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CLINICAL INVESTIGATION PLAN

Official title of the study: Evaluation of a sound processor for a transcutaneous system

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CONFIDENTIAL

Clinical Investigation Title	Evaluation of a sound processor for a transcutaneous system
Investigation Code	BC114
Investigational Device (s)	Sentio 1 sound processor
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Sponsor	Oticon Medical AB Datavägen 37 B 436 32 Askim Sweden
Date	05-10-2022

Revision history:

Revision no	*Date*	*Description*
0	05-07-2022	First version
1	05-07-2022	No changes to the document made. Only made Revision 1 for consistency in the EDMS.
2	16-08-2022	• Implementation of comments from the Swedish Medical Products Agency: ○ Section 18 revised in accordance with MDR ○ Visit 1 assessments updated ○ PI contact details added ○ Information on financial agreements added • Secondary endpoint E clarified • Additional minor clarifications
3	05-10-2022	• Implementation of comments from Swedish MPA (LV) and Swedish Ethical Review Authority (EPM) (2022-09-16)
4	04-07-2023	• Amendment 1: Study prolongation (1 year) ○ A fourth visit is added in sections 6.2, 9.1, 9.4 ○ Information added regarding future CE-marked investigational device (Sentio 1) in section 9.1. ○ Timelines extended in section 9.3.5 • Additional minor clarifications

STATEMENT OF COMPLIANCE

This clinical investigation will be performed in consistency with the current versions of the Declaration of Helsinki, ISO 14155, Regulation (EU) 2017/745 (MDR) and applicable regional or national regulatory requirements as well as any additional requirements imposed by the Ethical Committee's.

This Clinical Investigation Plan contains privileged or confidential information, which is the property of the Sponsor. Information may not be disclosed to a third party without written authorization from the Sponsor

Referenced Documents, Regulations, Standards and Ethical principles

[A] Doc-00065319	C58 End of Trial Clinical Investigation Report (CIR)
[B] ISO 13485:2016	Medical devices – Quality management systems – Requirements for regulatory purposes
[C] Doc-00118033	Investigator's brochure BC114
[D] Doc-00119039	Audiological Manual Sentio 1 SP for BC114
[E] Doc-00062186	Clinical evaluation Plan Sentio system
[F] Doc-00067091	State of the art – BAHS
[G] Doc-00062127	O1 Clinical investigation report, primary endpoint
[H] Doc-00063566	BC101 Clinical Investigation Plan
[I] EU MDCG 2020-10/2	Clinical Investigation Summary Safety Report Form 1.0
[J] ISO 14971:2019	Medical devices – Application of risk management to medical devices
[K] Doc-00119094	Risk Management File study BC114
[L] ISO 14155:2020	Clinical investigation of medical devices for human subjects – Good clinical practice
[M] Doc-00117557	Clinical Investigation Report BC109 Investigation of an updated bone-anchored sound processor

1 SYNOPSIS

Clinical Investigation Title	Evaluation of a sound processor for a transcutaneous system
Investigation Code	BC114
Investigational Device (s)	Sentio 1 sound processor
Principal Investigator(s):	Ann-Charlotte Persson, certified audiologist, MSc Habilitation & Health, Hearing organization Södra Gubberogatan 6 416 63 Göteborg E-mail: ann-charlotte.l.persson@vgregion.se (emergency contact) Phone: +46 70 960 92 16 (emergency contact)
Sponsor:	Oticon Medical AB Datavägen 37 B 436 32 Askim Sweden
Methodology:	Prospective, single-center, comparative investigation with within-subject control design.
Inclusion/exclusion criteria:	Inclusion criteria: 1. Signed Informed Consent Form 2. Adult subjects (18 years or older) 3. Subjects implanted with an I1 implant 4. Fluent in Swedish Exclusion criteria: 1. Subjects who do not have the ability or are un-willing to follow investigational procedures/requirements, e.g., to complete questionnaires, according to investigator's discretion. 2. Subject deemed unsuitable for any medical or other reason as judged by PI or medical responsible

Objective(s):	Primary Objective • To assess the improvement of hearing with the Sentio1, PTA4 Secondary Objective (s) • To assess the improvement of hearing with the Sentio 1, across frequencies • To assess self-reported performance with the Sentio 1 compared to previous sound processor after at least one month field usage of the Sentio 1 • To assess the preference of sound processor. • To assess the degree to which Sentio 1 compensates for the BC hearing loss • To assess the difference between BC in-situ thresholds measured with Sentio 1 and conventional unmasked BC audiometry. • Assess safety with the Sentio 1 SP Tertiary Objective (s) • [redacted]

Endpoints	Primary Endpoint • Functional gain with Sentio 1, i.e., the difference in dB between unaided and aided sound field thresholds, calculated on average for frequencies 500, 1000, 2000 and 4000 Hz (PTA4), at 1 month follow-up visit. Secondary Endpoint(s) • Functional gain with Sentio 1, i.e., the difference in dB between unaided and aided sound field thresholds, for all measured frequencies. • Average SSQ12 scores with Sentio 1, current device and difference between the two for each question, sub-scales and in total. • Percentage (%) of subjects who prefer the Sentio 1 over current sound processor • Effective gain defined as the difference in dB between aided sound field thresholds with Sentio 1 and unmasked BC thresholds on the aided ear(s). The effective gain is calculated for PTA4 and for all measured frequencies. • Difference in dB between Sentio 1 BC in situ thresholds and BC thresholds measured with conventional unmasked BC audiometry for the frequencies 500, 1000, 2000, 3000 and 4000 Hz • Tabulation of AEs occurred throughout the investigation and percentage of individuals with reported AEs Tertiary Objective (s) • [redacted]
Duration of investigation period:	Expected investigation start: 15 November 2022 Expected investigation end: 15 February 2025
Number of screened subjects:	16
Estimated number of enrolled subjects:	12-14
Estimated number of subjects completing the investigation:	11
Investigation plan prepared by:	Marianne Philipsson, Sr. Clinical Trial Manger, Oticon Medical AB Åsa Nilsson, Sr. Clinical Trial Manager, Oticon Medical AB

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3 LIST OF ABBREVIATIONS

AE	*Adverse Event*
ADE	*Adverse Device Effect*
BAHS	*Bone Anchored Hearing System*
CIP	*Clinical Investigation Plan*
DD	*Device Deficiency*
EC	*Ethical Committee*
eCRF	*Electronic Case Report Form*
GCP	*Good Clinical Practice*
GDPR	*General Data Protection Regulation*
ISF	*Investigator Site File*
IRB	*Institutional Review Board*
ISO	*International Organization for Standardization*
LMV	*Läkemedelsverket (Swedish Medical Products Agency)*
MDCG	*Medical Device Coordination Group*
OM	*Oticon Medical*
OSN	*Open Sound Navigator*
PI	*Principal Investigator*
PRO	*Patient Reported Outcomes*
SAE	*Severe Adverse Event*
SADE	*Serious Adverse Device Effect*
SSQ	*Speech, Spatial and Qualities of hearing*
USADE	*Unanticipated Serious Adverse Device Effect*

4 INTRODUCTION

4.1 Background

Bone conduction hearing systems use the body's natural ability to transfer sound through bone conduction. The bone conduction system picks up sound and converts it into vibrations that are transferred through the skull bone to the inner ear(s) (cochlea), thus the sound-transmissions independent of the function of the ear canal and middle ear. For patients with conductive or mixed hearing losses, the vibrations are bypassing the conductive impairment in the ear canal or middle ear, stimulating the ipsilateral cochlea directly. For single sided deaf patients, the vibrations are transmitted in the same manner via the scull bone to the (functioning) cochlea on the contralateral side.

Bone conduction systems currently on the market can be divided into two main types: direct drive (or direct transmission) and skin-drive (or skin-transmission) system [1]. Direct drive systems where the vibrations are transmitted directly to the bone and can be further divided into percutaneous (skin-penetrating) and active transcutaneous (non-skin penetrating) systems. In direct drive systems, the vibrations are transferred directly to the bone via a screw or a flat surface attachment. In a skin drive system, the vibrations are transmitted through intact skin. Skin drive systems can be further divided into non-surgical transcutaneous systems (conventional bone conduction systems) and passive transcutaneous systems. In non-surgical (or conventional) bone conduction systems, all components are kept outside the skin, while the passive transcutaneous system contain a passive implanted part with retention magnet(s).

