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Your hearing · Our passion

A comparative, controlled, clinical investigation of a currently marketed hearing aid programmed with two different fitting methods

Protocol

Document dated: 2017.12.21

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A comparative, controlled, clinical investigation of a currently marketed hearing aid programmed with two different fitting methods.

Clinical Study Protocol

Study Type:	Clinical Investigation with Medical Device (MD)
Study Categorisation:	Category C: Medical Device without CE mark
Study Registration:	SNCTP, clinicaltrials.gov
Study Identifier:	BF002-1707
Sponsor	Bernafon AG Morgenstrasse 131, 3018 Bern
Principal Investigator:	Barbara Simon bsim@bernafon.com +41 31 998 16 84
Investigational Product:	Fitting software; HearToo Studio
Protocol Version and Date:	Version3.0; Final Document

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Signature Page(s)

Study number	SNCTP; clinicaltrials.gov; registration number TBD
Study Title	A comparative, controlled, clinical investigation of a currently marketed hearing aid when programmed with two different fitting methods.

The Sponsor-Investigator and trial statistician have approved the protocol version [3.0 (dated 21.12.2017)], and confirm hereby to conduct the study according to the protocol, current version of the World Medical Association Declaration of Helsinki, ICH-GCP guidelines or ISO 14155 norm if applicable and the local legally applicable requirements.

Sponsor:

Printed name of Sponsor Representatives:

Erich Spahr, General Manager

Bruno Keller, Senior Director Marketing and Channel Support

Bern, 21.12.2017 _____
Place/Date Signature

Bern, 21.12.2017 _____
Place/Date Signature

Printed name of Investigator: Barbara Simon

Bern 21.12.2017 _____
Place/Date Signature

Printed name of Statistician: Christophe Lesimple

Bern, 21.12.2017 _____
Place/Date Signature

Head of RA

Printed name of ~~Quality Manager~~: Asif Muhammad

Copenhagen, 2017.12.21 Asif Muhammad
Place/Date Signature

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STUDY SYNOPSIS

Sponsor / Sponsor-Investigator	Bernafon AG
Study Title:	A comparative, controlled, clinical investigation of a currently marketed hearing aid programmed with two different fitting methods.
Short Title / Study ID:	BF002-1707
Protocol Version and Date:	Version 3.0; 2017.12.21
Trial registration:	SNCTP, clincialtrials.gov
Study category and Rationale	Category C: Medical Device without CE mark
Clinical Phase:	Pre-market validation study involving human subjects. This clinical investigation is designed to evaluate different methods of fitting a currently marketed hearing instrument system. As human subjects are involved, this validation test falls under the definition of a clinical investigation. The validation addresses the subjective benefit of the instrument when fit with different approaches. Does the end user perceive a difference between the fittings? Evaluating the overall safety is important for pre-market performance and safety validation.
Background and Rationale:	Benefits of amplification and accessories used with it outweigh anticipated risks in mild to profound hearing-impaired subjects. The basic benefit of amplification should be present with any method that the trained professional fitting the instruments uses. The goal of this study is to compare two fitting methods and determine whether the end user perceives more benefit from one fitting method over the other. The objective benefit is expected to be the same; however, the subjective benefit may be different due to a possible psychological effect from more effort or time spent by the trained professional. Bernafon will conduct this clinical investigation to test current hearing instruments fitted with the standard procedure and a self-directed procedure. Safety and performance validation of the new self-directed fitting software is needed before release to the market. The reason for this study is to evaluate a currently marketed, CE certified, hearing aid and determine whether different fitting methods provide the same perceived benefit. Additionally, this study will validate the safety of the fitting procedure as well as collect post market safety information about the devices themselves. The goal is to evaluate the audiological performance objectively as well as the subjective benefit. Furthermore, it is important to identify unexpected, unwanted behavior from the fitting software and the devices.
Objective(s):	The purpose of this research is to determine the potential of a narrative influence on the subjective benefit of the hearing instruments with the traditional fitting method versus the self-directed method. Furthermore, the objective benefit of the hearing instruments should not be affected by using a different fitting method. The gain applied by each fitting method should be the same and will be controlled by electro-acoustical measures.

Outcome(s):	Primary Endpoint: • Primary Outcome is the subjective benefit with the standard fitting compared to the self-directed fitting (using questionnaires) Secondary Endpoints: • Audiometry will be compared using the standard measurement made by the Investigator as a control against the self-directed measurement • Comparison of the objective performance of the devices (using speech testing) • Procedural safety meaning that there are no unwanted noises or artefacts heard from the devices (as reported by the subjects) • Scores from speech tests and questionnaires will be compared between the self-directed fitting and the standard fitting method. • No unexpected, unwanted behavior of the devices or unexpected device related AEs or SAEs.
Study design :	This is a controlled, randomized, cross-over, open label, comparative clinical investigation conducted at two sites within the canton of Bern. The study is based on a population of hearing impaired people that have hearing loss appropriate for the tested devices. The treatment assignment of participants is randomized as well as the test condition order during the lab testing. The standard fitting method will be used as a control. The hearing instruments will be exactly the same. There is no placebo or “fake” device that does not provide amplification. A randomized cross-over design is used with half of the test subjects wearing the device fit with the traditional fitting method first and the other half using the self-directed method and then switching after approximately 10 +/-5 days. A lab test will be used to test speech in a simulated environment. After each field trial period, the participants will be tested unaided and aided with speech material.

Inclu sion / Exclusion criteria:	Inclusion Criteria: • All types of hearing loss (sensorineural, conductive, mixed) • If the hearing loss is conductive or mixed it must first be approved for amplification by a physician • All shapes of hearing loss (flat, sloping, reverse slope, notch) • Severity ranging from mild to severe • First time hearing aid users (never worn hearing aids before) • German speaking • Both genders • Ages 18 and older • Ability and willingness to sign the consent form Exclusion Criteria: • Current hearing aids users • Contraindications for amplification • Active ear disease • Inability to follow the procedures of the study due to language problems, psychological disorders, dementia, or other cognitive problems of the participant • A reduced mobility unable to attend weekly study appointments • A reduced ability to describe auditory impressions and the usage of the hearing aids • Uncooperative so that it is not possible to record a valid pure tone audiogram • A strongly reduced dexterity • With psychological problems • Central hearing disorders • Bernafon employees • Family members of Bernafon employees
Measure ments and procedures:	A hearing test will be made using standard audiometry performed by the investigator and a hearing screening using the new self-directed software which includes an automated screening. Amplification is fitted either using the first fit procedure with the standard Oasis software (RMD) or with the new self-directed software (IMD) that uses a simplified version of the existing Oasis software. First fit in the context of this trial will mean without any additional fine tuning. During a normal first fit it is possible to make changes based on subject comments. However, to maintain that the acoustic fitting of the two sets of hearing aids is the same there will be no fine tuning performed. The subjects will complete a standardized questionnaire that measures their perceived handicap of the hearing loss (Gothenburg). Two additional questionnaires will be used to measure a possible narrative effect on the subjective perception of the fitting procedures. A standardized questionnaire, IOI-HA, and a custom product questionnaire will be used after each 10-day field test to evaluate the benefit of amplification with the RMD and the IMD. Also, a custom packaging questionnaire will be used after each fitting to measure the usability of the packaging of the RMD and the IMD. At the last appointment the participants will complete a preference questionnaire. Speech intelligibility tested in quiet will be measured with both fittings. The speech material will be a multi-syllable word test called the Freiburger Wörttest (FST) with the speech presented from a speaker in front of the subject. Safety is measured by reported unexpected sounds from the hearing aids verbally. Safety is also measured by AEs or SAEs reported at visits.

Study Product / Intervention:	HearToo Software The new self-directed fitting software is not CE marked. It is a combination of two entities: a self-directed hearing screening based on a known algorithm from Audiology Inc. sold in an automated audiogram by Grason Stadler, GSI (Eden Prairie, MN) and a simplified version of the Oasis software. The flow of the new software is driven by the end user, but a trained professional should always assist with the fitting. The new software will first perform a hearing screening on the end user and then recommend a hearing aid and prescribe amplification to the hearing aid based on the hearing screening results. Please see the IB for a full description of the self-directed fitting device. An additional medical device used for the trial is the Juna 7 behind-the-ear (BTE) hearing device. It was released to the market in 2015.
Control Intervention (if applicable):	The reference intervention is the standard accepted method of fitting hearing instruments. The software version used to program the Juna 7 devices with the traditional fitting is CE marked and has been used on the market since the release of the Juna product in 2015. The performance and subjective benefit of a self-directed fitting method will be tested against the standard. For the purposes of this trial the standard fitting method will be referred to as the RMD and the new self-directed fitting software will be the IMD.
Number of Participants with Rationale:	There will be an exploratory analysis of data only. The total number of participants will be a minimum of 24 (no more than 40), and the explanation for this sample size is as follows: A literature search about this tested topic does not provide enough strong references to build a confirmatory analysis. It seems that results might be strongly influenced by the inclusion criteria (first time vs experienced hearing aid users) or test design (cross-over, multi-investigator, or between group designs). There is no article to our knowledge that includes a multi-investigator effect in the test design when looking at the effect of different fitting procedures. Adding a treatment interaction term seems to be mandatory if this trial wants to determine the effect that different investigators may have. Each investigator shall treat the same amount of subjects. The 24-40 subjects will participate in 2 field studies, but randomized into different fitting/intervention groups with half the number of subjects in each group.
Study Duration:	Approximately 3 months The screening of the participants will begin in February of 2018 and the final data collection appointments will occur in April 2018.
Study Schedule:	The first participant is expected to begin in February 2018. The last participant is expected to finish the testing in April 2018.
Investigator(s):	Barbara Simon, Research Audiologist, Doctor of Audiology Morgenstrasse 131 3018 Bern, CH bsim@bernafon.com +41 31 998 16 46
Study Centre(s):	The testing will be performed at two clinical sites in canton Bern, Switzerland.
Statistical Considerations:	The analysis and documentation will be performed by the statistician using the latest validated R version with R Studio as IDE. Appropriate data analysis will be performed with parametric and non-parametric tests on questionnaire outcomes, hearing threshold measures, and speech test scores.

GCP Statement:	This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP or ISO EN 14155 (as far as applicable) as well as all national legal and regulatory requirements.

STUDY SUMMARY IN LOCAL LANGUAGE

This study is designed to investigate the benefits of the hearing aid in the laboratory and in daily life when fitted with two different methods. Subjective and objective evaluations will be made. The aim is to show the benefits of the hearing aids with both fitting methods with the help of data obtained, and to improve the available fitting methods in order to further increase the benefit for people with hearing disorders in situations where the standard method and those trained to perform it are not available.

