1: p \geq 80\%$ *p<0.05*
G	Subjects reported ability to ambulate over **typical environmental obstacles** with the investigational device is no worse than with previous prosthesis.	Self-report: *PMQ (Question 2-7)* *Likert scale 0-4* *PLUS M*	*Total score of PMQ questions 2-7 and PLUS M T-score compared to comparator.*	*For PLUS-M:* $H_0: \mu_1 \geq \mu_2 + \lvert M_{NI} \rvert$ $H_1: \mu_1 < \mu_2 + \lvert M_{NI} \rvert$ $\lvert M_{NI} \rvert = 10T$ *For PMQ questions:* $H_0: \mu_1 \geq \mu_2 + \lvert M_{NI} \rvert$ $H_1: \mu_1 < \mu_2 + \lvert M_{NI} \rvert$

				$\lvert M_{NI}\rvert = 3$ *p<0.05*
H	Subjects safe and stable **stance phase perception** no worse than previous prosthesis.	Self-report: *Modified PEQ 13A (rate your **safety** (during stance phase) when walking with your prosthesis/test prosthesis)* *Likert Scale 1-10*	*Average score compared to comparator*	$H_0: \mu_1 \geq \mu_2 + \lvert M_{NI}\rvert$ $H_1: \mu_1 < \mu_2 + \lvert M_{NI}\rvert$ $\lvert M_{NI}\rvert = 1$ *p<0.05*
I	Provides **comfort in standing** no worse than previous prosthesis.	Self-report: *PEQ-Question 1D* *"Rate your comfort while standing when using your prosthesis/test prosthesis"* *Likert Scale 1-10*	*Average score compared to comparator*	$H_0: \mu_1 \geq \mu_2 + \lvert M_{NI}\rvert$ $H_1: \mu_1 < \mu_2 + \lvert M_{NI}\rvert$ $\lvert M_{NI}\rvert = 1$ *p<0.05*
J	The investigational device provides **easier setup for CPO** compared to previous version of power knee	Self-report: *Likert Scale 1-10*	*Average score compared to previous versions of PK*	$H_0: \mu_1 \geq \mu_2$ $H_1: \mu_1 < \mu_2$ *p<0.05*
K	The investigational device provides **no worse ease of setup for CPO** compared to SOTA passive MPKs	Self-report: *Likert Scale 1-10*	*Average score compared to SOTA MPKs*	$H_0: \mu_1 \geq \mu_2 + \lvert M_{NI}\rvert$ $H_1: \mu_1 < \mu_2 + \lvert M_{NI}\rvert$ $\lvert M_{NI}\rvert = 1$ *p<0.05*
M	The investigational device provides **acceptable noise level**	Self-report: *PEQ- Questions 3K, 3L* *Likert Scale 1-10* Support question (yes/no) *"Would the noise from the test device prevent you from preferring it as your usual prosthesis?"*	*Proportion of participants (p) with average score of PEQ 3K & 3L over 5 with investigational device.*	$H_0: p < 80\%$ $H_1: p \geq 80\%$ *p<0.05*
L	The investigational device provides **ease of use of gait functions no worse than previous device**	Self-report: *PMQ (Questions 1 and 3-6)* *Likert scale 0-4* Objective measure *L-test*	*Total score of PMQ questions1, 3-6.* *Proportion of subjects (p) successfully completing the L-test using gait functions.*	*For PMQ score:* $H_0: \mu_1 \geq \mu_2 + \lvert M_{NI}\rvert$ $H_1: \mu_1 < \mu_2 + \lvert M_{NI}\rvert$ $\lvert M_{NI}\rvert = 2{,}5$ *p<0.05* *For L-test:* $H_0: p < 80\%$ $H_1: p \geq 80\%$ *p<0.05*
M	**Side effects** N/A	*Side effects*	*Occurrence of side effects*	*N/A*