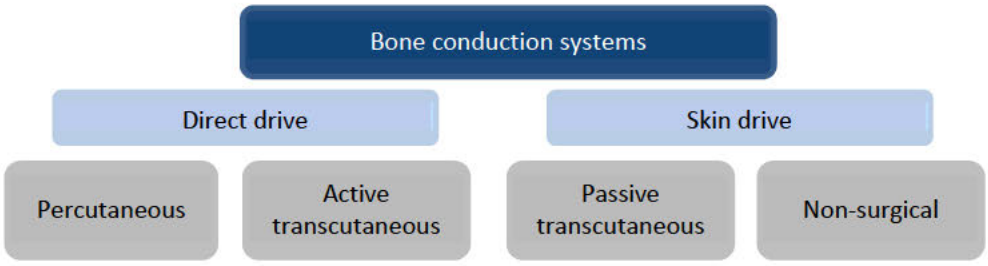

Figure 1 Bone conduction systems

In active transcutaneous, direct drive bone conduction systems the sound is picked up by the microphones in the external sound processor, processed and transmitted using a radio frequency link through the intact skin to an implant in the temporal and mastoid bone area of the scull. The receiver coil of the implant receives the signal that is converted to vibrations in the transducer. The vibrations are conveyed from the bottom of the transducer to the skull and thereafter by means of bone conduction to the cochlea. In the cochlea the vibrations are converted to signals that are transmitted to the brain through the auditory nerve. (Figure 2)

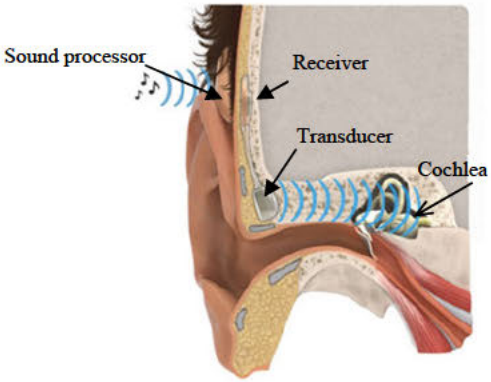

Figure 2 Active transcutaneous direct drive bone conduction device

Oticon Medical is developing a new active transcutaneous system – the Sentio system. A pivotal clinical investigation on the final design of the Sentio system (implant Sentio Ti and sound processor Sentio 1) is currently ongoing to provide sufficient evidence of the safety and performance of the system.

[redacted]

[redacted]

The current investigation (BC114) will include the use of the final design of the sound processor, Sentio 1, and upgrade the subjects already implanted with implant I1 with this sound processor as this is the latest version of the Sentio sound processor. The purpose of the investigation is to confirm the performance with the Sentio 1 sound processor in this population of users.

5 IDENTIFICATION AND DESCRIPTION OF THE INVESTIGATIONAL DEVICE

5.1 Investigational Device description

The sound processor Sentio 1 is, together with an active transcutaneous bone conduction implant, intended for improvement of hearing [redacted]

[redacted]

Sentio 1 includes a magnet, directional microphones, battery lid, LED indicator, sound processing electronics (electronic amplifier) and a transmitting coil. The sound processor is powered by a standard zinc air hearing aid battery. The sound processor is delivered non-sterile.

The sound processor is kept in place on the intact skin by means of a magnetic retention. The materials in skin contact are all biocompatible and biological evaluation is performed, detailed description is found in the investigator's brochure (IB) [C]. There is one magnet in the sound processor and one in the implant both centered within the antenna coils. The sound processor is low-weight and the magnet in the sound processor can be exchanged to achieve the optimal retention to fit the patient's needs.

5.2 Manufacturer

The Sentio 1 is manufactured by Oticon Medical AB, Askim, Sweden. Oticon Medical AB is ISO 13485 [B] certified and has CE marked and FDA cleared other products for hearing healthcare on the market.

5.3 Identification of the Investigational Device

Table 1 summarizes the investigational devices to be used in the proposed investigation. Detailed information about the investigational devices can be found in the investigator's brochure (IB) [C].

Table 1 Overview of the investigational device

Name	Reference	Description
Sentio 1	[redacted]	Sound processor in three different colors, external part of an active transcutaneous bone conduction system

5.4 Traceability

During and after the investigation the investigational device, Sentio 1, will be traceable by a unique identification code/serial number. The serial numbers will be recorded in the electronic Case Report Forms (eCRF), and in the 'Investigational device accountability log' (for further details, see section 15).

5.5 Intended Purpose

The Sentio 1 is, together with an active transcutaneous implant, intended for improvement of hearing for patients [redacted]

5.6 Population and indications

[redacted]

5.7 Training and Experience

Prior to the initiation of the investigation, the hearing care professionals will be trained in all procedures related to handling and fitting the Sentio 1. Training and training content will take the assessment from the risk management process into account.

[redacted]

5.8 Installation and Use

Fitting of the Sentio 1 in will be conducted as per standard clinical routine for BAHS as described in the Audiological Manual from Oticon Medical [D]. The Sentio 1 will be fitted (adapted) to the subject's need by hearing care professionals.

6 JUSTIFICATION FOR THE DESIGN OF THE CLINICAL INVESTIGATION

A clinical evaluation including an assessment and analysis of clinical data concerning safety and performance of the Sentio system is summarized in the IB [C]. Finalized pre-clinical and clinical studies on earlier design iterations of the Sentio system demonstrates that the systems perform as anticipated. A pivotal, pre-market clinical investigation on the final design of the Sentio system is currently [H] ongoing to collect sufficient evidence of the safety and performance of the system.

The current investigation will focus on the performance with Sentio 1 on patients previously implanted with the I1 as a part of a planned upgrade of these patients to the latest Sentio sound processor.

6.1 Summary of comparable devices (state-of-the-art)

A systematic literature review of alternative treatment options for patients with the indication of Sentio system has been performed and is summarized in the IB [C] [redacted]

The literature review showed that although the performance measures used varies between studies, the data on the active transcutaneous devices consistently showed performance improvement over the unaided condition on all outcome measures. The most commonly used performance measure are sound field thresholds (typically presented as the difference between unaided and aided thresholds hereafter denoted as functional gain), speech intelligibility test in quiet and noise and self-reported outcome questionnaires. [redacted]

6.2 Justification of the investigation design and outcome measures

In order to answer the proposed hypothesis, that there will be a significant improvement in aided thresholds with the Sentio 1 compared to unaided, a prospective, within subject controlled clinical investigation will be performed.

The single-arm design and the primary endpoint evaluation of performance reflects a typical clinical investigation design in the field.

Thus, this investigation will be a pre-market, confirmatory investigation with the purpose to confirm the performance of the Sentio 1 sound processor on users previously implanted with the I1 implant. The investigation includes four visits and three field trial periods. On the first visit the subjects will be fitted with the Sentio 1 according to the audiological manual [D]. The first field trial period will allow the subjects to get adapted to the sound in the Sentio 1. After one month (visit window +4 weeks) a follow up visit is conducted to evaluate the Sentio 1 sound processor. The investigation design in regards of fitting of and adaptation time to the Sentio 1 corresponds to standard clinical practice. A field period is conducted after the second and third visit with the purpose to monitor the safety of the Sentio 1 to assure long term safety data. The follow

up visit after one and two years will be conducted as a physical or remote meeting depending on subjects' preference.

6.2.1 Outcome measures

To ensure a holistic understanding of the Sentio 1, the current investigation combines audiological assessments in the laboratory and subjective self-reported outcomes collected during and after field trial periods.

In the sections below, the justification and rational for using each outcome measure is outlined.

6.2.1.1 Ability to hear sounds – Functional gain and sound field-hearing thresholds

Outcome with sound field hearing threshold results can be presented as the absolute measured aided threshold level [dB HL], as the difference between unaided and aided thresholds [dB] ("functional gain") or in relation to the cochlear loss, defined by BC thresholds ("BC/effective gain"). Functional gain is the most common way of expressing benefit (improvement of hearing) in the state-of-the art literature [F]. Overall sound field thresholds are a reliable and language independent outcome typically included as part of clinical practice for bone conduction devices and is therefore included in this investigation.

6.2.1.2 Patient reported outcomes

Patient reported outcomes are commonly used in the state-of-the art literature [F]. In this investigation patient reported outcomes (PRO) will be used to evaluate subjective performance of the Sentio 1 compared to current sound processor. In addition, patient reported outcome will be used to evaluate the preference between Sentio 1 and current sound processor for further confirmatory assessment of the performance of the Sentio 1.

6.2.1.2.1 SSQ12

The Speech, Spatial and Qualities of Hearing scale (SSQ; Gatehouse and Noble [3]), and its abbreviated scale SSQ12 [4], are validated questionnaires useful for evaluating self-reported performance with a hearing device and have therefore been deemed suitable to use in this investigation.

