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A comparative, controlled, clinical investigation and quality control of a new hearing aid in comparison to the currently marketed device

Clinical Investigation Plan

Study Type:	Clinical Investigation with Medical Device (MD)
Study Categorisation:	Category C: Medical Device without CE mark
Study Registration:	SNCTP, clincialtrials.gov
Study Identifier:	BF001-1611
Sponsor, Sponsor-Investigator or	[redacted]
Principal Investigator:	[redacted]
Investigational Product:	[redacted]
Protocol Version and Date:	Version 3.0 Final Document

Signature Page(s)

Study number	SNCTP, clincialtrials.gov; registration number
Study Title	A comparative, controlled,clinical investigation and quality control of a new hearing aid in comparison to the currently marketed device

The Sponsor and the Investigator have approved the protocol version [3.0 (dated 02.01.2017)], and confirm hereby to conduct the study according to the protocol, current version of the World Medical Association Declaration of Helsinki, ICH-GCP guideiines or ISO 14155 norm if applicable and the local legally applicable requirements.

Sponsor :

Printed name of Sponsor Representatives :

[redacted]

[redacted]

Place/Date Signature

Place/Date Signature

Printed name of Investigator [redacted]

[redacted]

Printed name of Statistician: [redacted]

Place/Date Signature

Printed name of Quality Manager [redacted]

Place/Date Signature

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STUDY SYNOPSIS

Sponsor	Bernafon AG
Study Title:	A comparative, controlled, clinical investigation and quality control of a new hearing aid in comparison to the currently marketed device.
Short Title / Study ID:	BF001-1611
Protocol Version and Date:	Version 3.0; 02.01.2017
Trial registration:	SNCTP, clincialtrials.gov
Study category and Rationale	Category C: Medical Device without CE mark
Clinical Phase:	Pre-Market, medical device validation study involving human subjects.
Background and Rationale:	Benefits of amplification and accessories used with it outweigh any risks in mild to profound hearing impaired subjects. Hearing aids undergo many innovation steps most of them are incremental improvements from already marketed devices. The new devices are expected to perform as well or better than the previous devices. Bernafon conducts clinical investigations in order to test whether new technology provides the same or more benefit than previous Bernafon devices. In addition the aim is to grant quality control prior to product launch according to Bernafon development requirements. The reason for this study is to evaluate a new hearing aid product generation replacing the one on the market. The goal is to evaluate the audiological performance, usability as well as features and functions in comparison to the hearing aid generation already CE marked. Furthermore, it is important to identify unexpected, unwanted behavior from the devices. This clinical investigation is a validation testing and is designed to evaluate the [redacted] hearing instrument system. As human subject are involved, this validation test falls under the definition of a clinical investigation. The validation addresses the performance of the device with a new chip, and additionally addresses whether the end user can understand speech as well as with the current device. Evaluating the overall performance of the [redacted] hearing instruments is important to verify that the end user is satisfied with the devices and that all User Requirements are fulfilled. All the features available in [redacted] with the exception of one new feature, have been validated and are used in devices currently on the market.
Objective(s):	The purpose of this research is to show that the performance of the device is as good as or better than the current device or previous hearing aid generation. Furthermore, speech should not be negatively affected with the addition of the new feature, the usability of the devices (that end users are able to handle the devices) should be as good as the current device, and there should be no artefacts or unwanted noises. Some measurements serve as quality control prior to product launch.

Outcome(s):	Primary Endpoint: • Primary Outcome is the speech intelligibility with the investigational device compared to the current device (using speech tests) Secondary Endpoints: • Comparing the subjective performance of the investigational device to the current device (using questionnaires) • Speech intelligibility with the new feature on and off (using speech tests) • Handling/usability of the devices (specified questionnaire) • Subjective preference testing (using interviews) • 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 should be as good as or higher than with previous devices. Handling of the devices should be the same or easier than previous devices. No unexpected, unwanted behaviour from the devices should occur.
Study design:	This is a controlled, open label, comparative clinical investigation conducted monocentric at the premises of Bernafon in Bern, Switzerland.
Inclusion / Exclusion criteria:	Inclusion Criteria: • All classifications of hearing loss (sensorineural, conductive, mixed) • If the hearing loss is conductive or mixed it must be approved for amplification by a physician • All shapes of hearing loss (flat, sloping, reverse slope, notch) • Severity ranging from mild to severe • German speaking • Both genders • Ages 18 and older • Ability and willingness to sign the consent form Exclusion Criteria: • 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 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

Measurements and procedures:	**Amplification** is verified and compared with targets using Real Ear Measured **Speech intelligibility** tested in quiet or with background noise. Tests used include: Oldenburg Sentence Test (OLSA), Wallenberg and Kollmeier Rhyme Test (WaKo), Oldenburg Logatom Corpus (OLLO). Speech tests are normally set up with speech in the front and noise in the back or at varying degrees around the test client. Some tests such as the OLSA have a varying signal depending on the SNR goal, and others are set to specific speech and noise signal level. **Noise acceptance** is tested with the Acceptable Noise Level (ANL) Test which uses the most comfortable listening level of the client and then allows the client to adjust the noise until it is too loud. **Interviews** are conducted with the subjects in order to gather more information about their experience with the hearing aids. The interview is guided with questions but allows for open comments and topics driven by the subjects' comments **Preference testing** is subjective testing that allows the test person to rate specific settings or devices when listening to the same sound environment. **Subjective perception of devices** with questionnaires asks the test clients various questions concerning the expectations and benefits of the hearing devices. They can be answered for two different devices or settings and then compared again one another. The questionnaires are the Device Oriented Questionnaire (DOSO), the Abbreviated Profile of Hearing Aid Benefit (APHAB), Speech, Spatial, and Quality Questionnaire (SSQ), and the NASA Task Load Index. Questionnaires designed to address specific topics concerning the new device will be used. **Usability and handling** is measured with the Practical Hearing Aid Skill Test which asks test clients to perform different handling activities with the devices. Other in-house questionnaires are also used that directly target new hardware or features of the hearing devices.
Study Product / Intervention:	[redacted] The new investigational device will be the [redacted] hearing device. The products will have the same features (with the exception of one new) and processing. The differences will be the hardware style and processing chip. Hearing instruments are generally worn for approximately 10 hours every day and removed at night. The test clients will wear the new devices for a time period of 2-3 weeks for each field trial period. In between periods they will wear their current devices. The tested medical devices will be in a stable stage of development. This means that system testing will be completed to ensure correct implementation and safe behavior of the devices before any testing on people is conducted. This also includes the software with which the devices are programmed. The software will be at a stable stage of development
Control Intervention (if applicable):	The reference devices are the subjects' current hearing instruments which are already CE marked, ie. previous technology Bernafon devices. The performance of the new devices will be measured against the previous technology.

