A clinical investigation comparing a standard hearing aid fitting protocol and a fitting protocol optimized for musicians

August 27, 2019

bernafon
Your hearing · Our passion

A clinical investigation comparing a standard hearing aid fitting protocol and a fitting protocol optimized for musicians.

Clinical Study Protocol

Study Type:	Clinical trial with an Investigational Medical Device (MD)
Study Categorisation:	Category A; MD with CE mark
Study Registration:	SNCTP, EudraCT
Study Identifier:	BF006-1902
Sponsor:	Bernafon AG Morgenstrasse 131, 3018 Bern
Principal Investigator:	Barbara Simon bsim@bernafon.com +41 31 998 16 84
Investigational Product:	Hearing Instrument; Viron 9 MNR
Protocol Version and Date:	Version 2.0, Final Document

CONFIDENTIAL

The information contained in this document is confidential and the property of Bernafon AG. The information may not - in full or in part - be transmitted, reproduced, published, or disclosed to others than the applicable Competent Ethics Committee(s) and Regulatory Authority(ies) without prior written authorization from the sponsor except to the extent necessary to obtain informed consent from those who will participate in the study.

Signature Page(s)

Study number	SNCTP; EudraCT, registration number (TBD)
Study Title	A clinical investigation comparing a standard hearing aid fitting protocol and a fitting protocol optimized for musicians.

The Sponsor-Investigator, Principle Investigator and trial statistician have approved the protocol version 2.0 (dated 27.08.2019) and confirm hereby to conduct the study according to the protocol, current version of the World Medical Association Declaration of Helsinki, ICH-GCP guidelines or ISO 14155 norm if applicable and the local legally applicable requirements.

Sponsor: Bruno Keller, Senior Director Marketing and Channel Support

Place/Date	Signature

Principle Investigator: Barbara Simon

Place/Date	Signature

Trial Statistician: Christophe Lesimple

Place/Date	Signature

Table of Contents

STUDY SYNOPSIS

Sponsor / Sponsor-Investigator	Bernafon AG
Study Title:	A clinical investigation comparing a standard hearing aid fitting protocol and a fitting protocol optimized for musicians
Short Title / Study ID:	BF006-1902
Protocol Version and Date:	2019.08.27; Version 2.0
Trial registration:	SNCTP; EudraCT
Study category and Rationale	Category A; Medical Device with CE Mark
Clinical Phase:	Post-market; Medical device study involving human subjects

Background and Rationale:	The intended use of hearing aids is to amplify sounds to compensate for hearing loss. The initial goal is to amplify speech and facilitate understanding speech especially in noise. Research shows that wireless hearing aids are efficacious for older adults (Humes et al. 2017), and in general, an increase in satisfaction and substantial benefits are characteristic for the wireless hearing aids brought to market during the last decade. Music is proven to enhance the lives of older people (Cohen et al., 2002; Lehmberg & Fung, 2010), but many people report a reduction in their ability to enjoy music with a hearing loss (Leek et al., 2008; Creech et al., 2013). Amplification can be used to overcome a hearing loss and return the joy of music to those with hearing loss. However, for listening to music or particularly, for musicians that play an instrument, the hearing aid settings used for amplifying speech often have adverse effects on music. Hearing perception abilities are different for normal hearing people compared to hearing-impaired, and musical training (i.e. history of playing an instrument or singing) further alters the perception and listening preferences. Normal hearing listeners and those with musical training prefer less compression, meaning less signal processing. While hearing-impaired participants may not strongly favor one condition over the other (Mussoi et al., 2015). For people using hearing aids, music should be treated as a special signal and a program devoted to music listening is recommended (Chasin & Russo, 2004). However, it is not possible to predict in advance the properties of the music signal as it can't be generalized like speech (different instruments, style, musical setup). For musicians the dedicated program may require further optimization and fine-tuning specific to their instrument and/or the situations in which they play music. For this study, Bernafon AG will carry out testing with participants with hearing loss to compare dedicated music programs. The current study will compare the standard music program available in the software to one that is fine-tuned for each participant. The Bernafon hearing aids used for the current study are CE- marked and have been on the market for almost one year. The goal is to determine whether musicians will perceive a difference and prefer a fine-tuned music program over the default music program in real-life situations.
Objective(s):	The purpose of this study is to compare the standard fitting protocol for hearing devices with a protocol that is optimized for musicians. Sound quality, specifically for playing music, should be improved with the optimized fitting.

Outcome(s):	Primary Endpoint: The primary objective is to assess whether the optimized fitting is better than the standard fitting. At the end of the trial the participants will complete a preference questionnaire and choose a preferred program (optimized music or default music) including the reasons for their preference. Secondary Endpoints: The secondary objective is to measure sound perception in a lab test in the clinic. The subjects will rate the perception of various aspects of music using both music programs. The overall sound quality and benefit from the device will be measured with product questionnaires that ask the subjects to rate the hearing aids in specific situations after using them during field tests. Safety Endpoint: The study aims to find any new risk factors and to ensure the safety of the device by monitoring all AEs.
Study design:	This is a controlled, single blinded, comparative clinical evaluation conducted monocentric at the premises of Bernafon AG 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 profound • German or French speaking • Play a musical instrument • Both genders • Ages 18 and older • Ability and willingness to sign the consent form Exclusion Criteria: • Normal hearing • Contraindications for amplification • Active ear disease • Don't play an instrument • 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 Measurements **Music perception** is tested with a rating scale that asks the participants about various aspects of recorded music and is performed in a sound studio as a lab test. **Subjective performance of devices** is tested with questionnaires asking the participants to rate aspects concerning the sound quality of the hearing devices. **Preference testing** allows the participant to choose the program that they prefer, which rates the fitting protocol (standard vs optimized).
Study Product / Intervention:	Viron 9 MNR The investigational medical device (IMD) will be the Viron 9 hearing instrument. The hearing aid was released to the market in early 2019. Hearing instruments are worn approximately 10 hours per day and removed at night. The participants will wear the devices for two field periods of 10 +/- 7 days. They will be current or new hearing aid users. There is no RMD as the comparison for the study is made using the same device. As the goal is to test fitting protocols, one device can be fitted with different programs within the same device. Participants can switch between the various programs to test them simultaneously in the situations in which they find themselves. The software version used during testing will be the final version of the software that was released to the market at the same time as the hearing aids.
Control Intervention (if applicable):	The control is the program with the standard fitting (default music) protocol.
Number of Participants with Rationale:	There will be an exploratory analysis of the data only. Based on the sample size calculation, the total number of participants will be approximately 18-20.
Study Duration:	Approximately 5 months. The screening of participants is planned for October 2019, and the final data collection appointments should occur in February 2020.
Study Schedule:	Planned First-Participant-in: October 2019 Planned Last-Participant-Out: February 2020
Investigator(s):	Barbara Simon, Research Audiologist, Doctor of Audiology Morgenstrasse 131 3018 Bern, CH bsim@bernafon.com +41 31 998 16 84
Study Centre(s):	The testing will take place at a single site in Bern, Switzerland at the Bernafon AG headquarters.
Statistical Considerations:	The analysis and documentation will be performed by the statistician using the latest validated R version with R Studio as IDE. Appropriate data analysis will be performed with parametric and non-parametric tests on questionnaire outcomes, hearing threshold measures, and music perception measures.
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.