6.2.1.2.2 Preference

To systematically assess the preference of the Sentio 1 compared to subject's current sound processor a preference scheme previously used for BAHS [M] will be used in this investigation.

6.2.1.3 [redacted]

7 BENEFITS AND RISKS OF THE INVESTIGATIONAL DEVICE, CLINICAL PROCEDURE AND CLINICAL INVESTIGATION

The risk assessment and analysis has been conducted according to internal procedures established in accordance with ISO 14971:2019 [J]. In addition, risk assessment and analysis for conduct of investigation has been conducted according to internal procedures [K] established in accordance with ISO 14155:2020 [L].

7.1 Anticipated clinical benefits

Together with an active transcutaneous implant, the Sentio 1 is expected to improve hearing [redacted]

7.2 Residual risks and anticipated adverse device effects

The risk assessment and analysis has been conducted according to internal procedures established in accordance with ISO 14971:2019 [J]and qualitative and quantitative aspects of clinical safety of risks have been examined and documented as part of the process. All identified hazardous situations in combination with harm have been evaluated for the probability of occurrence and the severity of harm. Based on this evaluation the risks have been categorized and control measures have been implemented to control and reduce the risks as far as possible. The identified risks have been mitigated as far as possible and all residual risks are acceptable according to the Sponsor's risk acceptability criteria.

The residual risks summarized below, including the characterization of their nature (hazards), incidence (occurrence), severity and outcome (harms), are disclosed in the IB [C] together with references to the complete risk management files.

7.2.1 Residual risks Sentio 1 sound processor

[redacted]

[redacted]

7.3 Risks associated with participation in the clinical investigation (6.2.3 in ISO14155)

The proposed clinical investigation has been designed to minimize the risks as far as possible. During the development of the CIP, systematic clinical investigation risk assessments according to internal procedures and ISO14155 have been performed. The inclusion of subjects has been limited to adults already implanted with an I1 implant. Exclusion criterion no. 2 has been set to exclude potential subjects with any medical or other condition, as judged by the PI or other medically responsible person, which could increase the risk associated with investigation participation to unacceptable levels. No procedures, measurements or assessments in the investigation add additional risks to the subjects. Since the investigation only aims at fitting a new sound processor on already implanted subjects the risk of participating in the investigation is considered low and comparable to any sound processor change or upgrade within clinical practice.

There is a minimal risk to the subject by means of violation of the General Data Protection Regulation (GDPR) by study personnel. Violations may include the accidental disclosure of personal identifiable information to unauthorized personnel or improper use of personal identifiable identification by authorized personnel.

7.4 Possible interactions with concomitant medical treatments as considered under risk analysis

7.4.1 Medications/pharmaceuticals

If medication is considered necessary for the subjects' safety and well-being during the clinical investigation, the investigator can refer to a physician according to normal clinical practice.

7.4.2 Medical treatments

- The sound processor contains a magnet and caution should be taken with subjects that have active implants (e.g., implantable defibrillators, CSF shunts, pacemakers).
- If the subject needs to undergo MRI, the sound processor must be removed.

7.5 Risk control and/or mitigation

The identified risks related to the use of the device have been mitigated as far as possible through verified design considerations, process validation and information and warnings disclosed in the instructions for use. In addition, the Sponsor will provide sufficient training on the specifics of the device prior investigation enrollment to minimize the risks associated with the devices.

The risk of violation of the GDPR is mitigated through the selection of a qualified site and investigator reduce the risk of unqualified study personnel. Additionally, at the site initiation visit, study personnel will undergo GDPR training by the Sponsor representative. This training will emphasize the violation of GDPR as a protocol deviation, which requires reporting to the Sponsor.

7.6 Rationale for benefit-risk ratio

Potential hazards associated with the use of the Sentio 1 have been through a comprehensive risk management process in accordance with ISO 14971:2019[J]. The identified risks have been mitigated as far as possible and no unacceptable residual risks have been identified according to the Sponsor's acceptability

criteria considering the anticipated severity of potential consequences/harm and probability of occurrence. Overall, the residual risks associated with the use of the Sentio 1 are comparable to similar products on the market when the sound processor is used as intended.

[redacted]

It is concluded that the benefits associated with the use of the Sentio 1 outweigh the overall residual risks. Furthermore, it is concluded that the anticipated risks associated with participation in the investigation are acceptable when weighted against the anticipated user benefits of participation.

8 OBJECTIVES AND HYPOTHESES

8.1 Primary objective

Primary objective	Corresponding primary endpoint/outcome variable(s)	Section
A. To assess the improvement of hearing with the Sentio1.	1. Functional gain with Sentio 1, i.e., the difference in dB between unaided and aided sound field thresholds, calculated on average for frequencies 500, 1000, 2000 and 4000 Hz (PTA4), at 1 month follow-up visit.	*9.5.3.2.1*

8.1.1 Primary hypothesis

Hypothesis 1A: The hypothesis for the primary objective is that there will be a significant improvement in subjects' aided thresholds with the Sentio 1 compared to unaided. The investigation will be declared successful if the primary endpoint is statistically significant (i.e., the null hypothesis H0 is rejected in favor of the alternative hypothesis H1) according to the following hypothesis.

- H0: Same or higher (worse) PTA4 with Sentio 1 compared to unaided.
- H1: Lower (better) PTA4 with Sentio 1 compared to unaided.

8.2 Secondary Objective(s)

Secondary objective(s)	Corresponding secondary endpoint/outcome variable(s)	Section
B. To assess the improvement of hearing with the Sentio1.	1. Functional gain with Sentio 1, i.e., the difference in dB between unaided and aided sound field thresholds, for all measured frequencies.	*9.5.3.2.1*
C. To assess self-reported performance with the Sentio 1 compared to previous sound processor after at least one month field usage of the Sentio 1	1. Average SSQ12 scores with Sentio 1 for each question, sub-scales and in total. 2. Average SSQ12 scores with current sound processor for each question, sub-scales and in total.	*9.5.4.1*

	3. Difference in SSQ12 scores between Sentio 1 and current sound processor for each question, sub-scales and in total.	
D. To assess the preference of sound processor.	1. Percentage (%) of subjects who prefer the Sentio 1 over current sound processor	*9.5.4.2*
E. To assess the degree to which Sentio 1 compensates for the BC hearing loss	1. Effective gain defined as the difference in dB between aided sound field thresholds with Sentio 1 and unmasked BC thresholds on the aided ear(s). The effective gain is calculated for all measured frequencies. 2. Effective gain with Sentio 1, see definition above, calculated in average for frequencies 500, 1000, 2000 and 4000 Hz (PTA4).	*9.5.3.2.2*
F. To assess the difference between BC in-situ thresholds measured with Sentio 1 and conventional unmasked BC audiometry.	1. Difference in dB between Sentio 1 BC in situ thresholds and BC thresholds measured with conventional unmasked BC audiometry for the frequencies 500, 1000, 2000, 3000 and 4000 Hz	*9.5.3.1* *9.5.1*
G. Assess safety with the Sentio 1 sound processor	1. Tabulation of AEs occurred throughout the investigation and percentage of individuals with reported AEs.	*18*

8.3 Tertiary objectives

Tertiary objective	Corresponding tertiary endpoint/outcome variable(s)	Section
[redacted]	I. [redacted]	*9.5.3.3*

9 DESIGN OF THE CLINICAL INVESTIGATION

9.1 General

The investigation is prospective, single-center, comparative investigation with within-subject control design. It is estimated that 12-14 subjects previously implanted with the I1 implant will be fitted with Oticon Medical Sentio 1 sound processor.

The investigation includes two laboratory visits at the research unit at Chalmers tekniska högskola (Hörsalsvägen 9, vån 7, 41258 Göteborg), with a field trial period between. Both visits will take between 2-3 hours including breaks. At the first visit the subject's current device is evaluated and Sentio 1 is fitted according to the audiological manual [D]. Audiological measurements will be conducted. If needed, finetuning will be applied according to the subject's preference. Retention will be assessed and the magnet in the sound processor will be adjusted according to the investigator judgement and subject needs and preference. The subjects will wear the Sentio 1 in their daily life for 1 month (visit window +1 month). During

the field trial the subjects will fill out one questionnaire. At the second visit, any AE that occurred in the field trial will be evaluated. Audiological measurements will be conducted. If needed, finetuning will be applied according to the subject's preference. Retention will be assessed and the magnet in the sound processor will be adjusted according to the investigator judgement and subject needs and preference. A preference questionnaire will be filled out during the visit. A third and fourth visit are scheduled after one and two years respectively of using the device, with the main purpose to monitor safety using the device. Visit 3 can be conducted at Chalmers or at the Hearing clinic in Gothenburg or as a telephone visit. Visit 4 will take place at the Hearing clinic in Gothenburg. [redacted]

Due to the nature of the end points (comparisons between aided and unaided, and Sentio 1 and current sound processor) there is no possibility to blind the investigation as the conditions are obvious for the subject.