N	**Mobility** using the investigational device **is no worse** than with the comparator	*PMQ total score (0-48)*	*Average total score of the PMQ*	$H_0: \mu_1 \geq \mu_2 + \lvert M_{NI} \rvert$ $H_1: \mu_1 < \mu_2 + \lvert M_{NI} \rvert$ $\lvert M_{NI} \rvert = 5{,}5$ *p<0.05*
O	**Activity level** increases with longer adaptation period on the investigational device	*Activity reports from the knee (daily steps, use time)*	*Activity level after 8-12w follow up compared to 2w follow up on investigational device*	$H_0: \mu_2 \geq \mu_3$ $H_1: \mu_2 < \mu_3$ *p<0.05*

Informative endpoint: In house usability questionnaire (Perceived weight, size, look, ergonomics, fit w/clothes, battery life, preference, falls questionnaire)

8 Design of the Clinical Investigation

8.1 General

The test will be a two group prospective cross-over design, within subject comparison. 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 subject's previous device.

All investigational activities will be conducted at MCOP Silver Spring Prosthetic Clinic (2421 linden lane, Silver spring Md, 20910), Medical Center Boston, MA Prosthetic Clinic (500 Lincoln Street, Allston, MA 02134) and Motus Research (975 W. Walnut Street Indianapolis, IN 46202).

As stated above the primary endpoint is the perceived exertion during walking measured by the Borg scale before and after 6MWT, see table 4, and the secondary endpoints are focused on the general mobility performance and efficacy of the investigational device, as well as performance of gait functions and ease of set up for average to highly active transfemoral/knee disarticulation amputees and CPOs. 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:

The Six Minute Walk test (6MWT) is simply a record of the distance traveled by a given patient at his or her self-selected walking speed over a period of six minutes. All that is required is a stopwatch and a walking corridor or track of known distance[5,6].

The Borg Scale of Perceived Exertion[7] is a subjective rating scale on which people indicate their perceived exertion and has been used with people with lower-limb amputation[8].

The Amputee mobility predictor (AMPro) is a 20-item scale that was originally developed to provide a more objective approach to the assignment of Medicare K-levels. The scale includes tasks intended to assess sitting balance, transfers, standing balance, gait, and obstacle negotiation and takes around 15 minutes to administer[6].

The Prosthetic Mobility questionnaire (PMQ) is a measure of perceived ability to perform a range of ambulation and transfer tasks with a lower limb prosthesis. PMQ has been reported to have high internal consistency, great test-retest reliability, and good convergent construct validity in people with lower limb amputation. PMQ will be administered as recommended by Franchignoni et al.[9] PMQ is scored from 0 to 4; higher scores indicate higher perceived ability.

The Prosthesis Evaluation Questionnaire (PEQ) measures prosthetic-related quality of life. It consists of 82 items grouped into nine subscales. In addition, there are individual questions not contained in the subscales regarding satisfaction, pain, transfers, prosthetic care, self-efficacy, and importance[10].

L-test of functional mobility is a modified version of the Timed up and go test (TUG) developed for more active lower limb amputees. The patient begins the test seated in a chair, ideally positioned in an exam room and facing the entrance to the hallway. The patient rises from the chair, walks three meters into the hallway, turns 90 degrees and then walks an additional seven meters down the hallway. Upon completing seven meters, he turns 180 degrees, returns down the hallway, turns 90 degrees to face the exam room, and returns the three meters to his chair, where he retakes his seat[11]

The Plus-M is a self-report instrument for measuring mobility of adults (age 18+) with lower limb amputation who have experience of using a prosthesis. PLUS-M measures prosthetis users' mobility (i.e., their ability to move intentionally and independently from one place to another). The questions assess respondents' perceived ability to carry out specific activities that require use of both limbs. PLUS-M questions cover movements that range from basic ambulation such as walking a short distance indoors to more complex outdoor activities such as hiking for long distances[12,13].

Video

Data logging by Össur Logic

See chapter **10.2 Sample size calculation** and **Table 4** for analysis of variables.