ABBREVIATIONS

AE	Adverse Event
BASEC	Business Administration System for Ethical Committees, (https://submissions.swissethics.ch/en/)
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, in Italian: OSRUm)*
Clinic	Clinic room at test site at Bernafon AG; not a hospital clinic
eCRF	Electronic Case Report Form
CTCAE	Common terminology criteria for adverse events
GCP	Good Clinical Practice
HCP	Hearing Care Professional
HRA	Federal Act on Research involving Human Beings *(in German: HFG, in French: LRH, in Italian: LRUm)*
IB	Investigator's Brochure
IDE	Integrated Development Environment
IMD	Investigational Medicinal Device
IP	Investigational Program
ISO	International Organisation for Standardisation
ITT	Intention to treat
MD	Medical Device
MedDO	Medical Device Ordinance *(in German: MepV, in French: ODim)*
MNR	miniRITE
P1	Program 1 (general program)
PI	Principal Investigator
RITE	Receiver in the Ear
RMD	Reference Medical Device
SDV	Source Data Verification
SOP	Standard Operating Procedure
SP	Standard Program
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File

STUDY SCHEDULE

Study Periods	Screening	Treatment/Intervention Period	
Visit	1	2	3
Day	0	10 +/- 7 days	20 +/- 7 days
Patient Information and Informed Consent	x		
Demographics	x		
Medical History	x		
In-/Exclusion Criteria	x		
Otoscopy	x	x	x
Audiometry	x		
Randomisation of treatment	x		
Administer Medical Device	x		
REM	x		
Optimized fitting		x	
Primary Variable (Preference questionnaire)			x
Secondary Variable (Lab test-music perception)	x	x	x
Other Variables (Product questionnaire)	x		
Other Variables (Music perception questionnaire)	x	x	
Adverse Events	x	x	x

1. STUDY ADMINISTRATIVE STRUCTURE

1.1 Sponsor

Bernafon AG

Morgenstrasse 131, 3018 Bern

Tel. +41 31 998 01 01

The role of the sponsor is to provide the site for the testing as well as the equipment used during testing. The sponsor will provide the hearing devices, the IMD, used for the study. The results will be used by the sponsor for further development activities as well as post-market safety assessment of the devices. The sponsor may audit the clinic as well as the processes and documentation performed by the investigators at that site.

1.2 Principal Investigator

Barbara Simon, Research Audiologist
Morgenstrasse 131, 3018 Bern

Tel. +41 31 998 16 46

Email: bsim@bernafon.com

1.3 Statistician ("Biostatistician")

Christophe Lesimple
Morgenstrasse 131, 3018 Bern

Tel. +41 31 998 17 03

Email: cles@bernafon.com

1.4 Laboratory

Not applicable – no samples

1.5 Monitoring institution

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

1.6 Data Safety Monitoring Committee

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

1.7 Any other relevant Committee, Person, Organisation, Institution

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

2. ETHICAL AND REGULATORY ASPECTS

Before the study is 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). Any amendment to the protocol must as well be approved (if legally required) by this institution.

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

2.1 Study registration

The study shall be registered in the EU registry of clinical trials, EudraCT (https://eudract.ema.europa.eu/eudract-web/index.faces). In addition, the study will be registered in German in the Swiss National Clinical trial Portal (SNCTP via BASEC).

2.2 Categorisation of study

The risk category for the clinical trial of these medical devices falls under Category A because the hearing aids will have the conformity marking at the time of the trial. The Investigational Medical Device (IMD) has had the CE Declaration of Conformity for almost one year and will be used with its original intended purpose for this trial.

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 (all changes in the research activity and all unanticipated problems involving risks to humans; including in case of planned or premature study end and the final report) within the allowed time frame. 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 is reported within 15 days. The regular end of the study is reported to the CEC within 90 days, 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)

Not applicable – category A device

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 Regulation on medical devices 2017/745 and the ISO Norm 14155 and ISO 14971, the Swiss Law and Swiss regulatory authority's requirements. The CEC 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 always in the best interests of Bernafon AG, its members and the 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 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. Consent is sought from each participant. They will be compensated with hearing aid accessories (i.e. Batteries, cleaning supplies) that will not exceed a value of 100 CHF.

The participant is 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. Enough time needs to be given to the participants to decide whether to participate or not. The first appointment is scheduled for 2 hours; however, if they require more time than the allotted 2 hours, they can take the information home and have 24 hours in which to decide.

Otherwise, the participants will sign the consent form in the clinic during the first visit if they choose to become a participant, and the first visit will proceed as described in the scheduling overview.

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

The participant should read and consider the statement before signing and dating the informed consent form and will be given a copy of the signed document. The consent form will also be signed and dated by the investigator (or his designee) at the same time as the participant signs, 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.

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.

For data verification purposes, authorised representatives of the Sponsor, Swissmedic, or an ethics committee may require direct access to parts of the medical records relevant to the study, including participants' medical history.

2.9 Early termination of the study

The Sponsor and/or CEC 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 PI is allowed to amend the protocol or to provide suggestions for a protocol amendment. Any plans for important protocol modifications (e.g., changes to eligibility criteria, outcomes, analyses) will first be approved by the relevant parties (e.g., other investigators, CEC) before amending the protocol. Substantial amendments are only implemented after approval of the CEC.

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

All non-substantial amendments are communicated to the CEC within the Annual Safety Report (ASR).

3. BACKGROUND AND RATIONALE

3.1 Background and Rationale

The intended use of hearing aids is to amplify sounds to compensate for hearing loss. The initial goal is to amplify speech and facilitate speech understanding especially in noise. Research shows that wireless hearing aids are efficacious for older adults (Humes et al. 2017), and in general, an increase in satisfaction and substantial benefits are characteristic for the wireless hearing aids brought to market during in the last decade.