Diese Studie soll untersuchen, ob es einen subjektiv wahrnehmbaren Unterschied gibt zwischen der Hörgerate Anpassung durch einen Audiologen oder eine Anpassung durch eine vom Hörbehinderten selbst bediente Software. Neben der subjektiven Wahrnehmung werden weiter subjektive und objektive Parameter in diese Studie erfasst. Insgesamt ist das Ziel dieser Studie, eine selbstbediente Anpassungsmethode zu testen, welche eingesetzt werden kann falls kein Audiologe zur Verfügung steht. Die Anpassung soll sich dabei nicht unterscheiden und die Hörqualität für den Hörbehinderten nicht leiden.

ABBREVIATIONS

Provide a list of abbreviations used on the protocol - to be completed

AE	Adverse Event
AMTAS	Automated Method for Testing Auditory Sensitivity
CA	Competent Authority (e.g. Swissmedic)
CEC	Competent Ethics Committee
CRF	Case Report Form
ClinO	Ordinance on Clinical Trials in Human Research (in German: KlinV, in French: OClin)
eCRF	Electronic Case Report Form
CTCAE	Common terminology criteria for adverse events
DSUR	Development safety update report
GCP	Good Clinical Practice
IB	Investigator's Brochure
Ho	Null hypothesis
H1	Alternative hypothesis
HCP	Hearing Care Professional
HFG	Humanforschungsgesetz (Law on human research)
HMG	Heilmittelgesetz
HRA	Federal Act on Research involving Human Beings
IMD	Investigational Medical Devic
IIT	Investigator-initiated Trial
ISO	International Organisation for Standardisation
ITT	Intention to treat
KlinV	Verordnung über klinische Versuche in der Humanforschung (in English: ClinO, in French OClin)
LPTh	Loi sur les produits thérapeutiques
LRH	Loi fédérale relative à la recherche sur l'être humain
MD	Medical Device
OClin	Ordonnance sur les essais cliniques dans le cadre de la recherche sur l'être humain (in German : KlinV, in English : ClinO)
PI	Principal Investigator
RMD	Reference Medical Device
SDV	Source Data Verification
SOP	Standard Operating Procedure
SPC	Summary of product characteristics
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File

STUDY SCHEDULE

Study Periods	Intervention Period		
Visit	Screening/1	2	3
Day	0	10 +/- 5 days	20 +/- 5 days
Patient Information and Consent	x		
Demographics	x		
Medical/Hearing History	x		
In-/Exclusion Criteria	x		
Randomization	x	x	
Otoscopy	x	x	x
Audiometry	x		
Administer Medical Device	x*	x*	
Baseline Measure (Gothenburg questionnaire)	x		
Primary Variable (IOI-HA questionnaires)	x	x	
Secondary Variables (audiometry)	x		
Other Variables (speech testing)		x	x
Other Variables (product questionnaire)	x	x	
Other Variables (preference questionnaire)			x
Adverse Events	x	x	x

*Depending on randomization subjects will be fit with IMD at the first or second visit. Everyone will use the IMD at the first visit to perform audiometry.

1. STUDY ADMINISTRATIVE STRUCTURE

1.1 Sponsor, Sponsor -Investigator

Bernafon AG

Morgenstrasse 131, 3018 Bern

Tel. +41 31 998 01 01

The role of the sponsor is to provide the sites for the testing as well as the equipment used during testing. The sponsor will provide the hearing devices, the IMD, and the RMD used for the study. The results will be used by the sponsor to prove the performance of the IMD. The sponsor may audit the clinics as well as the processes and documentation performed by the investigators at those sites.

1.2 Principal Investigator(s)

Barbara Simon, Research Audiologist
Morgenstrasse 131, 3018 Bern
Tel. +41 31 998 16 46
Email: bsim@bernafon.com

1.3 Statistician ("Biostatistician")

Statistics will be performed by Christophe Lesimple. Christophe Lesimple is an employee of Bernafon that works within the Product Management Audiology group and specializes in statistical analysis. He is also certified in GCP.

1.4 Laboratory

Not applicable

1.5 Monitoring institution

Bernafon is in charge of monitoring in order to verify that the conduct of the clinical investigation complies with the approved CIP, subsequent amendment(s), ISO14155, and the applicable regulatory requirement(s). There will be a specific person assigned as the Monitor (sec. 1.7).

1.6 Data Safety Monitoring Committee

There will not be a data safety monitoring committee employed. The data will be stored using an accepted and validated data storage management system.

1.7 Any other relevant Committee, Person, Organisation, Institution

Julie Tantau will monitor the investigation. She works within the Product Validation group at Bernafon. She is certified in GCP, and familiar with ISO 14155. She has also been certified in Clinical Monitoring and has a CAS I in Clinical Trial Practice and Management.

2. ETHICAL AND REGULATORY ASPECTS

Before the study will be conducted, the protocol, the proposed patient information and consent form as well as other study-specific documents shall be submitted to a properly constituted Competent Ethics Committee (CEC) and Swissmedic. Any amendment to the protocol must as well be approved (if legally required) by these institutions.

The decision of the CEC and Swissmedic concerning the conduct of the study will be made in writing to the Sponsor before commencement of this study. The clinical study can only begin once approval from all required authorities has been received. Any additional requirements imposed by the authorities shall be implemented.

2.1 Study registration

The study shall be registered in a registry by the US National Institutes of Health, an International Clinical Trials Registry Platform called Clinical Trials.gov (https://clinicaltrials.gov/ct2/home). In addition, the study will be registered in German in the Swiss National Clinical Trials Portal (SNCTP).

2.2 Categorisation of study

The clinical trial of these medical devices falls under Category C because although the hearing aids have the conformity marking and will be used in accordance with the instructions, the new self-fitting software does not. The IMD and focus of the trial is the software device.

Use of the devices is not prohibited in Switzerland.

2.3 Competent Ethics Committee (CEC)

The responsible investigator ensures that approval from an appropriately constituted Competent Ethics Committee (CEC) is sought for the clinical study.

The responsible investigator will report any changes as well at the end of study within the allowed time frame (including changes to the research activity and all unanticipated problems involving risks to humans; including in case of planned or premature study end and the final report). No changes will be made to the protocol without prior Sponsor and CEC approval, except where necessary to eliminate apparent immediate hazards to study participants.

Premature study end or interruption of the study will be reported within 15 days. The regular end of the study will be reported to the CEC within 90 days, and the final study report shall be submitted within one year after study end. Amendments are reported according to chapter 2.10.

2.4 Competent Authorities (CA)

The Sponsor will obtain approval from Swissmedic before the start of the clinical trial. CA approval is necessary for all studies category C (MD).

The Sponsor will report any changes as well as the end of study within the allowed time frame (including changes to the research activity and all unanticipated problems involving risks to humans, including in case of planned or premature study end and the final report). No changes will be made to the protocol without prior Swissmedic approval, except where necessary to eliminate apparent immediate hazards to study participants.

2.5 Ethical Conduct of the Study

The study will be carried out in accordance to the protocol and with principles enunciated in the current version of the Declaration of Helsinki, the guidelines of Good Clinical Practice (GCP) issued by ICH, in case of medical device: the European Directive on medical devices 93/42/EEC and the ISO Norm 14155

and ISO 14971, the Swiss Law and Swiss regulatory authority's requirements. The CEC and regulatory authorities will receive annual safety and interim reports and be informed about study stop/end in agreement with local requirements.

2.6 Declaration of interest

It is the policy of Bernafon AG that the conduct of employees and all other persons acting as its representatives should be at all times in the best interests of Bernafon AG, its members and the general public. In performing their duties, Bernafon AG representatives should not be influenced by desire for personal gain. Accordingly, Bernafon AG has adopted rules to guide disclosure of potential conflicts of interest and the society's response thereto that shall apply to those who agree to serve Bernafon AG in any official capacity.

2.7 Patient Information and Informed Consent

The participants will be informed about the study including what type of testing will be involved, how long it will last, and who will do the testing. Consent is sought from each participant. They will be compensated with 100 CHF cash.

The investigator will explain to each participant the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits and any discomfort it may entail. Each participant will be informed that the participation in the study is voluntary and that he/she may withdraw from the study at any time and that withdrawal of consent will not affect his/her subsequent medical assistance and treatment.

The participant must be informed that his/her medical records may be examined by authorized individuals other than their treating physician.

All participants for the study will be provided a participant information sheet and a consent form describing the study and providing sufficient information for participant to make an informed decision about their participation in the study. The participants will sign the consent form in the clinic during the first visit if they choose to become a participant.

The patient information sheet and the consent form will be submitted to the CEC to be reviewed and approved. The formal consent of a participant, using the approved consent form, must be obtained before the participant is submitted to any study procedure.

The participant should read and consider the statement before signing and dating the informed consent form, and should be given a copy of the signed document. The consent form must also be signed and dated by the investigator (or his designee) and it will be retained as part of the study records.

2.8 Participant privacy and confidentiality

The investigator will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspections and will provide direct access to source data and/or documents.

Additionally the investigator affirms and upholds the principle of the participant's right to privacy and that they shall comply with applicable privacy laws. Especially, anonymity of the participants shall be guaranteed when presenting the data at scientific meetings or publishing them in scientific journals.

Individual subject medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited. Subject confidentiality will be further ensured by utilising subject identification code numbers to correspond to treatment data in the computer files.

The subject identification numbers have no relation to any subject private data (e.g. Birthdate). The numbers are assigned as the subjects join the subject pool. The number and corresponding subject name are written in a document that is stored in a secured document management system. The document can be opened with a security access code of 11 characters that is only given to study personnel that work with subjects (e.g. investigators/ audiologists). For data verification purposes, authorized representatives of the Sponsor (-Investigator), Swissmedic, or an ethics committee may require direct access to parts of the medical records relevant to the study, including participants' medical history.

2.9 Early termination of the study

The Sponsor and/or CEC and/or Swissmedic may terminate the study prematurely according to certain circumstances, for example:

- ethical concerns,
- insufficient participant recruitment,
- when the safety of the participants is doubtful or at risk, respectively,
- alterations in accepted clinical practice that make the continuation of a clinical trial unwise,
- early evidence of benefit or harm of the experimental intervention

2.10 Protocol amendments

The Principal Investigator is allowed to amend the protocol or to provide suggestions for a protocol amendment. Any plans for protocol modifications will first be approved by the relevant parties (including, other investigators, CEC, and Swissmedic) before amending the protocol.

Substantial amendments are only implemented after approval of the CEC and CA respectively.

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 CEC/CA. Such deviations shall be documented and reported to the sponsor and the CEC/CA as soon as possible.

All non-substantial amendments are communicated to Swissmedic as soon as possible if applicable and to the CEC within the Annual Safety Report (ASR).