Number of Participants with Rationale:	There will be an exploratory analysis of data only. The total number of participants will be approximately 35. For 90% power at the 0.05 significance level, the required sample size is about 24 subjects to detect non-inferiority of the current marketed device with an SD of 2 dB and non-inferiority δ of 1.3 dB.
Study Duration:	Approximately 4 months The screening of the participants will begin in February of 2017 and the final data collection appointments will occur in May 2017.
Study Schedule:	The first participant is expected to begin in February 2017. The last participant is expected to finish the testing in May 2017.
Investigator(s):	[redacted]
Study Centre(s):	The testing will be performed at a single site in [redacted] at the [redacted].
Statistical Considerations:	The analysis and documentation will be done by the statistician using R (version 3.3.2) a statistical software package. R "stats" package will be used for the confidence interval, non-inferiority, and Wilcoxon tests. Documentation of the analysis will be done with R Studio under R Markdown format. Main outcome: speech reception threshold The paired t-test usually tests that the mean differences are zero. The non-inferiority test compares the difference to a non-zero quantity -δ.
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 performance of the investigational hearing aid in the laboratory and in daily life. In addition, the performance of the hearing aid will be compared with Bernafon aids that are already sold on the market. The hearing aids will be adjusted to the user's requirements. Subjective and objective evaluations will be made using speech testing, questionnaires, interviews, and usability testing. By using data obtained from the trial, the aim is to show that the performance of the investigational hearing aids is the same as or better than the current CE marked hearing aid.

Language of subjects (German):

Diese Studie wurde konzipiert/erstellt, um die Leistung des Hörgeräts sowohl unter Labor- als auch unter Alltagsbedingungen zu untersuchen. Zusätzlich werden die Leistungsdaten des Hörgeräts mit den von Bernafon bereits auf dem Markt verfügbaren zu vergleichen.

Die Hörgeräte werden gemäss der Benutzeranforderungen angepasst. Es werden sowohl subjektive als auch objektive Evaluierungen durchgeführt mittels Sprachtests, Fragebögen und Usability-Tests. Mit der Verwendung der durch die Studie erhobenen Daten wird beabsichtigt aufzeigen zu können, dass der Nutzen des untersuchenden Hörgeräts identisch oder höher ist als die gegenwärtig CE gekennzeichneten Hörgeräte. Ein weiteres Ziel ist es, die Anpassung des Hörgeräts zu verbessern, um den Nutzen für Menschen mit Gehörschaden weiter zu steigern.

ABBREVIATIONS

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

AE	Adverse Event
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
HFG	Humanforschungsgesetz (Law on human research)
HMG	Heilmittelgesetz
HRA	Federal Act on Research involving Human Beings
IMD	Investigational Medical Device
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

A tabular listing of schedule of events and assessments and procedures of the study

Study Periods	Intervention Period						Follow-up
Visit	Screening/1	2	3	4	5	6	7
Day	0	14+/-3d	24+/-3d	38+/-3d	45+/-3d	59+/-3d	70+/-7d
Patient Information and Consent	x						
Demographics	x						
Medical History	x						
In-/Exclusion Criteria	x						
Randomization	x *	x **				x **	
Otoscopy	x	x	x	x	x	x	x
Audiometry	x						
Real Ear Measurement	x		x		x		
Administer Medical Device	x		x		x		
Primary Variables (speech)		x				x	
Secondary Variables (interview)		x		x		x	
Other Variables (evaluation of questionnaire)		x		x		x	
Other Variables (usability)				x		x	
Adverse Events	x	x	x	x	x	x	x

* Randomization of field trial period

**Randomization of lab trial test conditions

1. STUDY ADMINISTRATIVE STRUCTURE

1.1 Sponsor, Sponsor-Investigator

Bernafon AG is [redacted] The role of the sponsor is to provide the location for the testing as well as all of the equipment used during testing. The results will be used by the sponsor to prove the performance of the new hearing aids. The sponsor will audit the clinic location as well as the processes and documentation performed by the investigator.

[redacted]Principal Investigator

[redacted]

1.3 Statistician ("Biostatistician")

Statistics will be performed by [redacted] is an employee of Bernafon that works within the [redacted] group and specializes in statistical analysis.

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

[redacted] will monitor the investigation. She works within the [redacted]. She is certified in GCP, and familiar with ISO 14155. She has also been certified in Clinical Monitoring.

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 should 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, registration in a national language in the Swiss Federal Complementary Database (Portal) is required.

2.2 Categorization of study

The clinical trial of these medical devices falls under Category C because it will not have the conformity marking at the time of the trial. There are no great differences between the new devices and those on the market that already have the conformity marking and will be used with the same intended purposes as those with the conformity marking.