Enrollment of subjects is expected to occur in the second half of 2022, after approvals from the Ethical Committee (EC) and Regulatory Authority (Läkemedelsverket, LMV). The investigation will be considered completed when the last subject has completed the last visit.

9.2 Investigational device(s) and comparator(s)

The investigational device is the Sentio 1, which has been described in section 5. For secondary objectives A1-3 and B1 the subject's own device will be the comparator device. [redacted]

Each subject will receive one investigational device. Additional spare devices will be available with the investigator in case of subjects losing or breaking a device. [redacted]

9.3 Subjects

Subject previously implanted with the I1 implant will be asked to take part in the study. Recruitment of the patients will be the responsibility of the Principal Investigator (PI). [redacted]

9.3.1 Inclusion criteria

Patients meeting following criteria may be included in the investigation:

1. Signed Informed Consent Form
2. Adult subjects (18 years or older)
3. Subjects implanted with an I1 implant
4. Fluent in Swedish

9.3.2 Exclusion criteria

Subjects meeting any of following criteria will not be permitted to participate in the investigation:

1. Subjects who do not have the ability or are un-willing to follow investigational procedures/requirements, e.g., to complete questionnaires, according to investigator's

discretion.

2. Subject deemed unsuitable for any medical or other reason as judged by PI or medical responsible

9.3.2.1 Relationship of investigation population to target population.

The target population for the Sentio 1 is patients with either a mixed/conductive hearing loss (MHL/CHL) or SSD. In the investigation on the S1 and I1 implant [G] only patients with mixed/conductive losses were included, thus only patients with MHL/CHL will be included in this investigation. No children will be included in this investigation.

9.3.3 Criteria and procedures for subject withdrawal or lost to follow up

Subjects are free to discontinue participation in the investigation at any time and are not required to give a reason for their decision. This will not affect the future treatment / medical care of the subject. However, subjects who discontinue the investigation should be asked about the reasons(s) for their discontinuation, and about the presence of any adverse event (AE) / adverse device effect (ADE) and if possible, be assessed by an investigator. If such withdrawal is due to problems related to the investigational device safety or performance, the investigator shall ask for the subject's permission to follow his/her status/condition outside the clinical investigation.

Subjects may be withdrawn from further participation in the investigation if the investigator judges that this is in the subject's best interest, or for safety reasons.

Other reasons for premature discontinuation may be severe non-compliance to the CIP as judged by the investigator and/or the Sponsor, or incorrect enrolment, i.e., a subject did not meet the required inclusion/exclusion criteria for the investigation.

Should a subject fail to show up on agreed visits the site personnel should use all reasonable efforts to get in contact with the subject to prevent anyone from being 'lost-to follow-up'. The contact attempts should be properly documented in the subject’s medical record.

The investigator will be thoroughly informed at the site initiation training that missing data should be avoided to the farthest extent reasonably possible as it could have deleterious effects on trial integrity and credibility.

Due to the prerequisites for participating in the investigations, subjects withdrawing, discontinuing or being lost to follow-up from the investigation will not be replaced. Collected data will be considered as far as possible in analyses.

9.3.4 Subject Follow-up and Care

After the investigation, the subjects will be receiving follow-up and care according to clinical standard procedures for patients with bone anchored implants and may be asked to participate in follow-up investigations. [redacted]

[redacted]

9.3.5 Number of Subjects

It is planned to screen 16 subjects to reach enrollment of 12-14 subjects in this investigation. The sample

size has been based on a power calculation of the primary endpoint and is described in section 11.1.

Number of screened subjects:	16
Estimated number of enrolled subjects:	12-14
Estimated number of subjects completing the investigation:	11
Point of enrollment:	Visit 1
Point of balanced randomization:	NA
Total expected duration of the clinical investigation:	27 months
Expected duration of each subject's participation:	24 months (+/- 3 months)
Enrollment period:	8 weeks

9.3.6 Information on vulnerable, pregnant and breastfeeding population, if applicable.

Pregnant and breastfeeding individuals will be offered to participate in the investigation as no risk in relation to usage of the investigational device for this population have been identified.

9.4 Clinical Investigation flow chart

Table 2. Flow chart of the investigation.

Protocol activity	V 1	V2	V3	V4	Un-scheduled visit(s)
	Fitting	Follow up	Follow up	Follow up	
	0	*1 month*	*1 year*	*2 years*	N/A
		Visit window (+1 month)	*Visit window (+/- 1month)*	*Visit window (+/-3 months)*	N/A
Subject Eligibility					
Informed consent	X				
Inclusion/exclusion criteria	X				
Demographics	X				
Audiological assessment & fitting					
Audiometry	X				
Fitting and/or adjustment of sound Processor	X	(X)	(X)	X	(X)
Sound field thresholds		X unaided X aided			
[redacted]	X current device X Sentio 1				
PRO's					
SSQ12	X current device	X Sentio 1			
Preference		X Sentio 1			
Safety					
Adverse events assessment	X	X	X	X	X

9.4.1 Clinical Investigation visits

9.4.1.1 Visit 1 (screening/baseline visit)

Following procedures will be carried out during the first visit. The flow below is a suggested flow, based on convenience for subject and investigator the order may be changed. Information, informed consent and screening will always be carried out before any investigation related procedures are conducted.

- The subject is thoroughly informed about the investigation including all investigation related visits. Time will be given for consideration and answering any questions the subject might have.
- Consent form is signed.
- Screening according to inclusion and exclusion criteria.
- The subject's demographical data as well as their personal data and subjects' characteristics are registered.
- Audiometry is performed
- Fitting and adjustment of the Sentio 1 is performed
    - Including BC in-situ and feedback management measurement.
    - Strength of retention magnet is considered and potentially changed according to the subject's needs and preference.
    - Finetuning is considered and Sentio 1 is adjusted according to the subject's needs and preference.
- [redacted]
- Questionnaire for evaluation the subject's current hearing solution is filled out.
- Questionnaires for evaluation of the Sentio 1 is handed out and instructions to fill them out prior to next visit is given.
- AEs are assessed.

9.4.1.2 Visit 2 follow up (1 month)

Following procedures will be carried out at visit 2. The flow below is a suggested flow, based on convenience for subject and investigator the order may be changed.

- AEs are assessed.
- Questionnaires is handed in and checked for completeness.
- Aided and unaided sound field thresholds are performed.
- Preference questionnaire is filled out.
- Adjustment of the Sentio 1 is considered.
    - Strength of retention magnet is considered and potentially changed according to the subject's needs and preference.
    - Finetuning is considered and Sentio 1 is adjusted according to the subject's needs and preference.

9.4.1.3 Visit 3 follow up (1 year)

Following procedures will be carried out at visit 3. The flow below is a suggested flow, based on convenience for subject and investigator the order may be changed. Based on subject needs and preference the visit might be a remote visit.

- AEs are assessed.
- Adjustment of the Sentio 1 is considered

- Strength of retention magnet is considered and potentially changed according to the subject's needs and preference.
- Finetuning is considered and Sentio 1 is adjusted according to the subject's needs and preference.

9.4.1.4 Visit 4 follow up (2 years)

Following procedures will be carried out at visit 4. The flow below is a suggested flow, based on convenience for subject and investigator the order may be changed.

- AEs are assessed.
- Change and adjustment of the Sentio 1 as applicable
  - Strength of retention magnet is considered and potentially changed according to the subject's needs and preference.
  - Finetuning is considered and Sentio 1 is adjusted according to the subject's needs and preference.
- Study termination

9.4.1.5 Unscheduled visit(s)

If need for extra adjustment of the Sentio 1 or if other aspects arise that requires the attention of the investigator the subject's will be booked for an extra appointment.

9.5 Clinical Investigation Procedures

9.5.1 Fitting and adjustment of Sentio 1

The fitting of the Sentio will follow clinical practice for bone anchored devices and will be made following the fitting procedure described in the Audiological manual [D]. [redacted] The fitting procedure includes measurement of feedback limit and BC In-situ threshold for the frequencies 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz. If needed, the sound in Sentio 1 can be finetuned according to the patient's needs and preference. Also, the retention and comfort in relation to the magnet connection between the Sentio 1 and implant will be assessed, and if needed the magnet in the sound processor will be exchanged to a weaker or stronger magnet. At follow up visits further adjustment regarding finetuning and magnet retention is assessed.