Music is proven to enhance the lives of older people (Cohen et al., 2002; Lehmberg & Fung, 2010), but many people report a reduction in their ability to enjoy music with a hearing loss (Leek et al., 2008; Creech et al., 2013). Amplification can be used to overcome a hearing impairment and return the joy of music to those with hearing loss. However, for listening to music or particularly, for musicians that play an instrument, the hearing aid settings used for amplifying speech often have adverse effects on music. The common type of compression used to amplify speech, Wide Dynamic Range Compression (WDRC) can lead to poor music quality including distortion, acoustic feedback, and reduced tone quality (Madsen & Moore, 2014). While fast acting WDRC compression is helpful to amplify the soft sounds of speech, for music it disrupts the overall shape of the temporal envelope causing a reduction in the spectral contrast of the music (Madsen et al., 2015). In order to sound natural, the large contrasts between loud and soft sounds of music should not be changed by compression.

Hearing perception abilities are different for normal hearing people compared to hearing-impaired, additionally, musical training (i.e. history of playing an instrument or singing) further alters perception and listening preferences. Normal hearing listeners and those with musical training prefer less compression, meaning less signal processing. While hearing-impaired participants may not strongly favor one condition over the other (Mussoi et al., 2015). For people using hearing aids, music should be treated as a special signal and a program devoted to music listening is recommended (Chasin & Russo, 2004). However, it is not possible to predict in advance the properties of the music signal as it can't be generalized like speech (different instruments, style,

musical setup). For musicians the dedicated program may require further optimization and fine-tuning specific to their instrument and/or the situations in which they play music.

For this study, Bernafon AG will carry out testing with participants that are musicians with hearing loss to compare dedicated music programs. The current study will compare the standard music program available in the software to one that is fine-tuned for each participant. The Bernafon hearing aids used for the current study are CE- marked and have been on the market for almost one year. The goal is to determine whether musicians will perceive a difference and prefer a fine-tuned music program over the default music program in real-life situations.

The devices used for the trial are the Bernafon Viron 9 miniRITE (MNR) behind-the-ear (BTE) hearing aids. The results of the trial will be used to examine differences in the benefit provided by the two music programs as well as identify further optimization possibilities of the default music program provided by the fitting software. Objective measures will be made with Real Ear Measures (REM) to verify the output of the hearing aids, and subjective differences will be measured with questionnaires and an adaptive music perception test (Kirchberger & Russo, 2015).

All participants are hearing impaired persons that play an instrument. The trial will consist of a total 3 appointments. For the field testing and the lab testing, the order of the programs (optimized or default) will be randomized. It is expected that the optimized program will perform better than the default program for perception and preference testing.

In summary, the primary goal of this study is to evaluate the currently marketed hearing aids regarding their performance with music and to further validate the safety of the devices.

3.2 Investigational Product (treatment, device) and Indication

The IMD is a class IIa medical device. The brand name is Viron 9, manufactured by Bernafon AG. The software used to program the device is Oasis^{nxt}. The device is intended for people with hearing loss that are over 36 months of age. The hearing aids have the CE Declaration of Conformity and are currently sold on the market. The device consists of a body made of plastic that houses the microphone(s), and chip. A speaker that is covered with a plastic dome or plastic mold is attached by a piece of thin plastic that goes over the ear. The plastic dome/mold is the only part that is in contact with skin inside the ear canal. 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 concerning the use of the device is qualified to use it. The device is non-invasive and requires no surgical procedures.

For further details please see the Investigator's Brochure.

3.3 Preclinical Evidence

Bernafon requires evidence of operational safety and medical effectiveness of the devices before testing them with human subjects. This evidence includes the device-related performance data in accordance with IEC 118-7: Measurement of the maximum output level and the maximum gain. In addition to the performance testing, the hearing aids are verified with system tests to ensure that they function according to the requirements. The safety of the fitting software is also demonstrated by a complete systematic software test and ensures the functionality of the hearing aids in combination with the software. Please see chapter 3E of the IB.

3.4 Clinical Evidence to Date

A clinical literature evaluation is maintained and has been updated in 2019. 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 and is used as post market analysis of the devices. The Viron device was validated with a clinical trial on volunteer participants and was

released to the market in early 2019. To date, there have been no adverse events reported on the U.S Food and Drug (FDA) Manufacturer and User Facility Device Experience (MAUDE) website.

A risk assessment is performed for all devices during development. The primary risk identified is the possibility of over amplification from excessive sound pressure levels (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, when this type of instrument is selected in the software, there is a message warning the hearing care professional (HCP) of the sound pressure capability. Overall, Bernafon AG has had no adverse event reported in the last 16 years including no required modifications or recalls of products.

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

The IMD will be used in accordance with the current use of hearing devices. The intended purpose of the study is to compare the performance of two different music programs (standard default and an optimized program) within the IMD which is currently sold on the market. The programs will be referred to as the Investigational Program (IP) for the optimized music program and the Standard Program (SP) for the default music program throughout this document. To make an effective comparison the test participants will wear the devices for approximately 10 days with a daily average use of 8-10 hours.

3.6 Explanation for choice of comparator

The comparator program will be the current standard default music program (SP) available in the fitting software. The hearing aids are always fit with an initial program (P1) that is a general program to be used in most situations. The default music program (SP) is an optional additional program that offers a range of 1-4 dB of more gain (in reference to the general program) at specific frequencies to enhance music. The test participants will be fit with the devices with both the SP and the IP as a second and third program (randomized) to make a side by side comparison of the programs in various music situations.

3.7 Risks / Benefits

A device risk analysis and risk assessment have been conducted for the Viron 9 hearing aid according to EN ISO 14971. This describes the anticipated adverse device effects, residual risks associated with the device and the procedures involved in its use. It also explains that the anticipated clinical benefit outweighs the potential risks. Please see the Risk Assessment for details.

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 data collection, the risk for the test participants is judged to be extremely minor. However, the following risks shall be addressed:

Risk of hearing loss to residual hearing at too high a level in audiological and psychoacoustic experiments: The hardware can provide an output that exceeds 132 dB SPL; however, only those with appropriate hearing loss (moderate to profound) will be fit with such devices reducing the risk to participants' residual hearing. During audiometry (test of hearing loss with audiometer) a level of more than 100 dB SPL must be used for test subjects who are profoundly hard of hearing. The risk is mitigated by the fact that the benefit of wearing hearing aids with a high output is higher than the risk to their minimal residual 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 of their own devices as needed for those that are hearing aid users.