Equipment required for each amputee subject:

- Pen/pencil
- Detailed protocol
- Printed out instruments and instructions (Case report forms, PEQ, PMQ, AMPro, PLUS-M, Borg scale, in-house questionnaire)
- Logbook/Notebook
- Stopwatch/phone for 6MWT
- Markers and a measured corridor/course of known distance for 6MWT and L-test
- Chair for L-test and AMPro
- Measuring tape
- 10cm obstacle for AMPro
- Investigational device: Power Knee Mainstream (along with test foot and components as applicable).
- Tools for fitting

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

8.2 Investigational Device(s) and Comparator(s)

The investigational device is a powered microprocessor controlled prosthetic knee, with the same intended use as the previous version of the device (POWER KNEE II, a CE- marked device). See full details on the investigational device in **Clinical investigators brochure [3].**

When the investigational device is on the market the device will be a single user device, with a typical use time of 5 years. Due to supply shortage, for clinical testing purposes the same investigational device may be used iteratively for periods of up to 3 weeks, maximum 3 times. Before refitting of a device, a reset to manufacturer settings will be performed as well as inspection for damage or malfunction. This supply shortage only refers to

visits 1 and 2 in the test procedure due to time limitations. For visit 3, investigational devices will be available for all users.

The subjects will be asked to use the investigational device as their primary prosthesis for **2-3** weeks. Individual exposure will differ between subjects. Subjects are expected to use the investigational device for their daily living activities as they would with any other prosthesis, for up to 18 hours a day depending on the individual. The comparator device will not be used within the timeframe of the intervention period of the study. Subjects will evaluate and provide feedback on their exposure of the comparator at baseline and prior to them being fitted to the investigational device or after, depending on the group they are assigned to. The investigational device is used with a smart app to adjust and interact with the knee. Össur Logic is an iOS smart app and it is required to adjust and interact with the knee. It is a standalone software as a medical device, used with other bionic devices as well, the app is documented separately, see **[1].**

The comparator device is the users current prosthesis, it may be any passive MPK or a previous version of the Power Knee (AMPK), depending on the subject. Both have the same intended use and population as the investigational device.

The subject will be using the remaining part of their current prosthetic system with the investigational device, as it was used with the comparator device. If this is not possible, an advanced ESAR foot will be used and provided by Össur.

No other device, medication or intervention will be used. Aside from the Össur Logic app which is used to interact with the knee.

15-18 subjects are to be enrolled and therefore **15-18** investigational devices will be used, as the devices are intended to be used by a single patient; one for each subject.

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	50Kg> body weight > 116Kg
K3-K4 amputees with unilateral transfemoral amputation or knee disarticulation	Bilateral amputees
Allows for 37mm knee center height to dome of pyramid alignment	Users with socket problems
Currently using a MPK or Power Knee	Users with co-morbidities in the contra-lateral limb, which affect their functional mobility
Older than 18 years old	Younger than 18 years old
No socket issues/changes in the last 6 weeks and no socket changes expected during the duration of the study period.	Users with stump pain
Comfortable and stable socket fit	Users with cognitive impairment
Willing and able to participate in the study and follow the protocol	Users involved in other clinical tests and/or receiving treatment that the testing might affect.

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 PI, if the participant wants to disclose those reasons. No further investigational procedures concerning the subject will be conducted, except for a statement explaining the reason for withdrawal (if disclosed), 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.

Subjects will be enrolled at the clinic, the investigational site that they were contacted from.

The total time period required to implement the clinical investigation is expected to be ***15-20 weeks***. Each individual subject is expected to participate in the clinical investigation for ***4-15 weeks***. The estimated time needed to include this number (enrolment period) is up to ***6 weeks.***

At least ***15*** subjects are required to finish the protocol (3 visits) for statistical data analysis, as specified in chapter **10.2 Sample size calculation**.

8.4 Procedures

i) Recruitment

Potential subjects will be identified from the customer base of the Local Principal Investigator (LPI). The LPI evaluates, based on previous experience of interaction with and servicing of patients, if a potential participant is cognitively capable. If a potential participant fits the inclusion and exclusion criteria the PI will contact them via telephone. During the telephone call the LPI will verify if they are interested in participating in a study. If interest is expressed at this point they will answer some screening questions and questions relating to the duration of the study, number of clinical visits required, and the investigational device will be answered and if the eligibility criteria are met they will be invited for the 1st visit.

ii) Test procedure

There are ***three*** scheduled and ***one*** optional study event, all testing procedures will be conducted at the study site. 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 ***13.8*** **Informed consent**.