9.5.2 Clinical assessments

9.5.2.1 Demographic Data and Baseline Measurements

Following subject characteristics will be collected upon enrollment:

- Gender
- Age
- Indication (MHL/CHL/SSD)
- Implanted side (L/R)
- Type of hearing loss on the non-implanted side (MHL/CHL, SSD, normal hearing, sensorineural hearing loss)
- Hearing solution on the non-implanted side (BAHS, conventional hearing aid, no hearing solution, other)
- Usage hours with current device

9.5.3 Performance Assessments

9.5.3.1 Audiometry

Conventional pure tone audiometry (air-conduction and bone conduction). Tested frequencies for air-conduction are: 250, 500, 1000, 2000, 3000, 4000, 6000, 8000 Hz. Tested frequencies for bone-conduction are: 500, 1000, 2000, 3000, 4000 Hz. Masking is applied as per clinical practice and standard audiometry equipment is used (air-conduction is measured via insert phone or headphones (TDH39), bone conduction via e.g. B71).

If audiogram less than 3 years old can be retrieved from patient files and subject have not experienced any change in his or her hearing this can be used and full audiogram according to above does not need to be performed. Regardless of prior audiometry, the unmasked BC for the fitted side will be measured for all subjects.

9.5.3.2 Sound field thresholds

Detection of thresholds for warble tones presented in sound field from loudspeaker placed at 1-meter distance, 0 degrees azimuth from the subject. Warble tones according to local clinical practice for sound field measurements at 250, 500, 1000, 2000, 3000, 4000, 6000, 8000 Hz are presented. All subjects have the non-operated ear blocked (but not masked).

Conditions	Directionality settings	Noise reduction	Feedback management system	Estimated time [min]
Sentio 1	Omni	Off	feedback management as prescribed	10
Unaided	/	/	/	10

9.5.3.2.1 Functional gain

The functional gain is a calculation and uses the sound field thresholds as described above. Functional gain is defined as the difference between unaided and aided thresholds. In this investigation, functional gain is calculated for frequencies 250, 500, 1000, 2000, 3000, 4000, 6000, 8000 Hz. The average functional gain (PTA4) is calculated as the average of frequencies 500, 1000, 2000 and 4000 Hz.

9.5.3.2.2 Effective gain

Effective gain is a calculation and is defined as the aided threshold relative to the BC (unmasked bone conduction) threshold and is calculated as the difference in dB between aided sound field thresholds and unmasked BC thresholds for the implanted ear. In this investigation, effective gain can be calculated for frequencies 250, 500, 1000, 2000, 3000, 4000, 6000, 8000 Hz. The average effective gain (PTA4) is calculated as the average of frequencies 500, 1000, 2000 and 4000 Hz.

9.5.3.3 [redacted]

[redacted]

9.5.4 Patient Related Outcomes (PRO)

9.5.4.1 Speech Spatial and Qualities of hearing scale (SSQ)

A reduced version of the Speech, Spatial and Qualities of Hearing Scale (SSQ) questionnaire [3], the SSQ12,

will be used in this investigation. The SSQ12 was developed and validated by Noble, Jensen [4] and contains 12 questions that reflect the perceived performance in speech intelligibility, spatial abilities, and sound quality. Each item is scored from 0 to 10, with larger values always indicating greater ability. The SSQ12 will be assessed at visit 1 (own device) and at visit 2 (Sentio 1).

9.5.4.2 Preference questionnaire

The preference scheme is developed by Oticon Medical and has often been used when comparing two devices. [redacted]

The preference scheme will be filled out by the subjects at the final visit (Visit 2).

10 MONITORING

During the investigation, representatives from Oticon Medical will have regular contacts with the investigational site with the purpose to oversee the investigation. Monitoring activities, including on-site visits, will be performed by appointed monitors according to applicable standards (i.e., ISO 14155) and internal guidance documents. The overall purposes of the monitoring are to ensure that:

- The rights, safety and well-being of human subjects are protected.
- Reported data are accurate, complete, and verifiable from source documents.
- The conduct of the clinical investigation complies with the approved CIP, subsequent amendments (if any), applicable standards (i.e., ISO 14155), and applicable regulatory and ethics committee requirements.

The monitor or other Sponsor personnel will be available between visits if the PI or other site personnel needs information and/or advise.

Authorized representatives of the Sponsor and/or Regulatory Authority may visit the site to perform audits/inspections, including source data verification.

The PI should guarantee access to source documents for the monitor and auditors as well as for inspection by appropriate Regulatory Authority and Ethics Committee, if required.

Source documents are further described in section 12. Data Management.

10.1 Monitoring Plan

The extent and nature of the monitoring activities (e.g., review of data entered in the eCRF, source data verification, review of investigator's site file etc.) will be described in an investigation specific Monitoring Plan. The monitoring strategy will be based on a risk-based approach according to ISO 14155:2020.

11 STATISTICAL DESIGN AND ANALYSIS

The statistical analysis of all efficacy variables will be performed according to the study Statistical Analysis Plan. The general methodology for the analysis of primary, secondary, and tertiary endpoints is described below. Wilcoxon signed-rank test will be used to test hypotheses. The decision of the hypothesis test is done at the 5% significance level. Pearson's correlations (or Spearman's if the data is not normally distributed) will be used to test correlations.

The distribution of continuous variables will be given as Mean, 95% confidence interval (CI) of the mean, standard deviation (SD), Minimum and Maximum (Mean (SD), (Min; Max)). The distribution of categorical and dichotomous variables will be given as number and percentage (n = (%)).

All subjects that consented to the investigation will be included in the safety population; all subjects enrolled and treated in the investigation will be included in the Intent-to-Treat (ITT) population. All subjects included in the investigation with no major protocol deviations will be included in the Per-Protocol (PP) population. The final decisions regarding the PP population will be taken after investigation completion, at the Clean File meeting before the database lock. All efficacy analyses will be performed on the PP population as main analysis. Complementary analysis for all efficacy variables will also be performed on the ITT population.

Details will be described in the Statistical Analysis Plan.

11.1 Sample size

The complete population implanted with I1 (N = 16) will be screened for participation in the investigation and the estimated sample size will be 12-14 patients enrolled, about 15% drop-out, and approximately 11 patients completing the study. Data from 11 patients will enable detection of a statistically significant difference between aided and non-aided functional gain of 9 dB or higher (based on normal approximation), with 90% power, 5% two-sided level of significance, and an estimated variability (SD) for the difference of 8 dB. This is considered well within the clinically relevant detection levels for functional gain as described by the systematic literature review on comparable devices [F]. The proposed sample size is also considered to ensure clinically relevant data for conclusions on the secondary end-point SSQ12, where the previous study on the I1 and S2 [A] has used a sample size of 10 patients, and 11 patients would enable detection of statistically significant differences in mean scores of 1 or higher (based on normal approximation), with 90% power, 5% two-sided level of significance, and an estimated variability (SD) for the difference of 0.9.

11.2 Timing for data analysis

One interim data analysis will be performed when all subjects have completed the second visit. The interim data analysis will include all investigation end-points at that time point. A final analysis will be made after all subjects have finalized the last visit and conclude on the safety assessment.

Data cleaning and database lock of the applicable data will be performed both before the interim analysis and prior to the final data analysis. Data cleaning activities and database lock procedures will be defined in a data management plan prior to investigation start.

11.3 Missing data handling

Missing data (e.g., single questions, experimental repetitions) will be treated as Not A Number (NANs) and will be disregarded from the analysis. A detailed description of missing data will be given in the Statistical Analysis Plan. Missing data will be handled in the same way for PP and ITT population.

11.4 Reporting deviations from the original statistical analysis plan

Any deviations discovered throughout the investigation from the original SAP, will be described with justification in a CIP amendment to the final report, as deemed appropriate.

11.5 Subgroups for analysis

No analysis on subgroups will be performed in the investigation.

12 DATA MANAGEMENT

Data management will be conducted according to the investigation specific Data Management Plan (DMP). Any deviations, i.e., discrepancies and additions from the process defined in the DMP will be described in an investigation specific database lock meeting minutes.

All personal data collected and processed concerning the subjects participating in the investigation are protected under the Regulation (EU) 2016/679 (GDPR) and will be handled accordingly. Further, professional secrecy regarding subject information and data applies to all involved personnel, including Sponsor representatives.

Names and/or other explicit personal identification information will not be collected or recorded for investigational purposes, with one crucial exception: it is the responsibility of the investigator to keep a 'Subject Identification Log' up to date, where personal identification information matches the Subject Identification Number (see below). The 'Subject Identification Log' must be kept up to date and stored in the Investigator Site File (ISF) in a secure location with restricted access. This log will not, at any time during and after the investigation, be available to any unauthorised party, nor available in the Sponsor files.