3.8 Justification of choice of study population

The choice of study population was determined by the goal of the study. No minors or otherwise vulnerable participants will be included. The intended purpose of the study is to compare the current Bernafon device fitted with a standard music program with an optimized music program and not the overall effect of amplification. Therefore, only participants that are hearing impaired and play an instrument will be included. Because this study requires musicians, the Bernafon database of test subjects that play an instrument will be exhausted and then recruitment from musical groups/orchestras will be required to find the number of participants required by the sample size calculation. These test subjects will not consist of employees of Bernafon or family members of employees.
The comparison between programs shall be made with hearing aid users. It is important to compare the performance of the devices and the subjective opinions 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 to be included in the study.
For emergency situations, the following applies:
The standard procedure is to recommend that a subject see the ENT with whom they have an established relationship. If a subject does not have an ENT then it is agreed with Dr. Carvacchio (Inselspital, Bern) that, if necessary, subjects from the trial could be referred to him.

4. STUDY OBJECTIVES

4.1 Overall Objective

The purpose of this study is to evaluate whether the IP provides better performance when listening to and/or playing music than the SP. The study aims to provide possible improvements to the development and to use the results as a post-market quality control of the IMD.

4.2 Primary Objective

The study will assess the performance of the IP in comparison to the SP using a preference questionnaire. After wearing the devices for at least 10 +/-7 days and using them in daily life and various music situations, the subjects will be asked to complete a preference questionnaire and choose between the two music programs.

4.3 Secondary Objectives

The secondary objective is to assess the benefit of the IP in comparison to the SP using an adaptive music perception test. The performance of the IP should not be inferior to that of the SP. Additionally, questionnaires will be used to control for a general acceptance of the hearing aids, sound quality of music, and to monitor for unexpected device behaviour.

4.4 Safety Objectives

The study aims to assess the overall safety of the IMD by testing for unexpected behaviour from the IMD and by the collection of AEs to identify any new risk factors since their release to the market.

5. STUDY OUTCOMES

5.1 Primary Outcome

The primary outcome is measured with a preference questionnaire where the subjects must choose which program they preferred for listening and playing music. They must also state how sure they are using a 10-point scale and indicate from a list of qualities what they based their decision on.

5.2 Secondary Outcomes

Secondary outcomes will be measured with an adaptive music perception test (AMP) developed by Kirchberger and Russo (2015). The test uses recordings and asks the subjects to judge different aspects of music such as meter and timbre. The overall sound quality and benefit of the hearing aids in daily life will be measured with product questionnaires. The product questionnaire for the general P1 will be used to control for a general acceptance of the hearing aids and will answered one time after the first field period. The music perception questionnaire will be used to judge sound quality of music and will be answered three times, one for each hearing aid program. The music questionnaire will be answered for P1 at the end of the first field test and for P2 and P3 at the end of the second field test.

5.3 Safety Outcomes

The questionnaires used for the secondary outcome will also contain questions to measure the safety of the devices. These questions will specifically address unexpected noise or behaviour from the devices. Unexpected behaviour includes unprovoked feedback or whistling, distorted sounds or artefacts, spontaneous muting or the shutting off of the device, and any unexplained warning signals, beeps, or loud sounds.

6. STUDY DESIGN

This is a controlled, single blinded, comparative clinical evaluation conducted monocentric at the premises of Bernafon AG in Bern, Switzerland.
The exploratory study is based on a population of 18-20 hearing impaired people that have a hearing loss appropriate for the IMD.
As the comparator, the subjects will be fit with an SP in the same hearing aid as the IP. Additionally, a control situation will be the P1 or general program that is intended for all daily listening situations excluding music giving the subjects 3 programs within the IMD.
There is no placebo or device that does not provide amplification. The study consists of two field and three lab tests. A randomized and single-blinded, single-arm design will be used for the field tests. The lab test order will be randomized and single-blinded.
The study will consist of hearing-impaired subjects with hearing loss ranging from mild to profound and appropriate for testing of the IMD. The lab testing (AMP) will be single blinded and randomised and performed in a simulated environment. The blinding and randomization refer to the position that the SP and IP have within the programming. When multiple programs are fitted to the hearing aid the subject switches programs with a button that scrolls through the programs. The subjects will not know if the SP or the IP are in second or third position during both the field and the lab testing.
The subjects are expected to participate for approximately 1 month. The testing will include a combination of a field and lab tests. There are three lab tests during which the participants will not spend more than 2 hours in the clinic (including breaks). The field test periods will not last more than 10 +/- 7 days.
The sequence for the testing will begin with the screening appointment in which participants are invited to the clinic to determine if they are candidates for the trial. The entire test procedure will be

explained, and they will be given a Patient Information and Informed Consent which will need to be signed, dated, and returned before any testing begins. If they choose to participate, a hearing test will be made to determine if they have an appropriate hearing loss. They will be fitted with the IMD with a general program (P1) as all test subjects will first wear hearing aids for an initial field period of 10 +/- 7 days to become accustomed to the devices. They will perform the first lab test in the unaided and aided (P1) conditions. They will be randomized regarding the program placement (P2 or P3) for the IP and SP.
The following appointments will include the fitting of the SP and the IP (as either program 2 or 3, according to the randomization) and the lab tests in the clinic performed in the aided condition with P2 and P3. There will be a total of 3 appointments. There is an appointment before and after each field test. Each appointment will not exceed 2 hours. During the lab tests in the clinic they will participate in the AMP test. Test subjects will be given questionnaires to complete at home and in the clinic.
After they have completed all appointments, they will be notified that the trial is over. They will be reminded that they are welcome to come to the clinic for any maintenance or other follow-up of their own hearing aids.

6.1 Methods of minimising bias

6.1.1 Randomization

A randomized assignment of the position of SP and IP will be used for the field trial period that includes P2 and P3 and consequently the lab tests. The position of the SP and the IP (as either program 2 or 3) will be based on a list created by the statistician. This reduces bias by using a different scroll position as the earlier position has a better chance of scoring higher due to the more prominent placement and likelihood that subjects might not always scroll to the 3rd program. The randomization list will not be concealed from the PI but should be in the ISF so that the PI knows in which condition order to test each subject.

6.1.2 Blinding procedures

The field and lab tests will be blinded as the subjects will not know in which place the SP and IP are programmed. The statistician will create a permuted block list to randomize the placement of the two music programs. The PI will follow this list.

6.1.3 Other methods of minimising bias

The IMD will be programmed with a P1 to be used in general listening situations. All test subjects will wear the hearing aids for the first field test of 10 +/- 7 days with this program to become accustomed to the amplification. They will continue to use P1 during the second field test with the SP and IP added as the second and third programs. P1 will serve as a control in the circumstance that the subject's rate both the music programs poorly, to determine whether only the music programs are the problem or whether they have not accepted the device overall.