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 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 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 B and C (IMP and 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.

Premature study end or interruption of the study will be reported within 15 days. The regular end of the study will be reported to Swissmedic 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.

2.5 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 are compensated for their time and effort with a box of batteries and cleaning accessories.

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 authorised 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 and to Swissmedic 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 (eg. 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 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 the 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.

Hearing aids undergo many innovation steps most of which are incremental improvements from already marketed devices. Studies have concluded that adding features such as noise reduction and frequency lowering add benefit to the primary goal of amplifying sound. Features provide comfort, speech intelligibility, and reduced listening fatigue (Stelmachowicz, et al. 2010; Houben, et al. 2013).

Bernafon AG will carry out studies of their new devices with test participants who have hearing loss in order to validate the new hearing system and to qualify the benefit for the user and also to identify areas of further optimization of the tested products. The aim is to validate speech comprehension in quiet environments and with background noise and to accomplish an ideal sound and hearing comfort.

Bernafon conducts clinical investigations in order to test whether new technology provides the same or more benefit than previous Bernafon devices. In addition the aim is to grant quality control prior to product launch according to Bernafon development requirements.

All participants were previously fitted with Bernafon's [redacted] Pico RITE BTEs (reference medical device) during testing for that product which has now been on the market for 2 years. The investigational medical device (IMD) will use a new chip with faster processing capability than the reference medical device (RMD). There is a new feature called [redacted]) that adapts the amount of compression applied to the signal based on the varying signal-to-noise ratio of a listening environment. Compression is standard in all hearing aids. The RMD applies compression based only on the non-linear level estimator while the new system applies compression based on the non-linear level estimator and the signal-to-noise ratio (SNR) estimation. The integration of [redacted]nto the system needs to be evaluated, including the overall effectiveness of the new feature. For the final test, all of the features will be available in order to test the overall performance of the devices in everyday use environments.

In summary, the primary reason for this study is to evaluate the new hearing aid product generation that will replace the current one on the market. The goal is to evaluate the audiological performance, usability as well as features and functions in comparison to the hearing aid generation already CE marked. Furthermore, it is important to identify unexpected, unwanted behavior from the devices.

3.2 Investigational Product (device) and Indication

The Investigational Product is a medical device. The brand name is [redacted], manufactured by Bernafon AG. The software version will be Oasis 2. The device is intended for people with hearing loss over 36 months of age. The devices are equivalent to those with CE Declaration of Conformity; however, do not yet have the physical marking on them. The device consists of a body made of plastic parts and non-toxic paint as well as plastic tubing that touches the skin. Only those trained as a hearing care professional in the fitting of hearing devices should program the device. However, anyone who receives a minimum amount of explanation for use is qualified to use the device. 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. The safety of the 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. The basic benefit of hearing aids does not change with newly released devices. 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.

Studies have concluded that adding features such as noise reduction and frequency lowering add benefit to the primary goal of amplifying sound. Features provide comfort, speech intelligibility, and reduced listening fatigue (Stelmachowicz, et al. 2010; Houben, et al. 2013).

A risk assessment is performed for all new devices. The primary risk identified is the possibility of over amplification from excessive sound pressure level (further described in sec. 3.7). This risk is mediated by printing a warning in the Instructions for Use for hearing aids with high sound pressure level output capability. Additionally, Bernafon AG has had no adverse events reported in the last 15 years including no required modifications or recalls of products.

For the IMD to be tested there is no available clinical research data to date.

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 hearing devices. The intended purpose of the study is to compare the performance of the IMD with the RMD currently on the market. In order to make an effective comparison the test participants shall wear the IMDs for a minimum of 2 weeks per test period.

3.6 Explanation for choice of comparator (or placebo)

The comparison device will be a current Bernafon hearing aid (RMD) that is available on the market. The test participants will have already worn these devices for a minimum of 6 months before comparing them to the IMD. The reason for using RMD is to control for performance differences caused by different signal processing or feature implementation used in competitor devices.

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 audiometry (test of hearing loss) a level of more than 100 dB SPL must be provided for test subjects who are profoundly

hard of hearing. This audiometry established for people who are profoundly hard of hearing

Post-trial care is organized in a manner that allows the test participants to contact the sponsor site and arrange an appointment for any maintenance for the devices as needed.

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.

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 current Bernafon device performance against the new device and not the overall effect of amplification. Therefore, only participants that are hearing impaired and experienced hearing aid users will be included. Bernafon has its own database of test subjects that come to Bernafon for updated fittings and general maintenance of their hearing aids. These test subjects do not consist of employees of Bernafon or family members of employees. The test subjects for the current study will be chosen from the internal subject database.

The comparison between devices shall be made with experienced Bernafon hearing aid users. It is important to compare the performance and the subjective opinion of the intended users. Testing normal hearing participants would not contribute information to this study. 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 [redacted]

4. STUDY OBJECTIVES

4.1 Overall Objective

The purpose of this study is to evaluate whether the IMD provides a similar or better performance than 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 performance of the IMD is as good as the RMD. 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 as expected in comparison with the RMD, meaning that the performance of the IMD should not be inferior to the RMD.

4.3 Secondary Objectives

Secondary objectives are to assess the performance of new features. The specific feature is the implementation of a new compression system called Dynamic Environment Compression System [redacted] The new feature should provide equivalent or superior benefit when activated compared with when it is not activated.

4.4 Safety Objectives

The study aims to validate the overall implementation of new and old features on the new chip used in 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 Speech Reception Threshold (SRT) measured in three conditions: unaided, with the control (RMD), and with the test device (IMD). Speech intelligibility scores should be equal to or better than those achieved with the RMD. The difference between control and test condition will be compared to the non-inferiority margin to test for non-inferiority. The unaided condition will be used as control of the investigational device benefit if non-inferiority could not be shown.