All subjects enrolled in the investigation will be provided with a Subject Identification Number (i.e., pseudonymization), consisting of a digit code, where the leading digit represents the investigation site number, for this single-site investigation all subject ID number will start with 100 and the two following numbers represents the consecutive subject number (e.g. 101 for the first enrolled subject 102 for the second enrolled subject.

Source documents

Source documents shall be created and maintained by the investigation site team as per clinical routine throughout the investigation. Source documents are the original records, including but not limited to worksheets (e.g., printouts of eCRF forms), physician or nursing notes, subject questionnaires etc. During each visit where printouts or copies of the source documentation are used for the investigation, these shall be signed and dated (i.e., certified) by a member of the investigation site team.

For investigation-specific variables, a possibility to use a combined worksheet/checklist will be made available to the investigation site. These worksheets will then, if used, constitute the source for the data noted in the worksheets. The site will store the worksheets in the ISF. The Sponsor may request a copy for remote monitoring. For variables entered directly into the eCRF, the eCRF is considered the source. To ensure consistency in the recording of source data, the use of worksheets versus entering data directly into the eCRF will be defined based on the preferred workflow of the site (if not directly entered into the medical record).

A source data agreement list will be created at each investigation site to define which are the source documents for the data gathered in the study and the location of them. This document will be completed at the first interim monitoring visit at the latest.

The Principal Investigator will provide direct access to source data during and after the clinical investigation for monitoring, audits, and regulatory authority review and inspections, if applicable. Permission for this

direct access to source documents needs to be obtained by the investigator from the subjects, hospital administration and local regulatory authorities as applicable, before starting the clinical investigation.

Case Report Form recording and processing

Data captured will be recorded, by the investigator and/or delegated site staff, in eCRFs by means of an EDC-system (SMART-TRIAL), provided/hosted by an external party (MEDEI ApS, Copenhagen, Denmark). The system has built-in features that enables users to be GCP and GDPR compliant. All data in relation to SMART-TRIAL is stored on secured Microsoft Azure hardware located in the EU, i.e., Dublin, Ireland. All users of the EDC system have personal accounts, accessed by two-factor authentication, allowing tracking of all data entries and changes in the system (i.e., audit trail).

The set-up, build and maintenance of the eCRF, incl. corresponding content (forms, events, data checks etc.), and testing/validation of the system, is performed by trained Sponsor representatives.

All data, subject- and product-related, must be accurately recorded in a timely manner (i.e., within 5 working days) into the EDC system by the delegated site staff.

NB. For Serious Adverse Events (SAE), Serious Adverse Device Effects (SADE) stricter timelines applies, see Section 18.4 for further reference.

The person entering the data into the database is not allowed to make any personal interpretation or to make any decisions on the data than self-evident corrections as listed in the data entry instructions or data handling report. All entered data must be consistent with the source documents, and if any discrepancies are found they must be corrected or explained in writing where applicable. The Principal Investigator is responsible for the data entered in the EDC-system and for signing the eCRF at the end of the clinical investigation.

The patient reported outcome (PRO) instrument used in this investigation will be completed on paper forms by the subjects themselves. The forms (i.e., source documents), marked with the Subject ID, will then be transferred by manual data entry to the corresponding form in the EDC-system by an authorized member of the investigation site team.

For screening failures following data will be recorded: reason for failure with reference to IE criteria and patient characteristics.

Data Management

To ensure data validity and accuracy, manual data cleaning and query handling will be performed remotely on a regular basis within the EDC-system. In addition, computerized edit checks will be utilised for identifying data values that are outside the allowed range, incomplete or inconsistent, and CIP deviations. The Data Validation Plan (DVP) specifies the checks that are to be performed on subject data for the clinical investigation.

Once all data has been captured and entered into the eCRF by the investigation site team, verified and validated by the appointed Sponsor representatives, and all reconciliation with the reported events and events reported to Oticon Medical Research and Development department, the clinical investigation database will be locked and the data will be analysed.

Storage of data

The investigator should retain clinical investigation records for at least 15 years after completion (or premature termination) of the investigation, or, in the event that the device is subsequently placed on the market, at least 15 years after the last corresponding device has been placed on the market. However, it is the responsibility of the investigator to make sure that the investigation record of clinical investigation subjects is retained in accordance with local legislation and in accordance with the maximum period of time allowed by the hospital. The investigator will continue having 'view access' to the study database even after

study closure.

The Principal Investigator must take measures to prevent accidental or premature destruction of these documents and at the end of the storage period, acquire a confirmation from the Sponsor before proceeding with the destruction of the documentation.

If the principal investigator leaves the investigation site, he/she will provide the Sponsor with the name and address of the person who will resume responsibility for the ISF. If the ISF will be transferred to another party (e.g., external archive, service provider etc.) this shall be discussed, agreed and documented in beforehand between the investigation site and the Sponsor.

The complete study database, which is a part of the TMF, will be securely stored at Oticon Medical, with restricted access. The TMF will be retained for 15 years after completion (or premature termination) of the investigation, or in the event that the device is subsequently placed on the market, at least 15 years after the last corresponding device has been placed on the market.

Missing data

Handling of missing data will be described in the SAP. In order to minimize missing data, the importance of complete follow up data sets will be emphasized to investigators and investigation site staff, as will the importance of recruiting subjects who are motivated to undergo treatment and participate in the investigation. The investigation site is leading in the field of bone conduction devices, thus familiar with the outcomes of the treatment, and what level of treatment compliance that can be expected from patients considering undergoing treatment with a device. The sites will also have experience in conducting clinical investigations and recruiting investigation subjects. The patient information will give the subjects a clear understanding of the design of the investigation and the visit schedule. The latter has been carefully considered to mimic the standard practice of treatment with a bone conduction device, but also to be feasible in relation to the burden on the investigation subjects as a mitigation measure to avoid drop-outs and/or missing appointments. In addition, subjects will be given the opportunity to complete out PROs at the applicable site visits if they have forgotten to bring them or to complete them on beforehand.

Monitoring through the electronic data capturing system will be performed all through the investigation period. Early and close monitoring of the eCRFs will enable the Sponsor to take action and get back to site if missing data and/or deviations are found. The Sponsors representatives will be in close contact to site to give support and training for general quality assurance of the data captured in the investigation

Audits and inspections

Audits of the clinical investigation may be conducted by the Sponsor or third parties designated by the Sponsor to evaluate compliance with the CIP, written procedures, this International Standard and the applicable regulatory requirements. These audits may cover all involved parties, systems and facilities and are independent of, and separate from, routine monitoring or quality control functions.

13 AMENDMENTS TO THE CIP

If changes to the CIP are needed, proposed amendments to the CIP shall be agreed upon between the Sponsor and Principal Investigator, and/or the coordinating investigator. Substantial amendments should be approved by the EC and Competent Authority (CA), as applicable, before incorporated.

In addition, substantial amendments to the Subject Information and Consent Form and/or other applicable documents previously approved by the EC/CA must be approved by the EC/CA before they will come into effect. For non-substantial amendments, local regulations regarding notifications to EC/CA should be followed.

14 DEVIATIONS FROM CLINICAL INVESTIGATION PLAN

A CIP deviation is an intentional or unintentional failure to follow the requirements of the CIP. Every effort should be made to comply with the requirements of the CIP and the Investigator, and other representatives of the investigational site team, is not allowed to deviate from the CIP, unless needed to protect the rights, safety and well-being of the subjects (i.e., emergencies). Under these circumstances, deviations from the CIP may proceed without prior approval by the Sponsor and favourable opinion from EC. Such cases should be documented and reported to the EC, as per local requirements, and to the Sponsor as soon as possible, but in no event later than 5 working days after the emergency occurred.

If other deviations occur, the Investigator should inform the monitor/clinical trial manager and make a record in the CIP Deviation Log provided in the EDC system. The implications of the deviation must be reviewed and discussed between the Sponsor and the Investigator. If deviations are found during monitoring visits, they should also be documented in the monitoring report and handled as above. This should be done as soon as possible after detection to avoid repetitive deviations. Continuous review of protocol deviations during monitoring visits aim to detect systematic errors and to identify retraining needs at the site. Frequency of monitoring is described in the monitoring plan and should be increased if systematic deviations are identified. All protocol deviations must be documented stating the reason, date, the action(s) taken, and the impact for the subjects and/or the investigation. If serious or repeated deviations occur, the Sponsor has the right to initiate early termination of the investigation.