3. BACKGROUND AND RATIONALE

3.1 Background and Rationale

According the World Health Organization (WHO, 2016) 360 million people worldwide suffer from disabling hearing loss. Hearing aid amplification is the most common treatment for hearing loss. Benefits of amplification and accessories used with it outweigh any risks in mild to profound hearing impaired subjects. A clinical literature evaluation is maintained and updated by Bernafon for new products. The evaluation concludes that, “Hearing device use is “a non-invasive, comparatively low risk option with considerable potential benefits”. As presented in the general literature evaluation, substantial scientific clinical literature shows that amplification of sound provides the claimed benefit for hearing impaired persons. The literature shows both significant improvements in speech intelligibility and improved life quality (Kochkin, 2011). The benefits are obtainable for both unilateral and bilateral fittings and are both short term and durable on long term.

Bernafon AG sells hearing aids internationally. They conduct trainings to teach people how to fit the hearing aids in multiple countries; however, it is not possible to train every person that fits a hearing aid. Different countries have different requirements for those that are allowed to sell and fit hearing aids. For example, the WHO has written a guideline for providing hearing aid services for developing countries. In that guideline it states that “Persons doing the fitting must have received the necessary training…” (WHO, 2004). The document later describes the necessary training as a 3-week training with follow-up supervision and refresher courses. With this in mind, Bernafon proposes a simplified and self-directed combined hearing screening and fitting software application that requires little training in order to complete a hearing screening and hearing aid fitting. The availability of such a system will make hearing devices available for more people around the world living in either remote areas or developing countries without enough equipment and trained personnel.

Bernafon AG will carry out studies of the IMD with test participants who have hearing loss in order to validate the performance and to qualify the benefit for the user when both the RMD and the IMD are used. Additionally, the results of the trial will be used to identify areas of further optimization of the tested products. The aim is to determine whether there is a narrative effect on the perceived benefit of the hearing aids from the RMD. Audiometry will be compared to ensure that similar results are achieved with the IMD as those from a standard audiometry test. Speech intelligibility will measure the objective benefit of the hearing aids. The trial will also provide safety information.

All participants are hearing impaired persons that have never used hearing aids before. They will be fit with hearing aids that have been on the market for 2 years, Juna 7 Nano BTEs. They will be fit two times during the trial, once with the RMD and once with the IMD.

The RMD is the standard first fit process of the Oasis software. The hearing thresholds are entered into the software and then used by the software to calculate the amount of amplification needed. The software has default settings for features such as noise reduction and directionality. The HCP saves the fitting and all settings are saved in the hearing aid. The IMD will use the same calculation algorithm to determine the amount of amplification; however, the hearing thresholds will be transferred directly to the software after the automated hearing screening. The same default settings will be applied, and the HCP will save the fitting. The hearing aids will be fit exactly the same electro-acoustically. The main difference is that the IMD is more patient driven; therefore, there could be a psychological effect that results in a higher rating for one hearing aid or the other.

In summary, the primary reason for this study is to evaluate the new self-directed hearing aid fitting software. It will not replace the current software but supplement markets that may not have the infrastructure or the trained personnel to use the current software. Or in markets that currently use the standard software, it could be used as an optional fitting method for other outlets beside the clinics where the standard software is used, such as a pharmacy. The goal is to evaluate the audiological performance, possible narrative effect, and safety of the new software before it’s released to the market.

3.2 Investigational Product (treatment, device) and Indication

The investigational product is a medical device (MD). The brand name is HearToo Studio, manufactured by Bernafon AG. The software component of the combined screening and fitting

software is Oasis 26. The device is intended for people over 36 months of age. The software does not have CE declaration. The device is a software application that can be downloaded onto a computer or a tablet. It will come with headphones and a soundcard to be used for the hearing screening. The hearing aids that can be fitted by the software are Bernafon Juna 7 hearing aids or Saphira 3 hearing aids, both of which are CE marked. They have been sold on the market for 2 years. The hearing aids will be used in accordance with their original intended use description. Consultants that receive a minimal amount of training will be able to use the IMD. The IMD is self-directed meaning that the person getting the hearing aids will drive the flow of the software. However, it is not intended to be used by the end user alone. A consultant will guide them through the fitting flow and help with explanations of the screening results, hearing aids, or other questions that arise. The headphones will be in contact with the outer portion of the ears. The hearing aids consist of a body made of plastic parts and non-toxic paint that touch the outer portion of the ears. Plastic tubing and a silicon dome are the parts that are fitted in the ear canal and come in contact with the skin. The device is non-invasive and requires no surgical procedures.

3.3 Preclinical Evidence

Bernafon requires evidence of the operational safety and medical effectiveness of the devices before testing with them. This evidence includes the device-related performance data in accordance with IEC 118-7: Measurement of the maximum output level and the maximum gain of the hearing aids themselves. The safety of the combined screening and fitting software is demonstrated by a beta version that has passed through a complete systematic software test and ensures the functionality of the hearing aids in combination with the software. Please see chapter B3e of the IB.

3.4 Clinical Evidence to Date

A clinical literature evaluation is maintained and has been updated in 2016 for the hearing aids. They are designed to amplify sound. The benefit of hearing aids has been shown in various studies (Kochkin, 2011). The evaluation includes an analysis of adverse events for Bernafon products as well as competitor devices. The basic benefit of hearing aids does not change with newly released devices.

A new literature search was completed in June of 2017 specifically for self-directed hearing test and fitting devices. In 2013 a study was completed by Eikelboom et al. to compare the results of standard audiometry to an Automated Method for Testing Auditory Sensitivity (AMTAS) system. The standard deviation between methods across frequencies was 6.4 dB. Using standard audiometry a 5 dB test retest difference is acceptable. The 6.4 dB difference using an AMTAS system is slightly higher than the expected but not significant. According to a study by Convery et al. (2015), self-directed hearing tests show good test-retest reliability. Also, a study was completed by Convery et al. (2017) with a combination system similar to the IMD in which subjects completed a self-directed hearing test and fitting. Fifty-five percent were able to complete the process with no errors at all. The results show the importance of good training material.

A risk assessment is performed for all new devices. The primary risk identified is the possibility of achieving incorrect screening results if there is too much background noise. For the study purposes the test will be completed in a clinic; therefore, this risk is not applicable. However, in everyday use the environment in which the system is used cannot be controlled. The risk is mitigated by providing training material for the consultant that describes the type of environment needed to run the hearing screening. Additionally, no adverse events for any currently marketed self-fit hearing instrument systems have been reported.

The current study will provide further data for self-directed hearing tests and fitting systems.

3.5 Medical Device: Rationale for the intended purpose in study (pre-market MD)

The IMD will be used in accordance with current use of self-testing devices and fitting software. The intended purpose of the study is to compare the performance of the IMD with the RMD. In order to make an effective comparison the test participants shall wear the hearing aids fitted with both methods

(IMD and RMD) for a minimum of 10 days per field test period.

3.6 Explanation for choice of comparator (or placebo)

The comparator device is the standard Oasis software and fitting procedure that is used by HCPs. Additionally a standard audiological test completed by the investigator will be compared to the results from the self-directed procedure. A placebo is not justified because the goal is not to test unaided versus aided, but the fitting procedure itself and how it impacts the perceived subjective benefit of the participants. Therefore, the current accepted standard will be compared to a new automated procedure.

3.7 Risks / Benefits

The audiological and psychoacoustic investigations are conducted using volunteer test participants with sound pressure levels that will not endanger their residual hearing. The test participants will be advised of the type, content, extent, and possible risks of the test beforehand. As psychometric methods are involved in the methods used, the risk for the test participants is judged to be extremely minor. However, the following precautions should be taken:

Risk of hearing loss to residual hearing at too high a level in audiological and psychoacoustic experiments: Due to the test design (use of noise level up to a maximum of 100 dB SPL) on the construction of the measuring equipment (maximum output of loud speaker, maximum level control of headphones-output-stage) the maximum provided sound level is limited. During the screening (test of hearing loss) a level of more than 100 dB SPL must be provided for test subjects who are profoundly hard of hearing. Only the standard audiometry test controlled by the investigator has the capability of such levels. The automated test is limited to an output of 80 dB SPL.

A device risk analysis and risk assessment has been conducted for the new device according to EN ISO 14971. This describes the anticipated adverse device effects, residual risks associated with the investigational device and the procedures involved in its use. It also describes that the anticipated clinical benefit outweighs the potential risks. Please see the Risk Assessment for details.

Post-trial care is organized in a manner that allows the test participants to return to the clinical sites where they were originally recruited and arrange an appointment if they choose to purchase hearing aids.

3.8 Justification of choice of study population

The choice of the study population was determined by the goal of the study. The intended purpose of the study is to compare the current standard of fitting to the new self-directed device. Therefore, only participants that are hearing impaired with a hearing loss that is indicated for amplification will be included. Experienced hearing aid users will be excluded because they have experience with the standard testing and fitting procedure that will bias their judgement of the two processes used for this particular study.

Test subjects will be chosen as they appear in either the Bern Audika clinic or the Thun Audika clinic for appointments that they have made for an initial hearing test. No employees of Bernafon or family members of employees will be included in the study. The participants will have the study explained and be consented before any trial activities take place. If they would like to participate, they will sign the consent form along with the investigator and trial activities for day 0 can begin. All trial activities including the initial hearing test to determine candidacy will take place at either the Bern or Thun Audika clinics.

If they do not wish to participate in the study they can cancel the appointment or they can continue with the normal hearing aid purchasing process.

Testing normal hearing participants would not contribute information to this study. It would not be ethical to fit normal hearing people with hearing aids. Test participants must be able to sign and understand the consent form otherwise they will not be included.

Vulnerable participants and those incapable of making their own judgments will not be included.

For emergency situations, the following applies:

-The standard procedure is to recommend that a subject see the ENT with whom they have an established relationship. If a subject does not have an ENT then it is agreed with Dr. Carvacchio (Inselspital, Bern) that, if necessary, subjects from this trial could be referred to him.

4. STUDY OBJECTIVES

4.1 Overall Objective

The purpose of this study is to compare the performance of the IMD to the RMD. The study aims to provide a final validation and quality control of the IMD before it is released for sales.

4.2 Primary Objective

The study seeks primarily to determine if the subjective benefit of the hearing aids fitted with the IMD is as good as the RMD. Does one fitting method provide a psychological effect that influences the participants? As a second primary objective the study seeks to proactively determine if there is any unknown and/or unwanted behavior from the IMD. The study seeks to validate that the performance of the IMD is not inferior to the RMD.

4.3 Secondary Objectives

Secondary objectives are to assess the performance of the hearing aids after being programmed by both fitting methods. The hearing aids will be the same electro-acoustically and should provide equivalent aided benefit.

4.4 Safety Objectives

The study aims to validate the overall implementation of the IMD. The study will test for unexpected behavior from the IMD and new risk factors to ensure safety of the devices before they are released to the market.

5. STUDY OUTCOMES

5.1 Primary Outcome

The primary outcome variable will be the subjective benefit of the hearing aids measured with a standardized questionnaire: the International Outcome Inventory for Hearing Aids (IOI-HA) and a custom questionnaire based on the questionnaire used in the Naylor et al. (2015) study. A comparison will be made between the subjective benefit measured with the hearing aids fitted with the control (RMD), and with the test device (IMD).