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5.2 Secondary Outcomes

A secondary endpoint will be the speech intelligibility measured with the feature, [redacted], and without [redacted] The subjective performance of [redacted] will be measured with questionnaires and interviews.

5.3 Other Outcomes of Interest

Further endpoints will be the subjective benefit measured with questionnaires. These measures help understand the overall performance and perceived benefit of the IMD as well as assess potential negative effects.

5.4 Safety Outcomes

The test participants will be asked to keep a diary during the field trial and to write down anything unexpected that occurs. 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, comparative clinical investigation conducted monocentric at the premises of Bernafon in Bern, Switzerland.

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

As an RMD the subjects' current hearing instruments (Bernafon device) will be used. Additionally, a control situation may be when an unaided test condition is used or a test condition with a feature on or off.

There is no placebo or "fake" device that does not provide amplification. A single group assignment design is used with test subjects that have worn the RMD for at least 6 months and will now be fit with the IMD. Most of the testing will be unblinded as the subjects are familiar with the RMD which will be used as the control. They will recognize when they are using a different device. In situations where one device is used but programmed with two different programs the test subjects will be blinded. They will not be told the difference between the two programs. They will, for example, have a feature on in one and off in another.

A randomized test order will be used to test in a simulated environment. The test subject will be tested using unaided and aided conditions in a randomized manner for speech testing, listening effort, and subjective evaluations of sound and benefit perception. Or as stated above, the testing may be single-blinded by using only the IMD and programming different states into the device for comparison testing in which the test subject will not be aware of the differences.

The participants will be expected to participate for approximately 4 months for a combinations of field tests and lab tests. For lab tests they will not spend more than 2 hours in the clinic for testing, but will be expected to come for 5-6 sessions. Field trial periods will not last more than 14 +/-3 days.

The sequence will begin with the preparation phase in which participants are invited to the clinic for testing to determine if they are candidates for the trial. The entire test procedure will be explained, and they will be given a Patient Informed consent form read which will need to be signed, dated, and returned before any testing begins.

The following appointments will include a series of field tests with corresponding lab test appointments. There could be up to 6 appointments, but will not exceed 2 hours each time. During these appointments they will participate in speech testing, listening effort testing, perceived loudness testing, and subjective evaluations of sound and benefit of the hearing aids. Subjects will be given questionnaires and diaries to complete with all field test periods.

After they have completed all appointments the clients will receive instructions about the continued use of the RMD and the reminder that they are welcome to come to the clinic for any maintenance of the aids.

6.2 Methods of minimising bias

6.2.1 Randomisation

For one period of the field tests the subjects will be divided into two groups. One group will begin the trial with the new feature [redacted]) programmed in the IMD and the other group will have the feature turned off. They will be given two sets of IMDs (one with and one without the feature). They will be instructed to wear one pair of devices for the first 7 days and then to switch to the other pair of devices. After two weeks (+/-3d) of use they will return to the clinic for an appointment. The allocation to the groups will be randomized using stratification in order to maintain balance between the two test groups. The stratification will be based on degree of hearing loss and frequency lowering prescription (on/off). For lab tests the assignment to the test condition will also be randomized.

6.2.2 Blinding procedures

The subjects will know that there are two programs (or two pairs of aids), but they will not know what the differences between them are. The program setting/device set up will be randomized so that not all test subjects have the same setting of [redacted] for program one and for program two. For example, program/device one may have [redacted] programmed for some subjects and for others program/device two will have [redacted] programmed. This will also help control any bias toward one program. The PI will be blinded concerning the two sets of devices. The statistician will create the randomization list and any pre-programming of devices needed to blind the PI.

6.2.3 Other methods of minimizing bias

Validated questionnaire will be used to minimize bias. Diaries will be recorded by the subjects of their experience, and questions during interview sessions during the appointments will be created in a non-leading manner.

6.3 Unblinding Procedures (Code break)

The statistician will maintain the documentation of blinding procedures. The [redacted]eature testing will be blinded and will be managed by the statistician. For all other testing the difference between the IMD and the RMD will be clear to the subjects due to the differences in hardware.

7. STUDY POPULATION

The study will take place in the clinic at Bernafon AG in Bern. There will be no other sites used for the testing.

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 combine 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
- 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
- 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

Bernafon has its own database of test subjects that come to Bernafon for updated fittings and general maintenance of their hearing aids. These test subjects do not consist of employees of Bernafon or family members of employees. The test subjects for the current study will be chosen from the internal subject database. Bernafon does not advertise as a method of recruiting participants. Participants are collected and added to the database by word of mouth. Current subjects will refer another person as a potential candidate to participate as a test subject. Additionally, if someone knows of another person with hearing loss they may give them the contact information of an audiologist within Bernafon. The person can then contact Bernafon if they wish to have a hearing test and determine if they're eligible to participate in a study. They first have a diagnostic audiological exam to determine if they have a hearing loss and the severity. If there are any medical indications it is recommended that they see a physician and then return if there are no contra-indications for hearing aids. During the hearing exam and medical history discussion it is determined whether the person is cognitively able to act on their own behalf. Additionally if the person comes alone or if they are accompanied will help to determine their level of independence. The potential study will be explained to the patients at this time and an approximate timeline will be outlined with an estimation of how much time/number of appointments would be required of them. It is explained that there is compensation of time by means of a box of batteries and clearning accessories.