At the end of the investigation, or in connection to a predefined interim analysis, protocol deviations will be re-categorized as minor or major and their consequence on analysis populations will be determined.

15 DEVICE ACCOUNTABILITY

The devices will be shipped or delivered by a Sponsor representative, as applicable, and kept in a locked area at the site. The Sponsor will keep records of the shipped / delivered investigational devices. A device accountability log will be held on site including date of reception, unique serial number, expiry date, subject identification, date of fitting and date of return of unused products (if applicable). The serial number will be noted in the eCRF at the fitting visit. If any devices are exchanged for any reason during the investigation the new unique serial number will be noted together with date of exchanging the device (both on the investigational device log and in the subjects eCRF).

All unused investigational devices must be returned to the Sponsor when treatment of the last subject has been completed. Return of devices by the end of investigation will be logged by Sponsor in Sponsor records.

The monitor will verify the accountability process at the monitoring visits.

16 STATEMENTS OF COMPLIANCE

The clinical investigation will be performed in consistency with the current version of the Declaration of Helsinki, ISO 14155, Regulation (EU) 2017/745 (MDR) and applicable regional or national competent authority regulations and requirements as well as any additional requirements imposed by the EC.

The final clinical investigation plan, including the final version of the patient Information and Consent Form must be approved in writing by an Ethics Committee (EC), and Competent Authorities (CA) if applicable, before enrolment of any subject into the investigation. The Principal Investigator is responsible for informing the Ethics committee of any amendment to the investigation plan as per local requirements.

The clinical investigation will not be commenced until approvals from the applicable Ethics Committee (EC) and Competent Authority (CA) have been received.

Any additional requirements imposed by the EC or national Competent Authorities shall be followed.

16.1 Insurance

The Sponsor will be responsible for ensuring adequate insurance covering any injuries to the subject caused by the investigational device. [redacted]

17 INFORMED CONSENT PROCESS

The Principal Investigator will ensure that the potential subject is given full and adequate oral and written information about the nature and purpose of the investigation, including possible benefits and risks involved. Alternatives to the treatment suggested in the CIP must be discussed to allow the potential subject to have an informed choice. Potential subjects must also be notified that they are free to decline participation in the investigation, and that they are free to discontinue at any time, without any consequences to their future care. Sufficient time will be given for consideration and the opportunity to ask questions before signing the informed consent form will be provided. The signed informed consent must be obtained before conducting any procedures specific for the investigation.

By signing the informed consent form, the subject agrees to participate in the investigation and that the results obtained may be used in authority assessments, and/or submissions for presentation or publication in scientific meetings and/or journals, with the condition that privacy and confidentiality are preserved.

The informed consent will be signed and dated by the subject and investigator who gave the verbal and written information. A copy of the patient information sheet including the signed informed consent form should be given to the patient and the original of the consent form must be filed in the ISF.

If any new information becomes available during the investigation that possibly could influence the subjects' willingness to participate, they will be informed and asked to sign a revised informed consent, if applicable.

18 ADVERSE EVENTS, ADVERSE DEVICE EFFECTS AND DEVICE DEFICIENCIES

18.1 Definitions

The definitions and procedures for reporting Adverse Events (AE), Adverse Device Effects (ADE), Serious Adverse Events (SAE), Serious Adverse Device Effects (SADE), Device Deficiencies (DD), Unanticipated Serious Adverse Device Effects (USADE) and Serious public health threats are presented in the subsections below. It is of outmost importance that all staff involved in the investigation is familiar with the definitions and procedures and it is the responsibility of the Principal Investigator to ensure this.

18.1.1 Adverse Event (AE)

Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs, including an abnormal laboratory finding, in subjects, users or other persons, in the context of a clinical investigation, whether or not related to the investigational device.

Note:
a. This definition includes events that are anticipated as well as unanticipated events
b. This definition includes events occurring in the context of a clinical investigation related to the investigational device, the comparator or the procedures involved. For the purpose of safety reporting all activities related to the use of a medical device may be considered procedures.

18.1.2 Adverse Device Effect (ADE)

An adverse device effect is an adverse event related to the use of an investigational medical device.

Note 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
Note 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.
Note 3: This includes 'comparator' if the comparator is a medical device

18.1.3 Serious Adverse Event (SAE)

Any adverse event that led to any of the following:

(a) death,
(b) serious deterioration in the health of the subject, that resulted in any of the following:
- (i) life-threatening illness or injury,
- (ii) permanent impairment of a body structure or a body function,
- (iii) hospitalisation or prolongation of patient hospitalisation,
- (iv) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
- (v) chronic disease,

(c) foetal distress, foetal death or a congenital physical or mental impairment or birth defect;

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

18.1.4 Serious Adverse Device Effect (SADE)

A serious adverse device effect is an adverse device effect that has resulted in any of the consequence characteristics of a serious adverse event.

18.1.5 Device deficiency (DD)

Any inadequacy in the identity, quality, durability, reliability, safety or performance of an investigational device, including malfunction, use errors or inadequacy in information supplied by the manufacturer.

18.1.6 Unanticipated Serious Adverse Device Effect (USADE)

An Unanticipated Serious Adverse Device Effect is an effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment. Procedures associated with the use of a device should be addressed in the risk assessment, which makes it possible to determine whether the procedure related SAEs are Unanticipated Serious Adverse Device Effect or not. SAEs related to procedures imposed by the clinical investigation plan but not with the use of the device should not be considered Serious Adverse Device Effects.

Note: Anticipated Serious Adverse Device Effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.

18.1.7 Serious public health threat

An event which could result in imminent risk of death, serious deterioration in a person's state of health, or serious illness, that may require prompt remedial action, and that may cause significant morbidity or mortality in humans, or that is unusual or unexpected for the given place and time.

18.2 Methods for discovering and documenting AE/ADE and DD

All subjects will be asked about the occurrence of AEs from the first day and until completion of the investigation. Events prior to enrolment will be considered medical history. The Principal Investigator (PI) or delegate will collect safety information using a non-leading question “have you experienced any new health problems or worsening of any existing condition?”. Events directly observed or spontaneously reported by the subjects will also be recorded throughout the investigation

All AEs falling into any of the previously defined definitions must be recorded as an AE in the eCRF. Clearly related signs, symptoms and abnormal diagnostic procedure results should be grouped together and reported as a single diagnosis or symptom whenever possible.

All AEs, but not limited to events reported by the subject or reported in response to an open question by the PI or member of the investigation team, which fall into any of the previously defined definitions must be recorded as an AE in the eCRF and should include the following information:

- Brief description of the event(diagnosis)
- Date of event onset (and time, if relevant)
- Date of event resolution (and time, if relevant)
- Severity
- Seriousness
- Causality assessment (i.e., relationship to medical device and/or procedure)
- Event treatments
- Event outcome

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance shall be reported as a device deficiency (DD) without unnecessary delay to the Sponsor by using the device deficiency form. It is the PI’s responsibility to record every observed device deficiency together with an assessment. The Sponsor shall review all device deficiencies and determine and document in writing whether they could have led to a SADE. Device Deficiencies that are assessed to or have SADE potential should be subjected to expedited reporting as described in Section 18.4.

AEs/ADEs and DDs should be reported to Sponsor as described in section 18.4.1. SAEs/SADEs/USADEs and DDs with SADE potential should be subject to expedited reporting according to section 18.4.2.

18.2.1 Severity

Severity describes the intensity of an AE and will be assessed as:

- Mild: does not interfere with subject’s usual function.
- Moderate: interferes to some extent with subject’s usual function
- Severe: interferes significantly with subject’s usual function

18.2.2 Causality

The relationship between the use of the medical device (including the medical - surgical procedure) and the occurrence of each adverse event shall be assessed and categorized.

During the causality assessment activity, clinical judgement shall be used and the relevant documents, such as the Investigator's Brochure, Clinical Investigation Plan and risk analysis report shall be consulted, as all of the foreseeable serious adverse events and the potential risks are listed and assessed there. The presence of confounding factors such as concomitant medication/treatment, the natural history of the underlying disease other concurrent illness or risk factors should also be considered.

The investigator and Sponsor will use the following definitions to assess the relationship of the serious adverse event to the investigational device, the comparator or the investigation procedure:

1. **Not related:** Relationship to the device, comparator or procedures can be excluded when:

   - the event has no temporal relationship with the use of the investigational device, or the procedures related to application of the investigational device;
   - the serious adverse event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
   - the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible - and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious adverse event;
   - the event involves a body-site or an organ that cannot be affected by the device or procedure;
   - the serious adverse event can be attributed to another cause (e.g. an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors);
   - the event does not depend on a false result given by the investigational device used for diagnosis, when applicable;

   In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious adverse event.