Procedure for resetting and inspection of investigational devices between users:

In Ossur Logic App, default parameters of the knee will be restored using the default profile.

An activity report is generated in order to record the number of steps performed on the device before the next user starts using the device.

Visual inspection of the device condition performed to identify any signs of wear or damaged parts. If damaged parts or sign of wear are observed, the knee shall be segregated and not fitted to a new user.

Following the instructions provided in the Instruction for Use, the knee exterior surface and the battery pack complete outer surfaces will be cleaned.

Visit 1:

The subject will be consented and enrolled after verification of the inclusion/exclusion criteria. Potential risk of participating in the investigation will be explained to the subject.

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

Subjects will be randomized into 2 groups, using a random number generator. Half of the subjects (Group 1) will then be fitted with the investigational device. Prior to fitting the subjects of Group 1 will be asked to provide feedback on the current prosthesis, by filling in a set of questionnaires **and performing the AMPro, L-test and 6MWT with Borg scale,** to obtain baseline data. Subjects may be videotaped during fitting and while performing functional tests, care will be taken to blur out faces and other personally identifiable markers such as tattoos and birthmarks.

Users will be fitted within the standard methods of prosthetic fitting, alignment, introduction, training and walking on various terrain. After being fitted with the investigational device subjects will receive functional training on the investigational device prior to going home and using it as their usual prosthesis for approximately 2-3 weeks. They will be given an appointment for the follow up visit prior to leaving the testing site.

The other half (Group 2) will stay on their prescribed prosthesis until the next visit in 2-3 weeks.

CPO subjects will provide feedback on the ease of setup and fitting, they will also be videotaped during setup. Care will be taken to blur out faces and other personally identifiable markers such as tattoos and birthmarks.

Visit 2:

During the second visit subjects in Group 1 will perform the same functional tests as in the first visit (**6MWT, L-test, Borg scale**) on the investigational device and answer questionnaires on the performance of the investigational device, and then be fitted back to their prescribed prosthesis. Subjects in Group 2 will perform the tests/questionnaires on their prescribed prosthesis and then be fitted with the investigational device. A new appointment is made after approximately 2-3 weeks.

CPO subjects will provide feedback on the ease of setup and fitting.

Visit 3:

During the third visit all subject will repeat the tests and questionnaires on the prosthesis they are fitted with. Subjects will have the option to use the investigational device for an additional 8-12 weeks, those who choose that will be fitted with the investigational device or stay on it, depending on which they are fitted with. They will be given an appointment for the fourth visit 8-12 weeks later. They will be contacted via telephone 4-5 weeks later and asked to provide feedback on their experience with the device so far, see script in **Appendix 18.1**.Those that choose not to keep using the investigational device will be fitted back on their prescribed prosthesis and end their participation in the study at visit 3.

Visit 4 (optional):

During the fourth visit subjects will answer the same questionnaires and complete the same functional tests as the other visits and data will be collected from the knee on activity (step count, use time). They will then return to their prescribed prosthesis. End of study.

iii) Measurements and data collection

The same questionnaires, consisting of four valid instruments (PMQ, PEQ, PLUS-M, Borg) and in-house questions on the performance of the investigational device, will be used and filled in at three-four separate points in time. The same functional tests (L-test and 6MWT) will also be carried out at two points in time (except for those that elect the optional 8-12week follow up period, there will be an addition visit with data collection and a follow up phone interview), the AMPro will be performed at baseline to verify users K-level. The activity report will be generated from the Investigational device software application. See Table 6 for visit schedule and study procedures.**Table 6 Visit schedule and procedures**