5.2 Secondary Outcomes

The secondary outcome variables are the audiometry as measured with the standard test and with the automated system. The data analysis will focus on the hearing threshold differences with both procedures in a nested model: ear-participant-investigator.

Additionally data logging from the hearing aids will be recorded as an indication of hearing aid use. The data will be averaged from each ear. The following data will be used:

1. Daily usage in hours per day,

2. Acoustical environment in percentage for the following listening environments: quiet, speech in quiet, speech in noise, and noise.

5.3 Other Outcomes of Interest

Explanatory variables include speech intelligibility testing using a multi-syllable word test called the Freiburger Sprachverständnistest (FST). This test will measure the objective benefit (difference from unaided and aided) from the hearing aids as fitted with the RMD and the IMD. Also the perceived handicap associated with hearing impairment may influence the perceived benefit from the hearing aids. The Gothenburg Profile (GP) will be used to quantify perceived handicap and the influence it may have on the primary outcome. A custom packaging questionnaire specific to hearing aids will test the usability of the packaging.

5.4 Safety Outcomes

The test participants will be asked whether anything unexpected that occurs during the field trial periods. Unexpected things include feedback or whistling from the device, unexpected sounds or artefacts from the device, discomfort, muting or shutting off of the device in mid-use, unexplained warning signals or beeping from the device, loud sounds, and occlusion. The information provided from the field trial will alert Bernafon to the potential for safety risks that should be addressed before the product is released to the market.

6. STUDY DESIGN

6.1 General study design and justification of design

This is a controlled, randomized, open label, cross-over, comparative clinical investigation conducted at two sites within Canton Bern, Switzerland.

The exploratory study is based on a population of hearing impaired people that have hearing loss appropriate for the hearing aids.

As a control, the RMD will be used to fit the hearing aids as well as the IMD. Additionally, a control situation will be implemented by using an unaided test condition in laboratory speech testing.

There is no placebo or “fake” device that does not provide amplification. A randomized cross-over design will be used with one group using the device programmed with the RMD first and the other using the device programmed with the IMD and then switching. The testing will be unblinded as the subjects can clearly see a difference between fitting methods. Although two hearing tests will be completed (standard audiometry and IMD screening), the hearing aids will be programmed only with the IMD screening results in order to reduce variability in the analysis of the results. Therefore, the hearing aids will be acoustically programmed the same, but this will not be explained to the participants.

The same randomized test order will be used to test in a simulated environment. At the end of the field test period the participants will return to the clinic. They will be given a speech test in the unaided condition and the aided condition with the hearing aids as they have worn them for the previous 10 days. They will then be fit with the other method (whichever they did not have in the first round), and then have speech testing again in the aided and unaided condition at the end of the field test period.

The participants will be expected to participate for approximately 1 month for a combination of field tests and lab tests. For lab tests they will not spend more than 1.5 hours in the clinic for testing. They will be expected to come for 3 visits in total. Field trial periods will not last more than 10 +/-5 days.

The sequence will begin with the screening visit which will also be the first intervention visit if they satisfy the inclusion criteria and if they choose to join the study. The entire test procedure will be explained, and they will be given a Patient Informed consent form to read which will need to be signed, dated, and returned before any trial procedures begin.

Subjects will be given questionnaires to complete with all field test periods. After they have completed all appointments the subjects will complete a preference questionnaire to determine their preference between the IMD and RMD. They will also be given the option to purchase hearing aids from the clinic. If they purchase the hearing aids they will receive all follow-up care at that specific clinic.

6.2 Methods of minimising bias

6.2.1 Randomisation

For the cross-over design, the participants will be divided into two groups. One group will begin the trial with hearing aids programmed with the IMD and the other group will begin the trial with hearing aids programmed with the RMD. Each field trial will last for 10 days (+/-5d). Then they will return to the clinic for an appointment. The allocation to the groups will be randomized using a block randomization method in groups of four. They will be assigned as they appear in the clinics for their appointments. All investigators at the sites should be assigned an equivalent number of participants.

6.2.2 Blinding procedures

There will be no blinding as it is impossible to hide the programming method because the differences are very distinct.

6.2.3 Other methods of minimising bias

Two of the questionnaires used in the study are validated. Two are custom questionnaires but based on similar questionnaires used in a study that was assessing the same narrative aspect as this study aims to measure.

6.3 Unblinding Procedures (Code break)

Not applicable.

7. STUDY POPULATION

The study will take place at two sites in canton Bern, Switzerland (Thun and Bern).

7.1 Eligibility criteria

Participants fulfilling all of the following inclusion criteria are eligible for the study:

- All classifications of hearing loss (sensorineural, conductive, combined)
- If the hearing loss is conductive or combined it must be approved for amplification by a physician
- All shapes of hearing loss (flat, sloping, reverse slope, notch)
- Hearing loss severity ranging from mild to severe
- First time hearing aid users
- German speaking
- Both genders
- Ages 18 and older
- Ability and willingness to sign the consent form

The presence of any one of the following exclusion criteria will lead to exclusion of the participant:

- Contraindications for amplification
- Experienced or current hearing aid users
- Active ear disease
- Inability to follow the procedures of the study due to language problems, psychological disorders, dementia, or other cognitive problems of the participant,
- A reduced mobility making them unable to attend weekly study appointments
- A reduced ability to describe auditory impressions and the usage of the hearing aids
- Uncooperative so that it is not possible to record a valid pure tone audiogram
- A strongly reduced dexterity
- Central hearing disorders
- Bernafon employees
- Family members of Bernafon employees

7.2 Recruitment and screening

The participants will be recruited by the Audika call center. The call center has a database of prospective clients that have either come in for a hearing test and not purchased hearing aids or have never come for an appointment. The call center will use the following text when phoning prospective participants:

Guten Tag, meine Name ist XXX von Audika. Wir führen eine klinische Studie über Hörgeräte durch und wollten Sie anfragen, ob Sie an der Studie teilnehmen möchten.

Die Teilnahme an der Studie umfasst das Tragen von Hörgeräten, Sprachtests und das Beantworten eines Fragebogens über den Anpassungsprozess von Hörgeräten.

Für die Studie werden insgesamt 3 Termine in einer Audika Filiale in Bern oder in Thun erforderlich sein. Zwischen den Besuchen liegt eine Testphase von ca. 10 Tagen, somit wird die Gesamtstudienzeit ungefähr 1 Monat betragen. Im ersten Termin stellen wir fest, ob Sie für die Studie geeignet sind oder nicht und erklären Ihnen ausführlich den weiteren Ablauf.

Am Ende des Versuchzeitsraumes haben Sie die Möglichkeit die Hörgeräte zu erwerben. Als Dank für Ihre Teilnahme erhalten Sie 100 CHF.

Wenn Sie teilnehmen möchten oder mehr Informationen benötigen, können wir einen Termin vereinbaren.

((When they don't want to make an appointment say:))

Gerne senden wir Ihnen alle Details der Studie noch einmal per Post zu und melden uns bei Ihnen in einer Woche noch einmal. An welche Adresse dürfen wir Ihnen die Unterlagen senden?

((When they choose not to participate say:))

Ich danke Ihnen für ihre Zeit und wünsche Ihnen einen guten Tag.

Do not send the person any information about the trial or contact them again about the trial.

At the appointment, the trial will be explained and Patient Information given to them to read if they have not already received it by mail. They will have time to ask questions.

If it is determined that their hearing loss is appropriate they will be given the opportunity to participate in the trial. If they choose to join the trial, they will be given the consent form to sign. No trial proceedings will begin until the consent form has been signed by the participant and the investigator. The visit described as the screening/V1 will then proceed as per the trial schedule.

7.3 Assignment to study groups

The participants are randomized by a block assignment as they appear at the trial sites. There will be 24-40 subjects. The test condition order will be randomized using a 2-factor randomization with a 6 block design. The first factor is the investigator with 4 levels, and the second factor is the test order with 2 levels. This will minimize the bias created when one test condition is tested in the first or last position all of the time.

7.4 Criteria for withdrawal / discontinuation of participants

Participants are allowed to withdraw from the study at any time and for any reason. They do not have to share the reasons with the investigator. They will be asked to return the hearing aids. If the decision is made by the investigator then they will inform the participant in person that they are no longer needed for the study. Reasons for withdrawing a participant from the study could be for non-compliance during testing, unreliable responses, medical reasons such as an ear infection, or the study may need to be stopped or postponed. Any data gathered from these subjects will be used for the current study. All data will remain encoded because results are only recorded using the identification code of the subject. There will be at least 5 "back-up" test participants to replace those that withdraw or are withdrawn. These are participants that have already been screened and determined to be appropriate for the testing.

8. STUDY INTERVENTION

8.1 Identity of Investigational Products (medical device)

The treatment will be approximately 1 month of use overall with hearing aids. During half of this time the participants will use hearing aids programmed with the IMD and during the other half the hearing aids will be programmed with the RMD.

There are 2 field test periods planned. They will continue wearing the hearing aids throughout both field tests and only have them reprogrammed at Visit 2. There is no need for a washout period or breaks between the fittings because amplification from hearing aids do not induce a carry-over effect.

At the end of the trial, the participants will return all hearing aids. They will have the option to purchase hearing aids, but they will be new serial numbers and not the devices used during the trial.