2. **Possible:** The relationship with the use of the investigational device or comparator, or the relationship with procedures, is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.

3. **Probable:** The relationship with the use of the investigational device or comparator, or the relationship with procedures, seems relevant and/or the event cannot be reasonably explained by another cause.

4. **Causal relationship:** the serious adverse event is associated with the investigational device, comparator or with procedures beyond reasonable doubt when:
   - the event is a known side effect of the product category the device belongs to or of similar devices and procedures;
   - the event has a temporal relationship with investigational device use/application or procedures;
   - the event involves a body-site or organ that
     - the investigational device or procedures are applied to;
     - the investigational device or procedures have an effect on;

- the serious adverse event follows a known response pattern to the medical device (if the response pattern is previously known);
- the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the serious adverse event (when clinically feasible);
- other possible causes (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
- harm to the subject is due to error in use;
- the event depends on a false result given by the investigational device used for diagnosis[10], when applicable;

In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious adverse event.

The sponsor and the investigators will distinguish between the serious adverse events related to the investigational device and those related to the procedures (any procedure specific to the clinical investigation). An adverse event can be related both to procedures and the investigational device. Complications caused by concomitant treatments not imposed by the clinical investigation plan are considered not related.

Any AE's that are assessed as possibly, probably or causally related will be classified as an ADE, which entails further information to be recorded, as specified in the corresponding eCRF.

Particular attention shall be given to the causality evaluation of USADE, since the occurrence of USADE could suggest that the clinical investigation places subjects at increased risk of harm than was expected beforehand.

In case of disagreement between the Sponsor and the Principal Investigator assessments of the AE, both opinions shall be communicated to concerned parties.

18.3 Reporting of safety events to Competent Authority by Sponsor

18.3.1 Reporting of SAE/SADE and Device Deficiencies with SADE potential

In accordance with MDR (EU) 2017/745, the following events are considered reportable events:

(a) any serious adverse event that has a causal relationship with the investigational device, the comparator or the investigation procedure or where such causal relationship is reasonably possible;

(b) any device deficiency that might have led to a serious adverse event if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate;

(c) any new findings in relation to any event referred to in points (a) and (b).

The period for reporting shall take account of the severity of the event. Where necessary to ensure timely reporting, the Sponsor may submit an initial report that is incomplete followed by a complete report.
For clinical investigations performed in line with the requirements of the Regulation (EU) 2017/745-Medical Device Regulation (MDR) Sponsor shall immediately, but no later than 2 calendar days after awareness report to CA events which indicate an imminent risk of death, serious injury, or serious illness and that requires prompt remedial action for other patients/subjects, users or other persons or a new finding to it. For any other reportable events, Sponsor shall immediately but not later than 7 calendar days report the event to CA.

In the absence of a fully functional EUDAMED database the MDCG template 'Summary Reporting Form' [I]. shall be used.

18.3.2 Reporting of Serious public health threats

Report of Serious public health threat shall be sent immediately to CA, but not later than 2 calendar days after awareness by Sponsor of new reportable event or of new information in relation with an already reported event.

18.4 Reporting of safety events to Sponsor by investigation site

18.4.1 Reporting of AE/ADE and DD

Any AE/ADE or DD shall be reported to the Sponsor via the eCRF within 5 working days after investigation site study personnel's awareness.

For device deficiencies that fulfil the SADE definition, the Investigator must provide Oticon Medical with detailed information and perform the steps described for SAE/SADE reporting section 18.4.2.

18.4.2 Reporting of SAE/SADE/USADE and DD with SADE potential

Any AE or ADE that is classified as serious, and any DD judged to have SADE potential shall be reported to the Sponsor via the eCRF, complemented with any additional information of the event as it become available. The signed report will trigger a system-generated e-mail notification to the Sponsor.

The report shall be registered in the eCFR immediately, but not later than 3 calendar days after investigation site study personnel's awareness of the event.

All SAEs/SADEs and DDs that could have led to a SADE should contain as much information as possible. In addition to information already collected and recorded for AEs/ADEs there is more detailed information required for SAEs/SADEs/USADs as specified in eCRF.

The occurrence of USADEs could suggest that the clinical investigation places subjects at increased risk of harm than was to be expected beforehand. Oticon Medical will handle and report USADEs to applicable authorities.

18.5 Reporting of safety events to EC by investigation site

It is the responsibility of the Principal Investigator to ensure that the local safety reporting requirements are adhered to regarding the extent of information and timing of reporting to the concerned EC.

Investigation study personnel shall provide Sponsor with all SAE/SADE/USADE related documentation and correspondence to the EC.

When the opinion on seriousness/causality differs between the PI and the Sponsor, the PI will be informed and is responsible for communicating both opinions to the EC, as required and agreed between Sponsor and PI.

18.6 Non-reportable events

Not applicable

18.7 Safety event follow-up

Medical follow-up of any type of safety event will continue until the symptoms/disease resolves, or an adequate medical explanation is apparent.

Documentation of all follow-up information regarding the AEs must be provided in the eCRF and, in accordance with the reporting requirements described above.

If the subject is withdrawn from investigation treatment due to an AE, the AE and the reason for withdrawal from the investigation is to be documented clearly in the eCRF.

18.8 Safety related contacts

Should the need for further guidance on safety-related issues and/or reporting be evident, the following contact details applies:

Oticon Medical

Phone:	+46 31 748 61 70 (vigilance)
Postal address:	Oticon Medical Datavägen 37, SE-436 32 Askim, Sweden
Mail:	QA@oticonmedical.se

18.9 Data Monitoring Committee

Based on the risk assessment, it has been concluded that a DMC is not needed for this open label, single arm, single center clinical investigation. The investigation will be conducted by experienced hearing aid professionals that are used to working with similar devices, with similar risk profiles.

19 VULNERABLE POPULATION (IF APPLICABLE)

Not applicable for this investigation

20 SUSPENSION OR EARLY TERMINATION OF THE CLINICAL INVESTIGATION

The investigator or Sponsor may at any time terminate the clinical investigation due to circumstances related to the rights, safety and welfare of the subjects enrolled, or conduct of the investigator/investigational site or company that preclude ongoing subject treatment.

If the investigation is suspended or terminated prematurely, the investigator will promptly inform the Sponsor and provide the reason(s) thereof (and vice versa). The applicable regulatory authorities and ECs/IRBs concerned will also be informed promptly in writing by the investigator. In case of suspension or terminated prematurely, subject included in the clinical investigation will fall under standard clinical care provided by the hospital.

21 PUBLICATION POLICY

A final report of the clinical investigation (CIR) (accompanied by a summary) will be completed, even if the investigation is prematurely terminated. The report will be prepared by the sponsor as referred to in Regulation (EU) 2017/745 (MDR) Chapter III of Annex XV, and Annex D of ISO 14155:2020. Irrespective of the outcome of the clinical investigation, the sponsor will within one year of the end of the clinical investigation or within three months of the early termination or temporary halt submit the CIR to the competent authority.

The results obtained in the investigation may be submitted for publication in scientific journals by the investigators, in cooperation with the Sponsor. Privacy and confidentiality of information about each subject will be preserved in any reports and any publications of the clinical investigation data.

Annual progress reports and final clinical investigation report will be submitted to the EC as applicable.

The clinical investigation will be registered in a publicly accessible database (www.clinicaltrials.gov) before recruitment of the first subject. Results will be registered once the clinical investigation and final investigation report have been completed.

22 CLINICAL INVESTIGATION AGREEMENTS

This is a sponsored investigation financed by Oticon Medical AB. The site 'Habilitation & Health, Hearing organization, Södra Gubberogatan 6, 416 63 Göteborg' will receive compensation [redacted] A clinical investigation agreement will be signed between Oticon Medical AB and 'Habilitation & Health, Hearing organization, Södra Gubberogatan 6, 416 63 Göteborg' before the investigation starts.

In addition, as the subject visits will be conducted at the site Chalmers University of Technology, a separate contract between Sponsor and Chalmers University of Technology will be fully executed before study start. Chalmers University of Technology will receive compensation [redacted]

23 SIGNED AGREEMENTS

23.1 Sponsor

On behalf of Oticon Medical AB I approve this clinical investigation plan.

Date and signature:

Name and title

23.2 Principal Investigator

I agree to the terms of this investigation plan. I will conduct the investigation according to the procedures specified herein and in consistency with the current versions of the declaration of Helsinki and ISO 14155 Clinical investigation of medical devices for human subjects — Good clinical practice.

Date and signature:

Name and title

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