7.3 Assignment to study groups

For the field tests the allocation to the groups will be randomized using stratification in order to maintain balance between the two test groups. The stratification will be based upon the hearing loss of the participants, and more specifically the pure tone average and individual frequency lowering prescription (on/off). The idea is to avoid that any results are affected by one of these factors being more heavily represented in one group versus the other. For lab tests the assignment to the test condition will also be randomized. The test condition order will be randomized using a latin square design. 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 IMD. 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 are normally at least five “back-up” test participants on the list 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 4 months of use with the IMD and breaks in between when they will return to the RMD. All participants will already be Bernafon hearing aid users; therefore, during the investigation they will stop using RMD and switch to the IMD for the assigned periods.

Additionally, there will be lab tests in which the participants will use the IMD for up to 2 hours at a time during testing in the clinic.

There are 3 field tests planned. In between each field test they will return to wearing RMD. At the end of the entire trial, and once the devices have been CE marked, the participants will have the choice to continue wearing the RMD or to switch and wear the IMD permanently.

8.1.1 Experimental Intervention (medical device)

The investigational product (IMD) is a medical device. It is a new version of a Bernafon hearing device. The name is [redacted] It does not significantly deviate from the current commercial product. The hearing aid still has the same intended use and the basic function of amplifying sound. The IMD uses a new chip to power the hearing aid. Performance is expected to be the same or better than the RMD. They are non-invasive devices. The hearing aid 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). The hardware of the BTE is painted with a non-toxic paint.

Figure 1: [redacted] device

8.1.2 Control Intervention (comparator treatment / medical device)

The Reference Medical Device (RMD) is called [redacted] and is a CE marked hearing aid. Its intended purpose is the same as [redacted]- to amplify sounds. The strength of the amplification is programmed according to the subject's individual hearing loss. There is no placebo treatment used during this study. The RMD and the IMD will be programmed based on the subject's individual hearing loss. The amplification will be the same from both devices with +/- 5 dB. The output amplification will be tested for both the RMD and the IMD to ensure that they are similar.

8.1.3 Packaging, Labelling and Supply (re-supply)

The IMD is labelled by printing the name of the device directly onto the device. There is an individual serial number printed in the battery drawer that identifies each specific device. Additionally the device comes in a blister pack that includes a small paper with the serial number, name and description of the device (style and color). The blister is removed by the healthcare professional, and the device is placed in plastic case for the subjects. The packaging and labelling are the same for both the IMD and the RMD (marketed) device.

8.1.4 Storage Conditions

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. The IMD and the RMD are stored in exactly the same way. They should not be exposed to temperatures below -25° and not above 60° Celsius during storage or transport. The storage is the same as for devices already in use. The storage of these devices is according to standard procedures.

8.2 Administration of experimental and control interventions

8.2.1 Experimental Intervention

The devices are worn over the ear with a piece that is worn in the ear. They are non-invasive. The RMD will have been worn for at least 6 months as all subjects are current hearing aid users. The amplification is prescribed based on the subject's hearing loss. Both the RMD and the IMD will provide the same amount of amplification. The IMD will be worn for at least 2 weeks per field test period in order to give the subjects enough time to wear the devices in various sound environments. They need to wear the device in different environments to make a comparison between the IMD and the RMD. The questionnaires ask questions about specific environments, and it's beneficial if the subject has experienced most of them. Normal use of a hearing device is 8-10 hours per day. The subjects will wear the IMD for the amount of time during the day that they wear RMD. The will not be told how long to wear it. The device should be worn as the subjects normally wear their current device (RMD).

The study procedure will use a single group assignment design in which the subjects will wear the IMD at the same time. Use of a new feature will be randomized so that some start the trial with it and some without it. As stated previously, the device is non-invasive and requires no surgical procedure. 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 test subjects will have been wearing the RMD for at least 6 months; therefore, they will not need additional training. The IMD is inserted in the same manner at the RMD. 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 RMD is the current device that the test subjects are using. They will have used the device for at least 6 months so that they are experienced with using hearing aids. They will interrupt the use of the RMD during the field trial periods to use the IMD. They need to wear the device in different environments to make a comparison between the IMD and the RMD. The questionnaires ask questions about specific environments and it's beneficial if the subject has experienced most of them. Normal use of a hearing device is 8-10 hours per day. The subjects will wear the IMD for the amount of time during the day that they wear the RMD device. They will not be told how long to wear it. The device should be worn as the subjects normally wear the RMD.

The study procedure will use a single group assignment design in which the subjects will wear the IMD at the same time. Use of a new feature will be randomized so that some start the trial with it and some without it. As stated previously, the device is non-invasive and requires no surgical procedure. 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 test subjects will have been wearing the RMD for at least 6 months; therefore, they will not need additional training. The IMD is inserted in the same manner at the RMD. 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 provide the same amplification as the subjects' RMD; therefore, they should not experience any significant negative differences that would make the subjects want to discontinue use of the device. If a subject reports certain differences that can be improved with fine tuning, for example, of amplification, this step will first be taken to see if the situation improves enough for the subject to continue with the trial. However, if the subject requests to discontinue they can immediately remove the IMD and return to the RMD. They will be asked to return the IMD to Bernafon AG, 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 only wear the IMD. However, the RMD are left in their possession in the event that the IMD does not work or if they find that they simply can't hear as well with the IMD as the RMD. For safety reasons the RMD are left with the subjects to use in the event that the IMD does not work. For ethical purposes, the subjects must have a back-up solution for their hearing impairment.

The software monitors the amount of time that the devices are worn. Therefore, it will be noted if the IMD has not been worn a standard or expected amount of time. 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 same follow-up as those subjects that complete the trial. They will already be Bernafon hearing aid users and, therefore, welcome to return to the clinic for follow-up fine tuning and maintenance as needed.