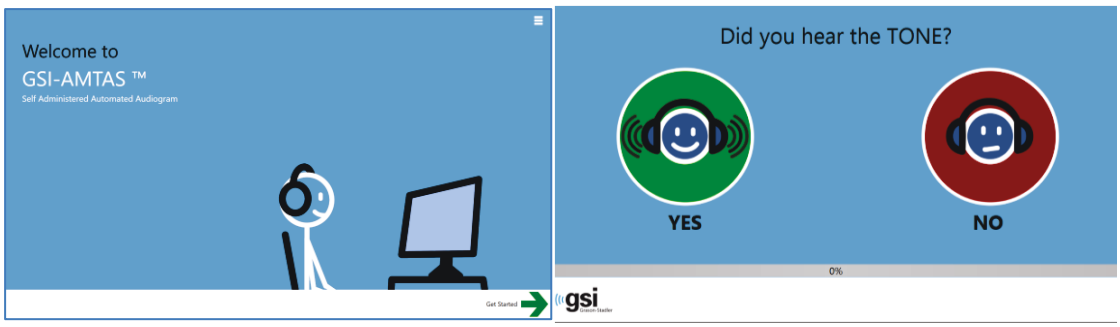
8.1.1 Experimental Intervention (treatment / medical device)

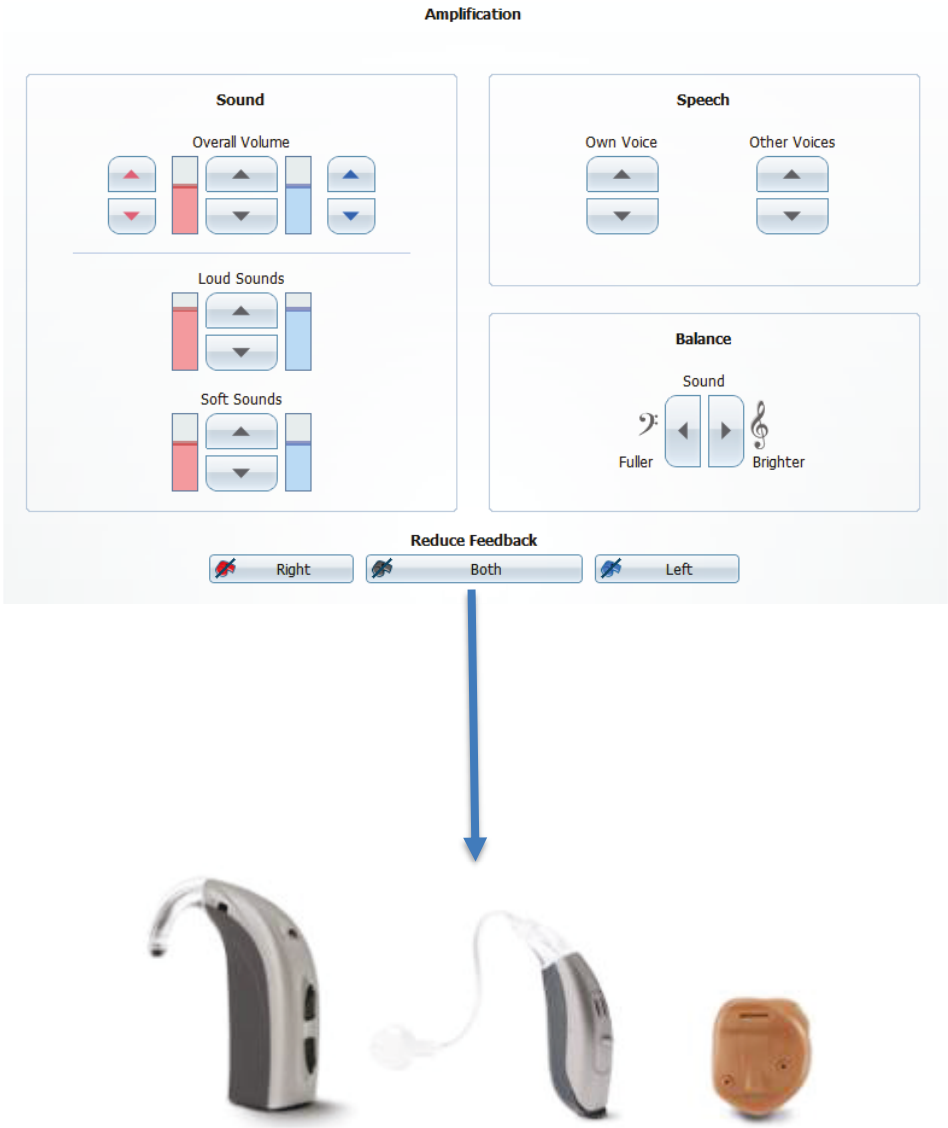
The investigational product (IMD) is a medical device. It is a new self-directed software that combines a hearing screening and the hearing aid fitting into one procedure. The name of the software is HearToo Studio. The hearing aid that the software will program for the trial is already CE marked and sold on the market for 2 years. It still has the same intended use and the basic function of amplifying sound.

The IMD will produce automated tones at a frequency range of 250 Hz to 8000 Hz with an output limit of 80 dB. A standard audiometer has an output of up to 120 dB at certain frequencies. The IMD only has an output of 80 dB to mitigate the risk of a person allowing the system to present too loud of tones by not responding. The user will respond when they hear the tone. The IMD transfers the screening results to a restricted version of Oasis software to implement the results into the hearing aid fitting. Traditionally, these results are input manually by the HCP into the software. The software will use the screening results to quantify the amount of amplification needed in the hearing aid in the same manner that it does in the current Oasis software. Performance is expected to be the same when programmed with the IMD as it is with the RMD because both fitting methods will use the IMD screening results to calculate gain. The hearing aids when programmed with either method will be the same electro-acoustically.

The version of Oasis software is a restricted and simplified version. There will only be 3 styles of hearing aids offered and one type of acoustics. Therefore, decisions that HCPs would normally have to make with the standard software have been removed and are automatically chosen in the software. The HCP cannot fit multiple programs to the hearing aid with the IMD, only one. They also can make simple fine-tuning as seen in the picture below. In the standard version of the software the HCP can adjust specific frequencies and input levels, as well as adjust features.

The new software is a non-invasive device. It uses supra-aural headphones to conduct the hearing screening. The hearing aid itself is worn behind/over the ear with a part that fits into the ear canal. The part that fits in the ear canal is either made of silicon or plastic that is covered with an acrylic coating (for custom molds or ITEs). The hardware of the BTE is painted with a non-toxic paint. Below is a picture of the process of the IMD. First the hearing screening, then the hearing fitting, and finally the settings are saved to the hearing aids.





8.1.2 Control Intervention (standard/routine/comparator treatment / medical device)

The Reference Medical Device (RMD) is the standard hearing aid fitting software used by an HCP. Normally, after they have completed a manual hearing test the HCP enters the results into the fitting software to perform the fitting. The intended purpose is the same; however, the IMD is automated and the RMD is manual. For the purposes of this trial the fitting process is the focus and not the hearing aid output. The standard audiogram results will only be used for inclusion/exclusion criteria and as a control. The fittings with both the IMD and the RMD will use the hearing screening results from the IMD to calculate the fitting targets. The resulting amplification will be the same from both devices. The hearing aids will be programmed only with the IMD screening results in order to reduce variability in the analysis.

8.1.3 Packaging, Labelling and Supply (re-supply)

The IMD product comes in a USB drive that the professional can download onto a computer or a tablet. The USB comes in a box with instructions for downloading printed in the inside upper flap of the box. Two USBs will be needed for the trial, one per site. Re-supply should not be necessary unless there is a defect with the USB.

Other medical devices used for the trial are the hearing aids. Each hearing aid has its own serial number that can be tracked back to production. These will be shipped to the trial sites. The sites will document which serial numbers that they receive. They will track which serial numbers are given to participants, and they will track that each of those serial numbers is returned to the site.

8.1.4 Storage Conditions

The IMD is stored on the computer or tablet once downloaded and will stay there for the entire study.

The hearing aids should be kept in a locked compartment, and only the site investigator should have access. This is to maintain control over the serial numbers handed out and received back at the site.

The devices are stored in the blister packs which are kept in boxes in a warehouse until shipped. They have a shelf life of years. They should not be exposed to temperatures below -25° and not above 60° Celsius during storage or transport. The storage of these devices is according to standard procedures.

8.2 Administration of experimental and control interventions

8.2.1 Experimental Intervention

At the first visit the participants will complete a hearing test using standard audiometry performed by the clinician and a screening using the IMD. The standard audiometry is used as a base test for the inclusion/exclusion criteria and as a control measure for the screening results of the IMD. The hearing devices will be programmed using both the RMD and the IMD during the course of the trial. The screening results from the IMD will be used for both fittings to ensure that the acoustic output of both methods is the same. The difference in the fitting process of the RMD and the IMD is the focus of the trial and not the actual output of the hearing aid.

The IMD will present tones from 250 Hz to 8000 Hz, and the participants will indicate when they've heard the tone. The tones are directed into the ears of the participants with supra-aural headphones. The test should take no more than 15 minutes. Depending on the randomization assignment, some participants will then start the fitting portion of the IMD. Hearing instruments will be connected using a wireless neck loop that the subjects will wear. Once the fitting has been programmed into the hearing aids the investigator will place the hearing aids in the subject's ears. The fitting process should not take more than 20 minutes. They will wear the programmed devices for approximately 10 hours per day for an overall time of approximately 20 +/-10 days for the trial. There are no surgical techniques used in the application of this device. It is a non-invasive device.

The study procedure will use a cross over design with two groups. One group will wear the hearing aids fitted with the IMD and one will wear the hearing aids fitting with the RMD. After 10 days they will switch to whichever method they did not have previously. As stated, the device is non-invasive and requires no surgical procedure. The device sound port will be inserted into the ear and the body of the device placed behind the ear each morning by the subjects themselves and removed each night by the subjects themselves. There is minimal training needed for a first time user to learn how to insert a hearing device. The subjects will be given an Instructions for Use booklet that explains how to insert the device and provides further instructions concerning cleaning, battery changing, and warnings.

8.2.2 Control Intervention

The hearing screening results achieved from the IMD will be manually entered into the standard Oasis software for the fitting with the RMD. The hearing aids will be connected to the software using the same wireless neck loop used for the programming with the IMD. The investigator will fit the hearing aids and then place them in the subject's ears.

The subject will then wear the hearing aids for 10 days. The device will be inserted into the ear and placed over the ear each morning by the subjects themselves and removed each night by the subjects themselves. There is minimal training needed for a first time user to learn how to insert a hearing device. The subjects will be given an Instructions for Use booklet that explains how to insert the device and provides further instructions concerning cleaning, battery changing, and warnings.

8.3 Dose / Device modifications

The IMD will fit the same amount of amplification to the hearing aids as the RMD; therefore, they should not experience any significant negative differences that would make the subjects want to discontinue use of the device. However, if the subject requests to discontinue they can, at any time, remove the hearing aids fitted either with the IMD or the RMD. They will be asked to return the

hearing aids to the site, but their data will still be included in the results for the current study. All data will remain encoded because results are only recorded using the identification code of the subject.

8.4 Compliance with study intervention

It is clearly explained to the subjects that during the periods of intervention it is important to the study that they wear the hearing aids. However, it is the responsibility of the subject to place the hearing aids in their ears every morning.

The software monitors the amount of time that the devices are worn. Therefore, it will be noted if the hearing aids from either field trial have not been worn the expected amount of time or if the time worn between trial periods is not similar. If the device has not been worn a sufficient amount of time the data will not be used for the study. The subjects will be asked to return the devices.

8.5 Data Collection and Follow-up for withdrawn participants

Withdrawn subjects' data will not be used in any final data analysis or report. Any data that is collected prior to withdrawal will be kept in the data management database. The data will remain encoded because results are only recorded using the identification code of the subject. Withdrawn subjects will have the opportunity to return to the clinic that recruited them for their hearing healthcare needs whether to purchase hearing aids or routine hearing tests.

8.6 Trial specific preventive measures

The performance of a hearing aid is not impacted by medication. The subjects will continue to take whatever type of medication that they normally take. There will be no impact on the study objectives.