Procedure/activity	Recruitment phase: 2-6 weeks prior to baseline	Group 1 visit 1: Baseline	Group 2 visit 1: Baseline	Group 1 visit 2: 2/3w F/U	Group 2 visit 2: 2/3w F/U	Group 1 visit 3: 4/6w F/U	Group 2 visit 3: 4/6w F/U	Visit 4 Optional 8-12w F/U
Potential subjects identified, fitting inclusion/exclusion criteria, by PI from customer database	X							
PI calls potential subjects and pre-screens by telephone	X							
Subject signs ICF, randomization		X	X					
Fitting, Training		X			X			
Subject fills in questionnaires		X		X	X	X	X	X
Subject performs 6MWT w/Borg scale and L-test		X		X	X	X	X	X
PI prints out activity report from investigational device				X			X	X
Subjects that choose to keep using the investigational device are given an appointment in 8-12 weeks from visit 3. Others are fitted with their prescribed prosthesis and end participation.						X	X	

All subjects still active are fitted back to their prescribed prosthesis, end of study.				X
CPO subjects provide feedback on fitting the investigational device	X		X	

For each subject there are three scheduled visits to the study site and questionnaires/tasks/measurements administrated three times during the course of the study, with an additional 4th visit which is optional.

8.5 Compensation

iv) Subject

Amputee subjects will be compensated for their spent time in the clinic with [redacted] in the end of each visit. CPO subjects will not be compensated.

8.6 Responsibilities

Sponsor Principal Investigator (Coordinating investigator)

- Identify sites
- Investigate possible vigilance cases/SAEs
- Train and explain the protocol to the sites
- Collect data via phone interview during optional 8-12w follow up

Monitor

- Monitor trial
- Collect data
- Analyze results
- Write report

Co-Investigator

- Collect Data
- Analyze results
- Write report
- Assist in conduct of trial procedures at investigators' site
- Assist in fitting users with trial device (and back to their prescribed prosthesis, if applicable)
- Perform reset and inspection of investigational devices between users (engineer).

Local Principal Investigator at site

- Screen subjects
- Explain trial to participants
- Responsible for obtaining informed consent from test subjects
- Conduct all trial procedures at investigators' site
- Fit users with trial device (and back to their current prosthesis, if applicable)

8.7 Study monitoring and Oversight

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

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

9 Investigational Device Accountability

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

The L**PI** 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

Outcomes at each timepoint will be visually inspected for normality using histograms and qq-plots. If the data are deemed to be normal the hypotheses will be tested using a two-tailed, paired, student's t-test. Non-normal data will be tested using the Wilcoxon signed-rank test.

Acceptance criteria for the data, as applicable, is defined in Table 4 **Endpoints, test methods and hypotheses**. 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 induvial 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

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

t tests - Means: Wilcoxon signed-rank test (matched pairs)

Options:	A.R.E. method		
Analysis:	A priori: Compute required sample size		
Input:	Tail(s)	=	One
	Parent distribution	=	Normal
	Effect size dz	=	0.7084529
	α err prob	=	0.05
	Power (1-β err prob)	=	0.8
Output:	Noncentrality parameter δ	=	2.6812808
	Critical t	=	1.7676466
	Df	=	13.3239449
	Total sample size	=	15
	Actual power	=	0.8150214

It is therefore expected that **at least 15** subjects are required to complete the protocol with a power of 0,**8** and significance at 0,**05**. Effect size was estimated for the primary endpoint based on a previous in-house study of the RHEO KNEE, a passive microprocessor controlled prosthetic knee.

Given a drop-out rate of **20**%, up to **18** subjects may be recruited.

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

10.3 Additional statistical matters

There is no provision for interim analysis and no criteria for early termination of the clinical investigation on statistical grounds.

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. Dropouts 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 for single site studies, 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/REB/REC 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/REB/REC 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 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.

[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 as opposed to using another **MPK prosthesis** commercially available. Compared to not using a MPK **prosthesis** the patient will benefit significantly in terms of mobility and ability to live independently. Further on the user will be trained on a new prosthetic component to experience the unprecedented functionality of the new component to mitigate the known deficiencies associated with his amputation. Within the test he/she will be trained on restoring physiological movement pattern closer to those of non-amputees.