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. All test subjects will already be hearing aid users and will have, therefore, used the RMD while receiving other types of care or medications. There will be no impact on the study objectives

8.8 Medical Device Accountability

The subjects will already be in possession of the RMD. The devices have serial numbers by which the individual device can be identified and the production history traced. The IMD will also have serial numbers to identify them. 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. Only IMD that are from a tested batch will be used in the study.

8.9 Return or Destruction of Study Drug / Medical Device

At the end of the study all of the subjects will return the IMD to the site in Bern. It will be noted in the documentation that the devices were returned and whether the subject would like to return to the clinic to be fitted with the IMD once available for release.

9. STUDY ASSESSMENTS

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

Study Periods	Intervention Period						Follow-up
Visit	Screening/1	2	3	4	5	6	7
Day	0	14+/-3d	24+/-3d	38+/-3d	45+/-3d	59+/-3d	70+/-7d
Patient Information and Consent	x						
Demographics	x						
Medical History	x						
In-/Exclusion Criteria	x						
Randomization	x *	x **				x **	
Otoscopy	x	x	x	x	x	x	x
Audiometry	x						
Real Ear Measurement	x		x		x		
Administer Medical Device	x		x		x		
Primary Variables (speech)		x				x	
Secondary Variables (interview)		x		x		x	
Other Variables (evaluation of questionnaire)		x		x		x	
Other Variables (usability)				x		x	
Adverse Events	x	x	x	x	x	x	x

* Randomization of field trial period

**Randomization of lab trial test conditions

9.2 Assessments of outcomes

9.2.1 Assessment of primary outcome

The primary outcome is the performance of the IMD compared with the RMD. It will be measured various times throughout the trial. The defining measurement will be on the 59th (+/-3d) of treatment when the subjects return to the clinic and will be measured with a questionnaire and lab tests. The results from this lab test will directly compare the IMD with the RMD as well as the unaided condition with no device. They will be compared to ensure that performance of the IMD is not poorer than the RMD.

9.2.2 Assessment of secondary outcomes

Subjective benefit regarding performance will be measured throughout the trial. Questionnaires will be collected and interviews conducted at 14, 38th, and 59th (+/- 3d).

9.2.3 Assessment of other outcomes of interest

Speech intelligibility will be assessed with the new feature on the 14 (+/- 3d). It will be assessed with speech in noise tests in a simulated environment in the clinic. The test conditions used will be made with the IMD with the feature on and off. The percentage of correct answers will be compared across conditions to ensure that speech intelligibility is not poorer with the new feature than without.

9.2.4 Assessment of safety outcomes

The test participants will be asked to keep a diary during the field trial and to write down anything unexpected that occurs. 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 instructed to write in their diary 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.

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 IMD. The follow-up procedure will be the same as for all active test subjects. They will be instructed to return to the clinic for any required maintenance or fine-tuning of the devices. Those that withdraw prematurely will already be wearing their RMD Bernafon devices; therefore, their follow-up treatment will be the same.

9.3 Procedures at each visit

9.3.1 Screening/First Visit

Screening visit, Day 0: Otoscopy is performed. Air and bone audiometry is performed to determine hearing loss. A history is taken that includes hearing history as well as general health history. The Patient Informed consent form will be explained to the subject and given to read, sign, and date. No trial activities will be performed before the Patient Informed consent form is signed and dated by the subject and investigator. Patients are given time during the appointmentto decide, whether or not to participate in the study. Subjects will receive a copy of the signed patient informed consent form and the patient information. Inclusion/exclusion criteria will be determined. The trial will be explained including how many visits are expected as well as the type of testing that they will complete. The subjects will be fit with a pair of IMD with [redacted] programmed and a second pair of IMD without [redacted]. Output will be measured with Real Ear Equipment. All other features will be set as prescribed by the software. They will receive an Instructions for Use (IFU). They will be given a questionnaire ([redacted]) and a diary to keep during the first period of the field trial. They will be scheduled for the First Visit. Any AEs will be reported in the CRFs.

9.3.2 Second Visit

Visit 2, Testing, Day 14 +/-3: The subjects will hand in the completed questionnaire given to them at the previous appointment. The clinician will conduct an interview based on the comments in the diary and prepared questions about user experience. They will be asked which pair of hearing aids they preferred. A lab test will be made to test speech intelligibility with the OLSA and WAKO tests (all features besides [redacted] will be set to off for the Lab testing). They will return the IMD and be instructed to use the RMD until the next appointment. Any AEs will be reported in the CRFs. They will be scheduled for the next visit.

9.3.3 Third Visit

Visit 3, Fitting, Day 24 +/-3: The subjects will be fit with the IMD. Output will be measured with Real Ear Equipment. All settings will be set to the defaults. They will be instructed to wear the IMD for the entire trial period. They will be given two questionnaires (specific to the device and the DOSO) and a diary to keep during the field trial. Any AEs will be reported in the CRFs. They will be scheduled for the next visit.

9.3.4 Fourth Visit

Visit 4, Testing, Day 38 +/- 3: The subjects will hand in the completed questionnaires given to them at the previous appointment. The clinician will conduct an interview based on the comments in the diary and prepared questions about user experience. The clinician will complete a PHAST test with the subject for usability of the IMD. They will return the devices and be instructed to use the RMD until the next appointment. Any AEs will be reported in the CRFs. They will be scheduled for the next visit.

9.3.5 Fifth Visit

Visit 5, Fitting, Day 45 +/- 3: The subjects will be fit with the IMD. Output will be measured with Real Ear Equipment. The subjects will be given three questionnaires (two device specific questionnaires and APHAB) and a diary to keep during the field trial. They will be instructed to wear the IMD for the entire trial period. Any AEs will be reported in the CRFs. They will be scheduled for the next visit.