8.7 Concomitant Interventions (treatments)

Test subjects will continue to receive any concomitant care and medication that they normally receive during the use of the IMD. Use of medication or other therapies will not affect the benefit of the hearing aids. There will be no impact on the study objectives.

8.8 Medical Device Accountability

The USB used to download the IMD software into each site's trial specific computer will be tracked with serial numbers. They will be shipped from Poland. Only IMD that are from a tested batch will be used in the study

The subjects will be assigned hearing aids with serial numbers. The serial numbers are tracked when fitted and tracked that they are received back by the sites on the last visit. The devices have serial numbers by which the individual device can be identified and the production history traced. They will be shipped from the production site in Poland. The serial numbers will provide the traceability of their production and from which batch they came.

8.9 Return or Destruction of Study Drug / Medical Device

At the end of the study the software will be uninstalled from the sites' computers (confirmed by the monitor), and the USB containing the software will be shipped back to the sponsor.

At the end of the study all of the subjects will return the hearing aids to the sites. The sites will return the hearing aids back to the sponsor. It will be noted in the documentation that the devices were returned.

9. STUDY ASSESSMENTS

9.1 Study flow chart(s) / table of study procedures and assessments

Study Periods	Intervention Period		
Visit	Screening/1	2	3
Day	0	10 +/- 5 days	20 +/- 5 days
Patient Information and Consent	x		
Demographics	x		
Medical History	x		
In-/Exclusion Criteria	x		
Randomization	x	x	
Otoscopy	x	x	x
Audiometry	x		
Administer Medical Device	x*	x*	
Baseline Measure (Gothenburg questionnaire)	x		
Primary Variable (IOI-HA questionnaires)	x	x	
Secondary Variables (audiometry)	x		
Other Variables (speech testing)		x	x
Other Variables (product questionnaire)	x	x	
Other Variables (preference questionnaire)			x
Adverse Events	x	x	x

*Depending on randomization subjects will be fit with IMD at the first or second visit. Everyone will use the IMD at the first visit to perform audiometry.

9.2 Assessments of outcomes

9.2.1 Assessment of primary outcome

The primary outcome is the subjective assessment of the IMD compared with the RMD. It will be measured two times during the trial. After each field trial when the subjects have worn the devices programmed with either the RMD or the IMD they will answer 2 questionnaires (IOI-HA and product) that measure their subjective opinion of the benefit they received from the hearing aids during that period of the trial. The results from the two trial periods will directly compare the IMD with the RMD. At the final visit they will answer one preference questionnaire where they will choose between the hearing aids fitted with the IMD or the RMD.

9.2.2 Assessment of secondary outcomes

The secondary outcome is the comparison of the two hearing results. The IMD combines an automated screening into the hearing aid fitting. The results from this screening will be compared with a standard audiometry test performed by the investigator. This will be measured at the first visit.

Additionally, the data recording from the hearing aids will be compared including the average amount of time in hours per day that the hearing aids are worn and in which listening environments: quiet, speech in quiet, speech in noise, and noise. This information will be collected at the end of each field trial period when the subjects return to the clinic.

9.2.3 Assessment of other outcomes of interest

Other outcomes of interest include speech testing as an objective measure of the hearing aids programmed with the IMD and the RMD. The Freiburger Sprachverständnistest consists of speech material that contains groups of 10 multi-syllable words which are numbers. The words are presented every 5 seconds. The participant must repeat the word immediately after they hear it. The goal is to find the presentation level at which the participant can repeat approximately 50% of the words correctly. This level will be measured for the unaided and aided conditions and recorded as test outcomes by the investigator. The differences between unaided and aided (IMD vs. RMD) will be used as an explanatory variable for the model.

Also, the perceived handicap associated with hearing impairment could potentially play a role in the perceived benefit from hearing aid. The Gothenburg Profile (GP) is a 20-item questionnaire with a 5 points scale (how often…? never, rarely, sometimes, often, and always). It will be given to the subjects on their first visit.

9.2.4 Assessment of safety outcomes

During the use of the IMD the subjects will be asked to alert the investigator to any unexpected or uncomfortable sounds heard during the screening or the fitting of the hearing aid.

Additionally, they will be asked about any adverse events or unexpected events that involve the hearing aids. Unexpected events or effects include feedback or whistling from the device, unexpected sounds or artefacts from the device, discomfort, muting or shutting off of the device in mid-use, unexplained warning signals or beeping from the device, loud sounds, and occlusion. The information provided from the field trial will alert the testers to the potential for safety risks that should be addressed before the product is released to the market. It is not expected that any of these things will occur and have not during testing on previous products.

9.2.4.1 Adverse events

For the recording of adverse events the subjects will be asked for a description of the event including how long it lasted, how many times it occurred, and if it caused discomfort or pain or a disruption of hearing ability. They will be recorded on the AE forms in the CRF.

9.2.4.2 Laboratory parameters

Not applicable

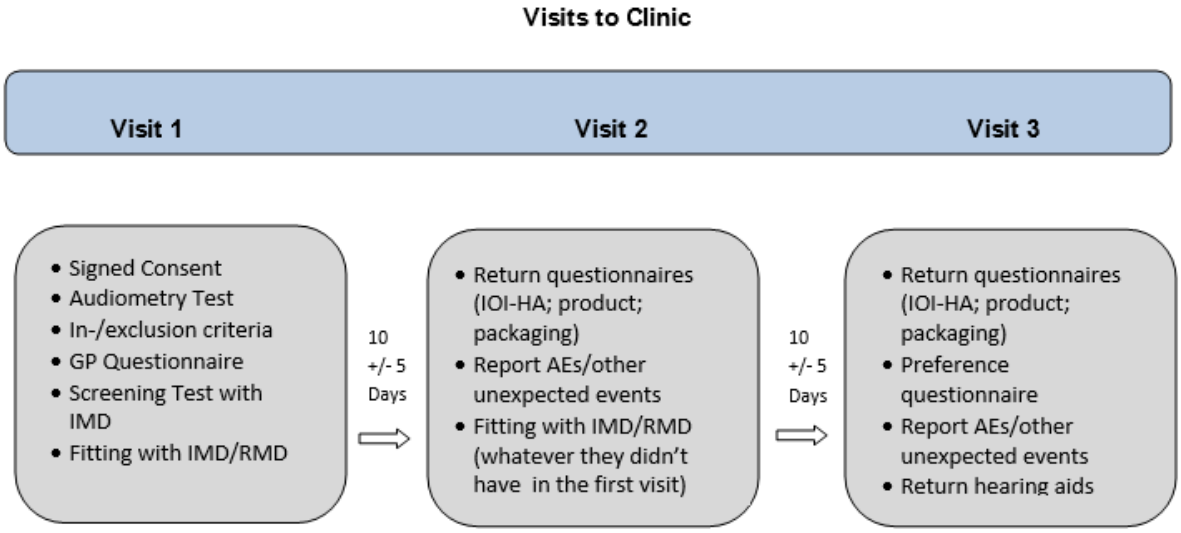
9.2.4.3 Vital signs

Not applicable

9.2.5 Assessments in participants who prematurely stop the study

After the study concludes the subjects will return the hearing aids. They will have the choice of purchasing hearing aids and continuing a regular follow-up procedure with the clinic that recruited them. Those that withdraw prematurely will also have the option to purchase hearing aids and continue with normal follow-ups as needed with the clinic that recruited them.

9.3 Procedures at each visit



9.3.1 Screening Visit/First Visit

Screening visit, Day 0: The trial will be explained including how many visits are expected as well as the type of testing that they will complete. They will be given the Patient Information sheet and everything explained to them by the site investigator. Subjects are given time during the appointment to decide, whether or not to participate in the study. If they choose to not take part in the trial they will not sign the consent form and the appointment will finish. They can still follow-up with the clinic for a standard hearing aid purchase if they choose. If they choose to join the trial they will sign and date the Patient Informed consent form. No trial activities will be performed before the Patient Informed consent form is signed and dated by the subject and investigator. Subjects will receive a copy of the signed patient informed consent form and the patient information. A hearing history is then taken and otoscopy is performed. The initial hearing test is performed to determine hearing loss including air and bone audiometry. Inclusion/exclusion criteria will be determined. The subjects will then complete a questionnaire to quantify their perceived hearing loss handicap (Gothenburg). They will complete a hearing screening using the IMD. Based on the randomization plan they will be fitted with hearing aids either with the IMD or the RMD. The investigator will make no fine tuning of the fittings. Gain and features will be set as prescribed by the software. They will receive an Instructions for Use (IFU) for the hearing aid. They will be given a standardized questionnaire (IOI-HA) and a custom product questionnaire to fill out during the first period of the field trial. The HCP will review the questionnaires to ensure that the subjects understand their task. They will be scheduled for the Second Visit. Any AEs will be reported in the CRFs.

9.3.2 Second Visit

Visit 2, Day 10 +/-5: Otoscopy is performed. The subjects will hand in the completed questionnaires given to them at the previous appointment. The investigator will review the questionnaires and inquire about AEs. Any AEs will be reported in the CRFs. A lab test will be made to test speech intelligibility with the FST.

Their hearing aids will be fit with either the IMD or RMD (depending on what they had for the first period). The investigator will make no fine tuning of the fittings. Gain and features will be set as prescribed by the software. They will be given a standardized questionnaire (IOI-HA) and a custom product questionnaire to fill out during the second period of the field trial. The HCP will review the questionnaires to ensure that the subjects understand their task. They will be scheduled for the Third Visit.

9.3.3 Third Visit

Visit 3, Day 20 +/-5: Otoscopy is performed. The subjects will hand in the completed questionnaires given to them at the previous appointment. The investigator will review the questionnaires and inquire about AEs. Any AEs will be reported in the CRFs. A lab test will be made to test speech intelligibility with the FST.

The subjects will return the hearing aids. The subjects will complete a custom preference questionnaire about the experience with both field test periods. They will report which period of the field trial that they preferred.

They will be given the option to purchase hearing aids from the clinic where they were recruited.

10. SAFETY

10.1 Medical Device Category C Studies

All adverse events (AE) including all serious adverse events (SAE) are collected, fully investigated and documented in the source document and appropriate case report form (CRF) during the entire study period, i.e. from patient's informed consent until the last protocol-specific procedure, including a safety follow-up period. Documentation includes dates of event, treatment, resolution, assessment of seriousness and causal relationship to device and/or study procedure.

The information on AEs is systematically collected by the clinician at each study visit. They will follow the procedures outlined in SOP-Medical Device Incident Reporting. The subjects are asked to keep a diary and write down any unexpected events. During the regular clinic visits the subjects are then asked questions about the event to gather details and to determine the severity of the event. If a subject reports pain that results in the inability to use the device he will be withdrawn from the study in order to avoid any pain from using the device and to remove partial data from the study. For reports of pain caused by insertion or the dome itself, the problem can be addressed in the clinic. For example, a different style or size of dome can be placed on the hearing aid, and re-training of insertion can be performed with the subject to avoid wrong or forceful insertion of the device. For reported pain they will be advised to not wear the device for 24 hours before resuming use.