6.2 Unblinding Procedures (Code break)

The blinding for the field and lab tests will be based on a permuted block list created by the statistician. The subjects will not know which program they have in the second and third positions, only that they are music programs. The list will be in the ISF so that the PI has access and knows which assignment to use for each appointment.

The study will take place in the clinic at Bernafon AG in Bern. No other sites will be used for the testing. A plan of action due to low enrolment will be to widen the number of orchestras or musical groups to which information about the trial is distributed. The initial plan is to distribute information to groups

located within a 20 km radius to avoid that participants must travel far.

7. STUDY POPULATION

7.1 Eligibility criteria

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

- 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)
- Hearing loss severity ranging from mild to profound
- German or French speaking
- Play a musical instrument
- 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:

- Normal hearing
- Contraindications for amplification
- Active ear disease
- Don't play an instrument
- Inability to follow the procedures of the study due to language problems, psychological disorders, dementia, or other cognitive problems
- 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 directory of test subjects that use the Bernafon clinic 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 first be chosen from the internal subject directory. Once the appropriate options from the internal list have been exhausted, a flyer with information about the trial will be shared with musical groups/orchestras within a 20 km radius of the city of Bern. The flyer will provide the email address of the PI of the study for further information. Additionally, participants may be recruited by word of mouth. If a current person from the directory or someone that is enrolled for the current study knows of another person with hearing loss, they may give them the contact information of the PI. The prospective person can then contact the PI if they wish to have more information and/or to make a screening appointment to determine if they're eligible to participate in the study. The PI will respond by email or phone (whichever is the preference of the possible test subject). The PI of the study is well informed and qualified to answer all questions and give information about the study. If there are any medical indications suspected during the screening, the subject will be recommended to see a physician and then return if there are no contra-indications for hearing aids. During the screening discussion it will be 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. It will be explained to the subjects that the general compensation for their time is by means of a box of batteries and cleaning accessories.

7.3 Assignment to study groups

For the field tests the allocation is a randomized single-arm design, meaning that all participants will receive the test program (IP) and the comparator (SP). Half of the test subjects will have the SP assigned to the second program position and half to the third with a possible maximum imbalance of 2.
For the adaptive music perception test in the lab, the assignment to the test condition order will follow the randomization of the field test. The subjects will perform the lab test with P2 at visit 2 and P3 at visit 3. Because the assignment to P2 and P3 is randomized it will automatically randomize the test condition order. This will minimize bias created when one test condition is tested in the final or last position all 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 to withdraw is made by the investigator, the PI will inform the subject 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. The “back-up” participants will have already been screened and deemed to be appropriate for the study.

8. STUDY INTERVENTION

8.1 Identity of Investigational Products (medical device)

The treatment will be approximately 20 days of use with the devices. For the first field test of 10 +/- 7 days they will use the devices to become accustomed to the amplification. For the second field test lasting 10 +/- 7 days they will use the devices with an additional two programs (IP and SP) to try when listening to music.

There will be three lab tests (one at each appointment) during which the participants will use the IMD, for up to 2 hours during testing in the clinic.

8.1.1 Experimental Intervention (medical device)

The investigational product (IMD) is a medical device. It is the current version of the marketed Bernafon hearing device. The name is Viron 9. It was released to the market in early 2019. One BTE hardware style will be used for the trial. It is called a BTE miniRITE (MNR) and is appropriate for mild to profound hearing losses (depending on the speaker that is used). The device uses a disposable battery that lasts for approximately 5-7 days of use.
The BTE MNR is fitted with the body of the device over the ear, and the speaker covered with a dome or earmold inside of the ear canal. The performance of the IP is expected to be the same or better than the SP. They are non-invasive devices. The dome that is worn inside the ear canal is made from non-toxic plastic and the earmolds are made of non-toxic plastic with an acrylic coating. An illustration of the IMD is shown in Figure 1.

Figure 1. Viron 9 miniRITE

8.1.2 Control Intervention (comparator medical device)

No Reference Medical Device (RMD) will be used for the trial as the comparison is between two programs which will both be fitted in the IMD.

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 that also printed on the device. The production batch can be tracked through this serial number. The hearing aids are shipped in a box with a label on the outside of the box that states the family name of the product, the serial number, a short description (colour and performance level), and an expiration date. Inside the box is a case that houses the hearing aids. The hearing aids are delivered inside a blister inside of this case. The HCP removes the case from the box and removes the hearing aids from the blister. The case is generally given to the end user in which to place the hearing aids whenever they are not worn.

8.1.4 Storage Conditions

The IMD devices are shipped from production when they are ordered. The conditions in which they should be shipped and kept by the end user are described in the IFU. They should not be exposed to temperatures below -25° and not above 60° Celsius.

8.2 Administration of experimental and control interventions

8.2.1 Experimental Intervention

The IMD is worn over the ear with the speaker covered by a dome or earmold anchored inside the ear canal. It is non-invasive. The amplification is prescribed based on the participant's hearing loss. The IMD will be worn by each participant for 10 +/- 7 days to give the subjects enough time to get used to the amplification and then a further 10 +/- 7 days to wear the devices in different environments and make a comparison between the IP and the SP. Normal use of a hearing aid is 8-10 hours per day. The participants will be instructed to use the IP for the same amount of time as the SP in music situations. The hours of daily use will be controlled with a data logging feature in the software that programs the hearing aids.
The study procedure will use a randomized single-arm design in which all of the subjects will wear the IMD programmed with both the IP and the SP. As stated previously, the device is non-invasive and requires no surgical procedure.
The subjects themselves will place the device in their ears each morning and remove them each night for sleeping. They will also be responsible for switching between the IP and SP programs to use both and compare them in music situations. It is expected that some of the test subjects will be experienced hearing aid users and some will be new users. However, they will require minimal explanation and/or training to use the IMD. They will be given an Instructions for Use booklet that explains how to insert the device and provides further instructions concerning cleaning, battery charging, and warnings.

8.2.2 Control Intervention

There is no RMD. The control intervention is the SP and will be programmed into the IMD.

8.3 Dose / Device modifications

The IMD will provide the amplification prescribed by the fitting rationale and will be measured with Real Ear Measures (REM). The SP and the IP will be programmed with the P1 gain as a reference with fine-tuning performed on the IP. Because the gain will be verified objectively and fine-tuned based on the patient's comments, it is not expected that any negative effects should be experienced that would make them want to discontinue use of the device. However, if a subject does report such differences, it will be possible to improve the programming with fine tuning. Fine tuning can improve the situation by making slight changes to the gain (higher or softer) enough for the subject to continue with the study. If the subject requests to discontinue they can immediately remove the IMD from their ear(s) and do not need to wait until their next appointment in order to do so. 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 the 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 intervention period it is important to the study that they only wear the IMD (in the case of current users with their own hearing aids). The importance of switching between the IP and SP during music situations is also explained. Additionally, they will receive an email as a reminder to use both programs during the field test. For current hearing aid users, their own hearing aids are left in their possession for safety reasons in the event that they choose to discontinue their participation in the trial, or a problem arises with the test devices. For ethical purposes, the subjects must have a back-up solution for their hearing impairment.
The data logging feature of the software monitors the average number of hours that the devices are worn each day and in each program. Therefore, it will be noted if the IP and the SP have not been worn a standard or expected amount of time.