9.3.6 Sixth Visit

Visit 6, Testing/Final, Day 59 +/- 3: The subjects will hand in the questionnaires given to them at the previous appointment. The clinician will conduct an interview based on the comments in the diary and prepared questions about user experience. A lab test will be made to test speech intelligibility with the OLSA. They will test in three conditions: unaided, aided with the RMD, and aided with the IMD. Any AEs will be reported in the CRFs. They will be told that the trial is complete.

9.3.7 Follow-Up

Visit 7, Follow-up, Day 70+/- 7: If subjects choose to have the RMD fine-tuned, they will make appointments as needed for follow-up adjustments and maintenance.

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 hospitalization, or
- results in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function
- 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

Reporting to Sponsor:

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

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

10.1.4 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.**Contact information in case of SAE / SADE**

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	[redacted]	[redacted]	[redacted]	[redacted]
2	[redacted]	[redacted]	[redacted]	[redacted]

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

11. STATISTICAL METHODS

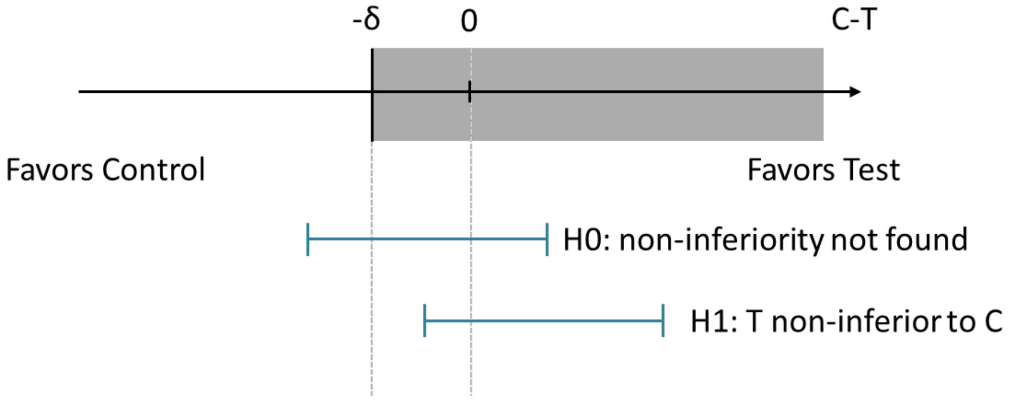
The goal of the trial is to show that the IMD performs at least as well as the marketed RMD. The platform that supports the IMD shows promising capabilities in terms of processing power and wireless capabilities. The intention with the development of the new generation is to port the main functionalities (amplification, feedback canceller, directional microphones and noise reduction) from the RMD to the IMD. For this reason, it is not expected to find that the IMD outperforms the marketed RMD.

11.1 Hypothesis

The goal of the test is to show that the IMD performs at least as well as the marketed RMD. A superiority hypothesis is used when a difference between performances is expected. To show that two devices have the same effect, the Committee for Proprietary Medicinal Products (CPMP) (2005) recommends using a non-inferiority test.

The non-inferiority margin is computed from the findings of the testing performed on the current marketed RMD with the primary outcomes (SRT) and other published results summarized in a meta-analysis. Lower SRT indicates a better performance, i.e. a positive difference between unaided and aided indicates an improvement with amplification.

Test condition labels: the marketed RMD as the Control (C), the IMD as the Test (T), and the non-inferiority Margin (δ). Positive value of SRT_C-SRT_T indicates and improvement with T:



Under H0: the IMD is not non-inferior to the RMD:

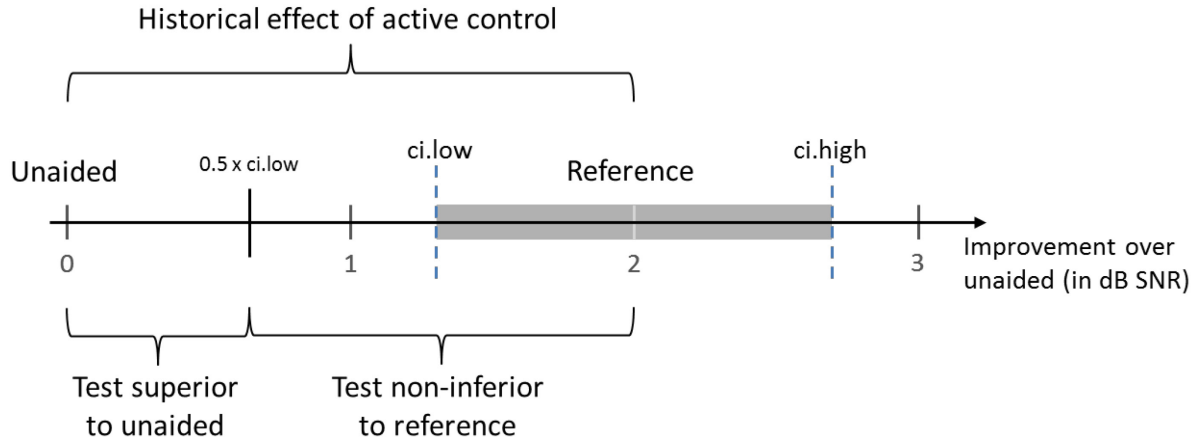
$$C - T \leq -\delta$$

Under H1: the IMD is not inferior to the RMD:

$$C - T > -\delta$$

Non inferiority margin is set with the following rationale (S. Kaul et al., 2005): *"One proposal for selecting the margin is to take one-half of the magnitude of the worst limit of this CI—the so-called "50% rule" or "95-95 method" recommended by the FDA"* with unaided condition instead of placebo.