Foreseeable adverse events outlined in the risk management file include discomfort caused by the domes, domes or filters falling off in the ear, no amplification coming from the device causing alarms or traffic to not be heard by the subject, skin reaction if chemical profile of device is changed, maximum output of the device exceeding 132 dB SPL, battery exploding or catching fire, and the device affecting other medical devices worn by the subject,. The incidence of all of these risks or adverse events is improbable. To mitigate the risk, the IFU describes how to insert the device, how to change the domes, and how to change a battery in case of no amplification. The IFU describes how to clean the device, domes, and filters in order to not introduce cleaning agents that might change the chemical profile of the hardware of the device. The labelling warns of the potential maximum output of the device. The IFU instructs the user to keep the device away from explosive environments, The IFU warns of interference with implantable devices.

10.1.1 Definition and Assessment of (Serious) Adverse Events and other safety related events

Adverse Event (AE)

Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in participants, users or other persons whether or not related to the investigational medical device [ISO 14155: 3.2].

This includes events related to the IMD or the RMD and to the procedures involved. For users or other persons this is restricted to events related to the IMD.

Adverse Device Effect (ADE)

Adverse event related to the use of an investigational medical device [ISO 14155: 3.1].

This includes any adverse event resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, operation, or any malfunction of the investigational medical device. This includes any event that is a result of a use error or intentional misuse.

AEs/ADEs include:

- Exacerbation of a pre-existing disease or condition.

- Increase in the frequency or intensity of a pre-existing episodic disease or medical condition.

- Any disease or medical condition detected or diagnosed after treatment with the study intervention device even though it may have been present yet undetected prior to the start of the clinical investigation.

- Any continuous persistent disease or symptoms present at baseline that worsen following the start of the clinical investigation.

- Events considered by the investigator to be related to any of the clinical investigation-mandated procedures.

- Abnormal assessments, e.g. physical examination findings, will be reported as AEs/ADEs if they represent a clinically significant finding that was not present at baseline or that has significantly worsened during the course of the clinical investigation.

- Test abnormalities will be reported as AEs/ADEs if they represent a clinically significant finding, symptomatic or not, which was not present at baseline or has significantly worsened during the course of the clinical investigation.

AEs/ADEs do not include:

- Pre-planned interventions or occurrences of endpoints specified in the CIP are not considered AEs/ADEs, if not defined otherwise.

- Unrelated medical or surgical procedures, e.g. surgery, endoscopy, tooth extraction, transfusion. However, the event leading to the procedure may be considered an AE. If this event is serious, the procedure will be described in the SAE/SADE narrative.

- Any pre-existing disease or medical condition that remains stable and does not worsen during the course of study participation.

- Situations in which an adverse change did not occur, e.g., hospitalizations for unrelated cosmetic elective surgery or for social and/or convenience reasons.

Serious Adverse Event (SAE)

Adverse event that:

- results in death, or
- led to a serious deterioration in health that either:
- results in a life-threatening illness or injury, or
- results in a permanent impairment of a body structure or a body function, or
- required in-patient or prolonged hospitalisation, or
- results in medical or surgical intervention to prevent life threatening illness, or
- led to fetal distress, death or a congenital abnormality or birth defect. [ISO 14155: 3.37].

This includes device deficiencies that might have led to a serious adverse event if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate. These are handled under the SAE reporting system. A planned hospitalization for pre-existing condition, or a procedure required by the protocol, without a serious deterioration in health, is not considered to be a serious adverse event.

Device deficiency

Inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labelling [ISO 14155: 3.15].

Health hazards that require measures

Findings in the trial that may affect the safety of study participants and, which require preventive or corrective measures intended to protect the health and safety of study participants.

Severity of adverse events/adverse device effects

The severity of clinical AEs is graded on a three-point scale: mild, moderate and severe, and reported in the CRF. If the severity of an AE worsens during medical device administration, only the worst intensity should be reported on the CRF. If the AE lessens in intensity, no change in the severity is required.

Mild: Event may be noticeable to subject; does not influence daily activities; the AE resolves spontaneously or may require minimal therapeutic intervention;

Moderate: Event may make subject uncomfortable; performance of daily activities may be influenced; intervention may be needed; the AE produces no sequelae.

Severe: Event may cause noticeable discomfort; usually interferes with daily activities; subject may not be able to continue in the study; the AE produces sequelae, which require prolonged therapeutic intervention.

Causal Relationship of Adverse Events

A causal relationship towards the medical device or study procedure should be rated as follows:

- Not related: The event is definitely not associated with device application or with study procedures; a relationship can be ruled out.
- Possibly related: The relationship between device application or study procedures and the event is possible, but other causes cannot definitely be ruled out.
- Related: The event is definitely associated with device application or study procedures.

Device deficiencies that might have led to an SAE are always related to the medical device.

10.1.2 Reporting of (Serious) Adverse Events and other safety related events

The following events are to be reported to the Sponsor within 24 hours upon becoming aware of the event:

- All SAEs
- Health hazards that require measures
- Device deficiencies

The Sponsor will evaluate SAEs with regard to causality and seriousness. Device deficiencies are assessed regarding their potential to lead to an SAE.

Reporting to Authorities:

In Category C studies it is the local Investigator's responsibility to report serious adverse events in Switzerland which are

- related or possibly related to the medical device under investigation
- related or possibly related to study procedures

within 7 days to the local Ethics Committee. The Sponsor-Investigator reports within the same timeline to Swissmedic (incl. events from abroad).

- Health hazards that require measures are reported within 2 days

All in the trial involved other Ethical Committees receive all mentioned reportable SAEs and health hazards having occurred in Switzerland via the Sponsor-Investigator within the same timeline. All participating investigators are informed regarding the occurrence of a health hazard.

Periodic safety reporting

In Category C studies a yearly safety update-report is submitted by the Investigator to the Ethics Committee and by the Sponsor-Investigator to Swissmedic.

10.1.3 Follow up of (Serious) Adverse Events

The adverse event shall be followed by the PI until its resolution or until the adverse event is recognised as permanent or stable condition by the PI. Follow-up investigations may be necessary according to the PI's medical judgement. In this situation, the follow-up does not have to be documented in the CRF but must be noted in the source documentation.

In case of SAE / SADE the sponsor can be contacted following the list below. If the first person in the list cannot be timely contacted, the PI should try to contact the next and so on.

Contact order

Contact order	Name	Mobile	Office	E-Mail
1	Michael Ernst	+41 31 998 15 57	Head of SIV	mier@bernafon.com
2	Bruno Keller	+41 31 998 15 92	Senior Director	brke@bernafon.com

Table 1: Contact information of the sponsor-investigator in case of SAE/SADE

11. STATISTICAL METHODS

The purpose of this study is to compare the performance of the IMD to the RMD. The study aims to provide a final validation and quality control of the IMD before it is released for sales. The hearing aids will have the same electro-acoustic characteristics with bot the IMD and the RMD. For this reason, it is not expected to find that the IMD outperforms the standard RMD.

11.1 Hypothesis

Both devices will have the same electro-acoustical performance; however, it is suspected that changing the fitting procedure might influence the subjective benefit for the hearing aid user. Research suggests that placebo effect might impact hearing aid trials (Dawes et al., 2013) and that clinician behavior might also modify the perceived benefit of hearing aids (Naylor et al., 2015). The designed test will investigate the potential effect of the IMD compared to the RMD on first time users.

The test should answer the following research questions:

1. Narrative effect of fitting procedure: Do different fitting procedures lead to differences in perceived benefit with hearing aids despite similar electro-acoustical performance? (Questionnaires)
2. Self-administrated audiometry: Is AMTAS self-administrated screening equivalent to standard clinical procedure? (hearing loss thresholds)

11.2 Determination of Sample Size

A literature search about this tested topic does not provide enough strong references to build a confirmatory analysis. It seems that results might be strongly influenced by the inclusion criteria (first time vs experienced hearing aid users) or test design (cross-over, multi-investigator, or between group designs). There is no article to our knowledge that includes a multi-investigator effect in the test design when looking at the effect of different fitting procedures. Adding a -by investigator- treatment interaction term seems to be mandatory if this trial wants to be determine the effect that different investigators have on the fitting procedure.

The sample size cannot be computed on reported effect sizes from previous experiment; however, the following summary shall be used as an indication to determine the sample size for participants per investigator:

•Naylor et al. (2015) about the narrative effect during the fitting with 24 experienced users and 16 first time users,

•Humes et al. (2017) about the performance with over-the-counter hearing aids compared to audiology best practice with 154 participants,

•Dawes et al. (2013) about the placebo effect in hearing aid trials with 16 experienced hearing aid users,

•Dawes et al. (2011) about the placebo effect in hearing aid trials with 20 experienced hearing aid users.

A placebo effect was found with sample sizes of about 20 participants in a single site study design. Adding an investigator effect in the design might bring new insights in this domain but requires a minimum number of participants per investigator to reduce imbalance between them.

With an effect size of 0.65 from the literature review, 2 degrees of freedom, 24 participants, and an alpha of 0.05, we can achieve a power of 0.82. Therefore, a minimum of 24 participants will be included in the trial overall. There will be 4 investigators with 6 to 8 participants per investigator.

11.3 Statistical criteria of termination of trial

A single statistical analysis is planned once all recruited subjects have completed the protocol (per-protocol). No interim analysis is planned for a test period of 14 days and no “stopping rules” are set from a statistical perspective. PI’s and clinician judgement are considered as reliable enough to stop the trial.

11.4 Planned Analyses

The analysis and documentation will be done by the statistician using R (latest available and validated version) downloaded from the official Comprehensive R Archive Network (https://cran.r-project.org/). R-Studio IDE will be used to integrate the analysis to the report. R provides adequate packages for descriptive statistics (base, stats, and Rmisc), data visualisation (ggplot2), mixed effect models (lmer, lmerTest, and nlme), and principal component analysis (FactoMineR).

A linear mixed effect regression will be used on the IOI-HA questionnaire, chi-squared distribution on the preference test and a paired t-test on hearing thresholds. The principal component analysis will be made on different outcomes and explanatory variables combinations.

11.4.1 Datasets to be analysed, analysis populations

Analysis population: a single group that had the same treatment (per protocol set).

The included subjects are first time hearing aid users with the same hearing aid model across the population. As hearing loss does not normally fluctuate, we assume that their hearing capabilities are stable over time and that the performance with a hearing aid can be compared over a longer period without any wash out period. Subjects’ individual auditory capacities (hearing loss degree, noise tolerance, speech recognition) vary, however the sample is considered as a homogenous population regarding their experience with the RMD. It will be ensured that the acceptance to generic amplification via hearing aids is not tested but an actual evaluation of the difference between the RMD and the IMD. A single assignment treatment will be considered representative of clinical intervention, i.e. when an experienced hearing aid user acquires a new device.