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

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

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 QM1673 Risk Management process, based on ISO 14971 (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 [3] and Chapter 7 in the Clinical Investigator´s Brochure [4]**.

The Hazard analysis document **[3]** contains analysis on foreseeable adverse events and anticipated adverse device effects, together with their likely incidence, mitigation or treatment.

Reasonably foreseeable misuses:

- Use of product by user exceeding the maximum user weight.
- Use of the product by user exceeding the activity or impact levels specified above.
- Use of the product for sport activities.
- Submersion of the product in water or exposure to quantity of water exceeding what is considered normal weather.
- 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.

13.3 Risk of Study (To Patient)

At each visit a PI/CI, a certified CPO/CO/CP or clinician, will be present to ensure the safety of the participants. The study adds no additional risk other than the risks identified above. Subjects will use the trial device as their primary prosthesis in the same manner as they would normally do on their prescribed 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 between study visits**.

13.4 Risk Mitigation

For each device designed by Össur risk mitigation is part of the design process according to ISO 14971 **[3]**. Furthermore, each participant fitted with **a MPK prosthesis** for the first time**, or an upgraded/adjusted version of the device,** will be trained by a fully qualified professional until the user can demonstrate sufficient understanding of the product operation and demonstrate minimum ability level in its operation. This process is the same as the usual training process deployed for normal fitting of a **MPK prosthesis**.

As part of the training process, the participant will be informed on the risks inherent in using a **MPK prosthesis in an uncontrolled environment**. Moreover, the participant will be provided with the product literature (e.g. Information for User), as well as being informed and trained on how to use the product.

13.5 Risk-to-Benefit 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 – Dynamic 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, Steinþóra Jónsdóttir, the Study Monitor. Continuous communication will be maintained between Össur and the IRB, as required. Moreover, communication will be maintained between the PI and the IRB, as required.

13.7 Vulnerable populations

No vulnerable populations will be enrolled.

13.8 Informed Consent

The Principal Investigator, 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 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 PI will contact each subject by phone and explain the new information as required and participants will be reconsented as applicable.

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

13.9 Participant confidentiality – Data management

Subjects will be assigned a random study identification (ID) number and a random investigational device (identified by the study serial number).

When recording video care will be taken not to include the face or other identifiable features, if they are accidentally captured they will be blurred or blackened.

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. A list connecting the ID to the subject´s name will be stored in a password secured file until the end of the study at which point it will be destroyed. Only investigators involved in the trial will have access to this information.

The screening form will be in paper format and will be stored by the PI in a locked container. All documents will be collected by Study Monitor and/or PI.

A Clinical Investigation Report (CIR) will be generated by 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 Hazard Analysis documentation **[3].**

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 14155:2011 for details.

14.2 Reporting procedures

Adverse events and device deficiencies are recorded and reported to the competent authority in all countries in which the trial is being conducted according to national guidelines.

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 the FDA. Any serious device related adverse event will lead to the immediate termination of the trial.

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 Principal 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 unexpected adverse event:

Ian Fothergill mobile: [redacted] for Investigational site 1# and 2#

Email: [redacted]

Jeffrey Denune mobile: [redacted] Investigational site 3#

Email: [redacted]

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 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.

15 Publication Policy

[redacted]

16 References

[redacted]

External Literature References:

1. Hafner, B. J., Willingham, L. L., Buell, N. C., Allyn, K. J. & Smith, D. G. Evaluation of Function, Performance, and Preference as Transfemoral Amputees Transition From Mechanical to Microprocessor Control of the Prosthetic Knee. Arch. Phys. Med. Rehabil. 88, 207–217 (2007).

2. Bellmann, M., Schmalz, T. & Blumentritt, S. Comparative Biomechanical Analysis of Current Microprocessor-Controlled Prosthetic Knee Joints. Arch. Phys. Med. Rehabil. 91, 644–652 (2010).

3. Pasquina, P. F. et al. Case Series of Wounded Warriors Receiving Initial Fit PowerKneeTM Prosthesis. J. Prosthet. Orthot. 29, 88–96 (2017).