The reference effect (unaided-aided) is about 2 dB improvement (SD = 2 dB). The lowest bound of the confidence interval is 1.3 dB. Following this rationale ($\delta = E\,t - 0.5 \times C\,lo$), we will set the non-inferiority margin to 1.3 dB. This rationale can be illustrated as follows (based on D'Agostino et al., 2003):



11.2 Determination of Sample Size

For non-inferiority testing, sample size calculations are the same as those for a 1-tailed test for superiority when the specified δ is the same as the superiority population difference to detect (Masha & Sessler, 2011). The sample size calculation follows the recommendation from Chow & Wang (2008), where sd is the standard deviation, α the significance level, 1-β the power, and δ the non-inferiority margin:

$$n = \frac{sd^2 \times (z_{1-\alpha} + z_{1-\beta})^2}{\delta^2}$$

For 90% power at the 0.025 significance level, the required sample size is about 24 subjects to detect non-inferiority of the marketed RMD with an SD of 2 dB and non-inferiority δ of 1.3 dB.(Chow & Wang, 2008, p. 52).

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 form 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 (version 3.3.2) a statistical software package. R "stats" package will be used for the confidence interval, non-inferiority, and Wilcoxon tests. Documentation of the analysis will be done with R Studio under R Markdown format.

Main outcome: speech reception threshold

The paired t-test usually tests that the mean differences are zero. The non-inferiority test compares the difference to a non-zero quantity -δ.

The assumptions of the paired t-test are:

1. The data are continuous (not discrete).
2. The data, i.e., the differences for the matched-pairs, follow a normal probability distribution.
3. The sample of pairs is a simple random sample from its population. Each individual in the population has an equal probability of being selected in the sample.

Secondary outcome: APHAB questionnaire

Data from comparative questionnaire represent a ranking more than a magnitude. The data are not continuous and normality of the data distribution is not expected. Therefore, a non-parametric statistical method like the Wilcoxon signed rank test on repeated measures will be used.

11.4.1 Datasets to be analyzed, analysis populations

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

The included subjects are experienced hearing aid users (minimum 6 months) 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.

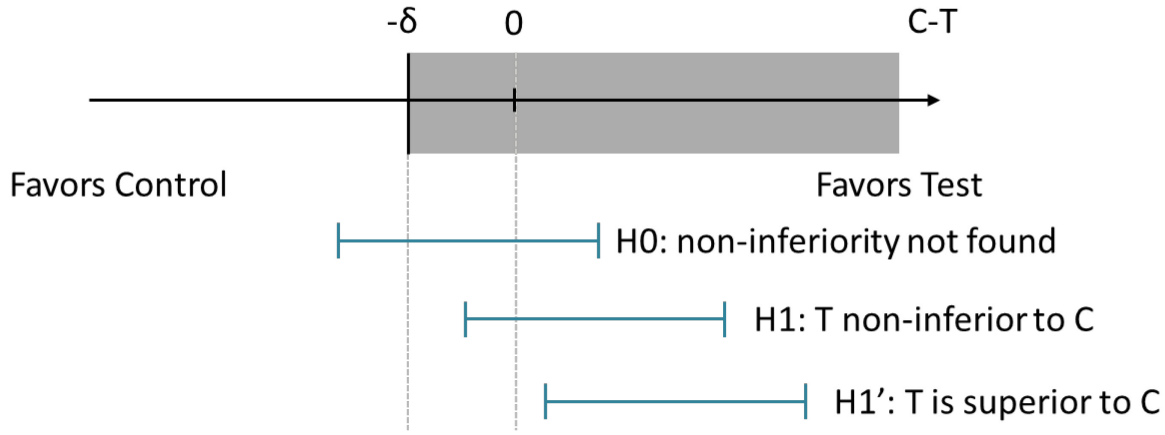
11.4.2 Primary Analysis

Speech Reception Threshold (SRT) will be measured in a single lab test under three test conditions: unaided, control (RMD), and test (IMD) after appropriate training. Test condition order will be randomized using a Latin square design to control any potential order effect. The difference between control and test condition will be compared to the non-inferiority margin to test for non-inferiority. The unaided condition will be used as control of the investigational device benefit if non-inferiority could not be shown.

11.4.3 Secondary Analyses

- Switching to superiority test will be considered as recommended by the CPMP (2001):

"If the 95% confidence interval for the treatment effect not only lies entirely above −M but also above zero then there is evidence of superiority in terms of statistical significance at the 5% level (P < 0.05). In this case it is acceptable to calculate the P value associated with a test of superiority and to evaluate whether this is sufficiently small to reject convincingly the hypothesis of no difference."



- Hearing loss degree will be added in post hoc analysis as a covariable.

11.4.4 Interim analyses

No interim analysis is planned according the test design.

11.4.5 Safety analysis

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

11.4.6 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.

11.5 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 switch back to his own device (RMD) and return the IMD.

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

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 the site. 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 locked clinic room. 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 Principle 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 treating physician must certify that the data entered into the Electronic Case Report Forms are complete and accurate. After database lock, the treating physician will receive a CD-ROM or paper copies of the patient data for archiving at the site.

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 OLSA test	PI
Results to WAKO test	PI
Results from [redacted] questionnaire	PI
Results from APHAB questionnaire	PI
Results from Interview	PI
Results from Journal/Diary	PI

Results from PHAST	PI
AEs / SAEs, ADE / SADE	PI
Name, date, signature of PI	PI

12.1.2 Specification of source documents

The PI 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.

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, 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 [redacted]. 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 analysed. The database will be locked at this time, recorded in special archiving format and securely stored for at least 1 year. In addition the treating physician 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 site will be monitored by a person at the site. 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 authorised person will be available during the visits to answer questions.

100% source data verification will be done for 10 patients. For the other 10 patients 50% source data verification will be done.

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 site.

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

16. REFERENCES

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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. Information for Use
8. Meta-Analysis