11.4.2 Primary Analysis

The narrative effect on the subject perception of the end user will be measured using a standardized questionnaire, the IOI-HA, and a custom product questionnaire. The questionnaires will be administered twice during the study, once after each field trial period. The responses for the IMD will be compared with those for the RMD. At the last visit the subjects will complete a preference questionnaire based on the Naylor et al. (2015).

11.4.3 Secondary Analyses

The standard audiological hearing test results will be compared to those completed with the automated IMD hearing screening. Data analysis will focus on hearing threshold differences with both procedures in a nested model: ear-participant-investigator.

11.4.4 Explanatory analyses

Speech intelligibility will be measured using the Freiburger Sprachverständnistest. The level at which 50% of words are correctly repeated will be recorded as test outcomes by the investigator for the unaided and aided conditions for each test session.

The differences between unaided and aided (for IMD and RMD) speech intelligibility will be compared and used as an explanatory variable for the model.

The subjects' perceived hearing handicap will be measured with a standardized questionnaire. Participants that are not often affected in their daily life by their hearing impairment, might report smaller benefit from amplification with a hearing aid. Understanding and quantifying their struggles with the principal component analysis could be used to improve the modelling of the results.

The usage of hearing aids will be recorded as another indication of hearing aid use. The data will be averaged from each ear. The following data will be used:

- 1. Daily usage in hours per day,
- Acoustical environment in percentage for following listening environments: quiet, speech in quiet, speech in noise, and noise

11.4.5 Interim analyses

No interim analysis is planned according the test design.

11.4.6 Safety analysis

Safety analysis is foreseen to be accomplished with the AEs reported by the participants during the trial. Clinical judgement from the PI will be used for the safety evaluation.

11.4.7 Deviation(s) from the original statistical plan

Any deviation from the original protocol has to be justified and reported in the final report. Post hoc analysis can be done on secondary outcomes and reported in the final report.

11.4.8 Further uses of data

Data collected from the study will potentially be used for further research purposes. The data will remain anonymized and stored in a secure document management system. The participant code list will be destroyed so that nobody will be able to connect the data to a specific test participant.

11.5 Handling of missing data and drop-outs

For missing data, the PI will contact the involved subject to evaluate the possibility of getting missing data from a questionnaire by post. If a test subject cannot come to the evaluation visit, after exhausting all the possibilities to reschedule a new one, the devices will be sent back per post. If a subject does not want to adhere to the protocol, he can easily withdraw from the study and return the devices.

Data will be immediately removed if the PI has some doubts about the data accuracy (especially about the understanding of the questionnaires).

Dropouts will not be replaced; therefore, extra subjects over the calculated sample amount will be included from the beginning to ensure enough completed cases with all data.

Analysis will be done on the complete case only.

12. QUALITY ASSURANCE AND CONTROL

The Sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs and working instructions, at all sites. The PI is responsible for proper training of all involved study personnel.

12.1 Data handling and record keeping / archiving

Data will be documented on paper and archived with an electronic data management system. The subjects will be given numbers to maintain anonymity. There are also hard copies of subjects' charts that are kept in a locked file cabinet inside of the clinic rooms. Only the PI, statistician, Monitor, and Auditor will have access to the information. The information will always be archived under the identification number with a key to the identification codes stored in another location (described in chapter 2.8).

12.1.1 Case Report Forms

Participant identities are coded using a participant identification number.

The PI or the Site Investigator will enter protocol defined data into a web based Electronic Case Report Forms using an EDC-software that conforms to 21 CFR Part 11 (FDA guidance) requirements. Site staff will be given access to the EDC system after a training. The data are checked automatically for plausibility and discrepancies. The generated appropriate error messages, allow the data to be confirmed or corrected before being saved in the database. At the end of the study, the PI must certify that the data entered into the Electronic Case Report Forms are complete and accurate. After database lock, the PI will receive a CD-ROM or paper copies of the patient data for archiving at the sites.

The CRF contains the following information:

Field	**Author**
Date of examination	PI
Participant identification number	PI
Age	PI
Sex	PI
Date of Informed Consent	PI
Inclusion / Exclusion Criteria	PI
Ear disease	PI
Control hearing device serial numbers	PI
Investigational device serial numbers	PI
Results to FST	PI
Results from Gothenburg questionnaire	PI
Results from IOI-HA questionnaire	PI
Results from preference questionnaire	PI
Results from product questionnaire	PI
Results from packaging questionnaire	PI
AEs / SAEs, ADE / SADE	PI
Name, date, signature of PI	PI

12.1.2 Specification of source documents

The Principle Investigator will maintain adequate and accurate records to enable the conduction of the study to be fully documented and the study data to be subsequently verified. These documents will be classified into two different categories: PI's file, and subject clinical source documents. There will be a PI file or Ivestigator Site File (ISF) for each site (Bern and Thun) as well as corresponding subject files with source documents pertaining to each site.

The PI's file will contain the CIP/amendments, IB/Instructions for use, CRFs, sites' standard operation procedures (SOPs) or reference to it, EC and CA approval with correspondence, informed consent, device records, staff curriculum vitae and authorization forms, screening and enrolment logs, site-specific subject identification code logs, and other appropriate documents/ correspondence as required by EN ISO 14155 and local regulations.

Subject clinical source documents include, but are not limited to subject hospital/clinic records, physician's and nurse's notes, appointment book, original laboratory reports, CT, X-ray, MRIs, pathology and special assessment reports, consultant letters, etc.

These two categories of documents must be kept on file by the PI for 10 years. If source documents are not durable as long as needed they must be preserved as a copy. When source documents are required for the continued care of the subject, appropriate copies should be made for storing outside of the site. The information will always be archived under the identification number with a key to the identification codes stored in another location (described in chapter 2.8).

For each subject enrolled an encoded electronic CRF must be completed and e-signed by the PI. This also applies to those subjects who fail to complete the study. If a subject withdraws from the study, the reason must be noted on the CRF.

Case report forms are to be completed after the visit.

CRF entries and corrections will only be performed by study site staff, authorized by the PI. All forms should be completed using a blue permanent pen and must be legible. Errors should be crossed out but not obliterated, the correction inserted, and the change initialled and dated by the PI, co-PI or study nurse.

The entries will be checked by the Monitor and any errors or inconsistencies will be checked immediately. The Sponsor-Investigator will collect original completed and signed CRFs at the end of the study. A copy of the completed and signed CRFs will remain on site.

12.1.3 Record keeping / archiving

All study data will be archived for a minimum of 10 years after study termination or premature termination of the clinical trial.

12.2 Data management

12.2.1 Data Management System

The CRFs in this trial are implemented electronically using a dedicated electronic data capturing (EDC) system. The EDC system is activated for the trial only after successfully passing a test procedure.

All data entered in the CRFs are stored on a Windows server in a dedicated database.

12.2.2 Data security, access and back-up

The server hosting the EDC system and the database is kept in a locked server-room in Biel. Only the system administrators have direct access to the server. A role concept with personal passwords (site investigator, statistician, monitor, administrator etc.) regulates permission for each user to use the system and database as he/she requires.

All data entered into the CRFs are transferred to the database using Secure Sockets Layer (SSL) encryption. Each data point has attributes attached to it identifying the user who entered it with the exact time and date. Retrospective alterations of data in the database are recorded in an audit table. Time, table, data field, original value and altered value, and the person are recorded (audit trail).

A multi-level back-up system is implemented. Back-ups of the whole system including the database are run several times per day. The back-up-data are stored in a secure place on a different storage-server.

12.2.3 Analysis and archiving

At final analysis, data files will be extracted from the database into statistical packages to be analyzed. The database will be locked at this time, recorded in special archiving format and securely stored for at least 1 year. In addition, the PI will receive a CD-ROM or paper copies of the patient data for archiving at the site.

12.2.4 Electronic and central data validation

Data can be entered into the database only after a check of completeness and plausibility. Furthermore, selected data points are cross-checked for plausibility with previously entered data for that participant.

12.3 Monitoring

The study sites will be monitored by an employee of the Sponsor. A minimum of five visits will be performed; one site initiation visit, 3 routine monitoring visits and one close out visit. The number of routine monitoring visits will be increased if needed based on the course of the study. The first routine monitoring visit will take place shortly after the first patient has been enrolled.

Source documents will be made available for the monitor and the principle investigator or a delegated and authorized person will be available during the visits to answer questions.

100% source data verification will be completed for 3 patients at the first interim visit. For another 3 patients 100% source data verification will be completed at the second interim visit, and an additional 3 at the third interim visit.

Subject to SDV for all patients are:

Patient Informed Consent Form

Eligibility criteria

Diagnosis

Visit dates

Study intervention details related to:

- Procedural success
- Procedure date and time
- (Serious) Adverse Events
- Device deficiencies

The content of Investigator Site File (ISF) will be checked during each monitoring visit.

12.4 Audits and Inspections

CEC as well as CA have the right to execute inspections at the study sites.

The study documentation and the source data/documents have to be made accessible to auditors/inspectors and questions have to be answered during audits/inspections. All involved parties must keep the participant data strictly confidential.

12.5 Confidentiality, Data Protection

Direct access to source documents will be permitted for the purposes of monitoring, audits and inspections and only authorized persons involved in those activities are allowed to have direct access to source documents and must keep participants data strictly confidential.

12.6 Storage of biological material and related health data

Not applicable

13. PUBLICATION AND DISSEMINATION POLICY

Trial results will be communicated to participants at the end of the trial. The trial results primary purpose are for internal product validation to ensure safety and performance of the device. The results will be communicated to other relevant groups (e.g., via publication, reporting in results databases, and other internal data sharing arrangements) as needed and for the purpose of sharing scientific information within the industry. The only people with authorship eligibility will be those that worked on the trial including the PI, statistician, and any other clinicians involved in testing. Any plans for writing will not include access to the full protocol but a description of it as well as a description of the participants. Statistics will be described sufficiently so that the reader understands the analysis and any conclusions made from it. Ultimately the decision to submit the report for publication and the ultimate authority over any of the activities is held by the Sponsor, Bernafon.

14. FUNDING AND SUPPORT

14.1 Funding

The Sponsor will financially support the trial including providing the clinic and all materials needed to complete the testing. This includes the devices themselves as well as equipment.

15. INSURANCE

Insurance will be provided by the Sponsor. A copy of the certificate is filed in each investigator site file and the trial master file.

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17. APPENDICES

1. IMD: IB or SPC
2. Medical Devices: IB (according to ISO 14155)
3. Medical Devices: Assurance of producer
4. Medical Devices: List of norms (vollständig eingehaltene, teilweise eingehaltene)
5. Case Report Form (e.g. CRF)
6. Patient Information and informed consent
7. Instructions for Use
8. Meta-Analysis