8.5 Data Collection and Follow-up for withdrawn participants

Any data that is collected will be kept in the Smart Trial data management database. The data will remain encoded because results are only recorded using the identification code of the subject. The analysis and report will include a summarized section based on the data available from all recruited subjects and another section based on the data from the subjects that complete the entire protocol. Withdrawn subjects will have the same follow-up as those subjects that complete the trial. Those subjects that are taken from the Bernafon directory, including those that withdraw, are welcome to return to the clinic for fine-tuning and maintenance as needed.

8.6 Trial specific preventive measures

The performance of a hearing aid is not impacted by medication or other conditions. 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 trial. Some test subjects will already be hearing aid users and will have, therefore, used them while receiving other types of care or medications. There will be no impact on the study

objectives.

8.8 Medical Device Accountability

The IMD devices have serial numbers by which the individual device can be identified, and the production history traced. The devices will be shipped from the production lab in Poland. The serial numbers will provide traceability of their production. All devices undergo testing in production before being shipped. 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 device accountability log and CRF that the devices were returned.

The PI will then return the devices to the Sponsor.

9. STUDY ASSESSMENTS

9.1 Study table of study procedures and assessments

Study Periods	Screening	Treatment/Intervention Period	
Visit	1	2	3
Day	0	10 +/- 7 days	20 +/- 7 days
Patient Information and Informed Consent	x		
Demographics	x		
Medical History	x		
In-/Exclusion Criteria	x		
Otoscopy	x	x	x
Audiometry	x		
Randomisation of treatment	x		
Administer Medical Device	x		
REM	x		
Optimized fitting		x	
Primary Variable (Preference questionnaire)			x
Secondary Variable (Lab test-music perception)	x	x	x
Other Variables (Product questionnaire)	x		
Other Variables (Music perception questionnaire)	x	x	
Adverse Events	x	x	x

9.2 Assessments of outcomes

9.2.1 Assessment of primary outcome

The primary outcome is the preference questionnaire. The hearing aids will be programmed with the two music programs, the SP with the standard default music settings and the IP with the optimized fine-tuned music settings. The subjects will use both programs during the second field test and then be asked to choose a preference for listening to music and/or when playing music. The questionnaire also asks that they rate how sure they are of their choice on a 10-point scale with 10 being completely sure and gives a list of reasons for the choice from which they can select as many as they choose.

9.2.2 Assessment of secondary outcomes

The Adaptive Music Perception (AMP) test will be run in the lab. The test is designed to assess aspects of music including meter and timber. The test is a computerized two-alternative forced-choice method run on a touch screen. The adaptation process uses a two-down, one-up rule and the score is the average of the last four reversal points. A reversal point is when the subject makes a correct selection and the adaptation reverses to a lower level.
They will also complete a product questionnaire with specific questions about feedback, sound quality, and unexpected behaviour for the general P1 program. The questionnaire is given to them to take home at the first appointment to be filled out and returned at the second appointment. The questions are rated with either a 5-point scale with 1 being the most positive outcome or yes/no answers. They will complete a music perception questionnaire for all three programs. The questions are rated with a visual analogue scale (VAS). The music questionnaire for P1 will be given to them at the first appointment and returned at the second. The music questionnaires for P2 and P3 will be given to them at the second appointment and returned at the third.

9.2.3 Assessment of safety outcomes

Questions concerning unexpected events, sounds, and behaviour are included in the product questionnaire that are given to them to take home at the first appointment to be filled out and returned at the second appointment. The questions are rated with yes/no answers.
In addition to the questionnaires, adverse events will be collected and monitored.

9.2.3.1 Adverse events

For the recording of adverse events the subjects will be asked for a description of the event including time/date of onset, how long it lasted, how many times it occurred, and if it caused discomfort or pain or a disruption of hearing ability.
Before the end of each appointment, the subjects will be asked if they have experienced any adverse events. It will be explained that adverse events are not restricted to problems related to the hearing aids or their hearing but can include allergies, broken legs, headaches, etc. They will be recorded on the AE forms in the CRF.

9.2.3.2 Laboratory parameters

Not applicable

9.2.3.3 Vital signs

Not applicable

9.2.4 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 their own devices. Those that prematurely withdraw from the study will

still be wearing their own devices; therefore, their follow-up treatment will be the same as for the other participants that finish the study.

9.3 Procedures at each visit

9.3.1 Screening/First visit

Screening visit, Day 0: The potential participants will be given the Patient Information and Informed Consent form. The trial will be explained including how many visits are expected as well as the type of testing that they will complete. They are given time during the appointment to read the information and decide whether to participate in the study. If they choose to not take part in the study, they will not sign the consent form, and the appointment will finish. If they choose to join the trial, they will sign and date the consent form. No trial activities will be performed before the consent form is signed and dated by the subject and the investigator. Subjects will receive a copy of the signed consent form. A hearing history is then taken, and otoscopy is performed. A hearing test is performed, and inclusion/exclusion criteria will be determined. The subject is then randomized regarding the assignment of the music programs (IP or SP) to program slots 2 or 3. They are fitted with the IMD based on a first fit in the software and adjusted using REM data to match the gain targets. The hearing aids will be fit only with a general program in the P1 slot. They will perform the lab test with the AMP in two conditions: unaided and aided with the general program. They are given an IFU for the hearing device. They are given a product questionnaire and a music perception questionnaire and instructed to complete them at home a day before their next appointment. Any AEs are reported in the CRF. They are scheduled for the second visit.

9.3.2 Fitting/Second visit

Fitting Visit, Day 10 +/- 7: Otoscopy is performed, and the subjects return the completed questionnaires. The IMDs are fitted with IP and SP as specified by the randomization carried out at the first visit. The IP is optimized and fine-tuned based on comments that the subject makes about the sound while they play their instrument in the clinic. The SP is programmed without any adjustment based on the default music program offered in the software. They are instructed to switch between programs two and three when playing and listening to music for the next 10 +/- 7 days. They perform the lab test with the AMP in one condition: aided with P2. The subjects are given the music perception questionnaires and instructed to complete them at home a day before their next appointment. One questionnaire pertains to P2 and the other to P3. Any AEs are reported in the CRF. They are scheduled for the third visit.

9.3.3 Lab/Third visit

Final Visit, Day 20 +/- 7: Otoscopy is performed. The subjects return the completed product questionnaires. They perform the lab test with the AMP in one condition: aided with P3. They complete a preference questionnaire during the appointment. They are notified that the trial has ended and those that normally wear hearing aids can return to using their own devices. They will return the IMD to the clinic. Any AEs are reported in the CRF. Those that are on the Bernafon subject list and normally wear devices fitted by the Bernafon clinic are reminded to return to the clinic for normal maintenance of their hearing aids. Anyone that would like to join the Bernafon clinic are also welcome to do so.

10. SAFETY

The Sponsor's SOPs provide further detail on safety reporting.

10.1 Medical Device Category A studies

Device deficiencies and 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 [ISO 14155, 6.4.1.].

The information on AEs is systematically collected by the PI at each study visit. They will follow the procedures outlined in SOP ID106_AE Reporting. The subjects are asked at each appointment if they have experienced any events since the last appointment. During the appointments 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, swallowing of a lithium battery, 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, and to keep them away from children or pets that might swallow the batteries. The IFU warns of interference with implantable devices.

10.1.1 Foreseeable adverse events and anticipated adverse device effects

No serious adverse events are anticipated. The hearing aid was tested before release to market for safety and has been on the market with no reported problems for almost one year. The following is a list of common and expected adverse device effects.

Headache	Likely	No treatment, self-medication with analgesic, remove device for a period, reduce gain
Sounds are too loud	Likely	Reduce gain, remove device for a period
Tinnitus	Likely	Reduce gain, remove device for a period
Discomfort or pain from device in or around ear	Likely	Remove device and refrain from using for a period, change of dome, change of speaker length
Habituation to the hearing aids and a possible new hearing	Likely	Continued use of hearing aids after the trial is finished.

perception.		

10.1.2 Definition and Assessment of (Serious) Adverse Events and 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 investigational device or the comparator and to the procedures involved. For users or other persons this is restricted to events related to the investigational medical device.

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.

Serious Adverse Event (SAE) [European regulation on medical devices 2017/745, art. 58].

Any adverse event that led to any of the following:

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

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 submitted to the EC via BASEC within 7 days. A planned hospitalisation 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 SAE [ClinO Art. 37].

Causal Relationship of SAE [MEDDEV 2.7/3 revision 3, May 2015].

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

- **Not related:** The relationship to the device or procedures can be excluded.
- **Unlikely:** The relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
- **Possible:** The relationship with the use of the investigational device is weak but cannot be ruled out completely. Alternative causes are also possible.
- **Probable:** The relationship with the use of the investigational device seems relevant and/or the event cannot be reasonably explained by another cause.

- **Causal relationship:** The serious event is associated with the investigational device or with procedures beyond reasonable doubt.

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

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

Reporting to Sponsor-Investigator:

All SAEs, device deficiencies and health hazards that require measures are reported to the Sponsor-Investigator within 24 hours upon becoming aware of the event. Device deficiencies are assessed regarding their potential to lead to an SAE.

Pregnancies – No pregnant participants will be included in the study

Reporting to Authorities:
In Category A studies, the sponsor is subject to the notification requirements specified in Art. 15 of the MedDO of 17 October 2011 (SR 812.213).
It is the Investigator's responsibility to report to the Ethics Committee via BASEC **device deficiencies** that could have led to serious adverse events if suitable action had not been taken, intervention had not been made, or circumstances had been less fortunate within 7 days [ClinO Art. 42].
Health hazards that require measures are reported to the Ethics Committee via BASEC within 2 days [ClinO Art. 37].

Periodic safety reporting:
A yearly safety update-report is submitted by the Investigator to the Ethics Committee via BASEC.
A report is submitted to Swissmedic by the Sponsor-Investigator, as defined in Art. 15a, b of the MedDO of 17 October 2011 (SR 812.213).

10.1.4 Follow up of (Serious) Adverse Events

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

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

Contact order

Contact order	Name	Mobile	Office	E-Mail
1	Bruno Keller	+41 31 998 15 92	Senior Director	brke@bernafon.com
2	Sabine Huemer	+41 31 998 15 34	Senior Director	shue@bernafon.com

Table 1. Contact information of the sponsor in case of SAE/SADE

11. STATISTICAL METHODS

11.1 Hypothesis

The assumption is that hearing aids that are optimized for hearing-impaired musicians should provide a better experience while playing an instrument with the following consequences: (a) improvement of the perception of music, (b) improvement of the ability to play, and (c) indirect improvement of the quality of life.

In summary, the primary reason for this study is to evaluate the new fitting protocol for musicians using hearing aids. The secondary reason is to evaluate the overall safety of the IMD by testing for unexpected behaviour from the IMD and by the collection of AEs to identify any new risk factors since their release to the market as a post-market quality control.

More specifically, the objective of the trial is to provide answers to following research questions:

- Does the fitting protocol optimized for hearing-impaired musician's individual needs make an audible difference compared to a standard fitting approach?
- Is the fitting protocol optimized for hearing-impaired musician's individual needs preferred over the standard fitting approach?
- Does the fitting protocol optimized for hearing-impaired musician's individual needs improve the perception of music compared to a standard fitting approach?

Null hypothesis: there is no audible difference or preference between the SP and the IP when the participants are playing or listening to music.

Alternative hypothesis: there is an audible difference or preference between the SP and the IP when the participants are playing or listening to music.

11.2 Determination of Sample Size

Vaisberg et al. (2018) is the only publication, to our knowledge, specifically focusing on hearing aids for hearing impaired musicians. They used a qualitative research methodology based on semi-structured interviews with 12 participants. Fullford et al. (2011) and Fullford & Ginsborg (2014) also used 12 participants for qualitative research studies about how hearing-impaired musicians experience sound and communicate while playing music. However, these publications are based on qualitative research methods which cannot be directly used for the sample size estimation.

Please refer to the Statistical Analysis Plan (SAP) for a complete list of articles used to determine the sample size. The SAP summarizes the sample sizes and population attributes from quantitative research tests in a lab, i.e. exclusion of online questionnaire-based research, with a topic related to the current study.

The sample size ranges between 9 and 21 participants when looking at studies including hearing aid users with a certain amount of musical training. This range can be used as a baseline for the sample size determination. However, there are some known limitations when using these references. Their study designs only include tests where the participants listen to predefined music samples and not when they are playing their own musical instruments. The definition of the sample size for this exploratory trial should take the population homogeneity and the recruitment potential into account.

On one hand, arguments for a sample size closer to the lower boundary might be justified by a relative homogeneous population reflecting a strong external validity potential because:

- The hearing loss is within the fitting ranges of the IMD, i.e. exclusion of participants with a too mild or profound hearing loss degree,
- The musical experience and practice are set as inclusion criteria, i.e. participants are regularly playing an instrument in different groups or ensembles,
- The recruitment process is restrictive. The target population must fulfil the inclusion /

exclusion criteria and be ready to bring their own instrument for the IP fitting. These criteria will eliminate potential participants with cognitive, social, or physical difficulties.

On the other hand, there are some unknown parameters that have also to be considered for the sample size determination:

- The effect of the instrument, i.e. the sound generation principle greatly varies between a string, a woodwind and a brass instrument. This might affect the perception of sound and interact with the range of the instrument, the hearing loss degree and type,
- The effect of amplification through hearing aids when musicians are playing. All the above-mentioned tests are based on passive listening experience. There are no publications, to the best of our knowledge, about the use of auditory feedback to control the production of music. We can assume that adaptation of their own voice production to the environment (Lombard effect) and perception of sound might show similarities when playing music,
- The effect of the IP which follows guidelines for hearing aids fitted to musicians. The guidelines are based on a project (Greasley et al., 2019) but no results based on quantitative research were published. It is therefore not possible to estimate an effect size when a personalized protocol like the IP is used with musicians.

The uncertainty from the test design and the unknown effect size from the IP motivates the choice for a larger sample size. Regarding recruitment possibilities, based on the principal investigator's input, the sample size was set to 18-20 participants for the current study.

11.3 Statistical criteria of termination of trial

There are no plans for early termination of the trial.

11.4 Planned Analyses

11.4.1 Datasets to be analysed, analysis populations

Primary analysis of the primary outcome will be based on the intention-to-treat (ITT). The ITT population will include all participants with associated primary outcome data, excluding only subjects who were deemed ineligible following the screening visit, those who withdrew from the trial and were unwilling for their previously collected data to be utilised or those who failed to provide baseline.

11.4.2 Primary Analysis

The study will assess the performance of the IP in comparison to the SP using a preference questionnaire. After wearing the devices for at least 10 +/-7 days and using them in daily life and various music situations, the subjects will be asked to complete a preference questionnaire and choose between the two music programs (SP and IP).

The preference score is rated on a 5-points Likert scale: SP much better, SP better, no difference, IP better, IP much better. The score distribution is described by the minimum, median, and maximum values and tested with a Wilcoxon signed-rank test with the assumption that ordinal scores from a Likert scale reflect the within subject difference. The null hypothesis is that there is no difference between the tested protocols and the alternative hypothesis is that there is a preference for a protocol. A two-sided test will be made as the IP has not been tested before.

Certainty and motivation of preference will be summarized and described separately. The results of this test will be used to answer the 1st and 2nd research questions.

11.4.3 Secondary Analyses

The secondary objective is to assess the perception of music with the IP in comparison to the SP using the adaptive music perception (AMP) test (Kirchberger & Russo, 2015). The AMP provides a means to

evaluate perception of details in music with various subscales, e.g. pitch, duration, loudness. The hypothesis is that the performance of the IP should not be inferior to that of the SP. Baseline scores for the AMP test are measured unaided and aided with the general listening program, i.e. not specific for music.

The AMP test is based on an adaptive procedure that provides the threshold reflecting the amount (time, loudness, pitch…) that each participant can detect above chance. The thresholds are measured on ratio scales: duration in milliseconds, pitch in hertz, loudness in decibels. Kirchberger & Russo (2015) indicate that the thresholds might be influenced by different covariates, like degree of hearing loss or music experience, and by the type of signal processing. Measured thresholds will therefore be modelled by a linear mixed-effect regression with backwards selection based on the variation inflation factor (VIF). This gives a complex picture for the coefficient interpretation as there are 4 test conditions: unaided, aided general program, aided SP, and aided IP. Planned contrasts will be considered:

1. Unaided vs Aided
2. General vs Music-specific programs
3. IP vs SP

The 3rd research question will be answered with a paired t-test on each subscale comparing threshold from the IP to the thresholds from the SP.

Additionally, a music perception questionnaire based on Rutledge (2009) will evaluate the perception of music in various environments with each listening program. Overall hearing aid benefit will be measured with a general product questionnaire

The results from the music questionnaire are scores from a visual analogue scale. The distribution of the scores will be visualized with boxplots for each listening program (General, IP, or SP program) and focus (own musical instrument vs other musical instruments). The effect of listening programs and focus will be evaluated with mixed effect regression model taking into account the hearing loss degree, own instrument category (string, woodwind, or brass), and music experience as fixed effects. Planned contrasts will be considered:

1. General vs Music-specific programs
2. IP vs SP

Results from the second contrast will be used to answer the 3rd research question.

11.4.4 Interim analyses

There are no plans for an interim analysis.

11.4.5 Safety analysis

The questionnaires used for the secondary outcome will also contain questions to measure the safety of the devices. These questions will specifically address unexpected noise or behaviour from the devices. Unexpected behaviour includes unprovoked feedback or whistling, distorted sounds or artefacts, spontaneous muting or the shutting off of the device, and any unexplained warning signals, beeps, or loud sounds.

The adverse event risks of taking part in the study have been assessed to be low. Numbers of adverse events and serious adverse events will be cross-tabulated for the IMD and categorised by severity. No formal statistical analysis will be conducted, but AEs and SAEs will be closely monitored throughout the process.

11.4.6 Deviation(s) from the original statistical plan

Due to the home-based nature of the trial, it is possible that there will be a few deviations from the study protocol, e.g. not wearing hearing aid, manipulation issues, misplacement, etc.

As well as non-compliance with the protocol, there could be other protocol deviations, for example if follow-up assessments take place outside the pre-specified ±10 days window. The numbers and proportions of participants with protocol deviations will be summarised with details of type of deviation provided. No formal statistical testing will be undertaken.

11.5 Handling of missing data and drop-outs

Unless specified otherwise in each objective, no statistical techniques will be used to impute missing data. If a subject's data are missing for any reason, that subject will not be included in that portion of the analysis. The number of subjects included in each analysis will be reported so that the potential impact of missing data can be assessed.

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. The PI is responsible for proper training of all involved study personnel.

12.1 Data handling and record keeping / archiving

Data will be archived with an electronic data management system. The subjects will be given numbers to maintain anonymity. There are also hard copies of subjects' charts that are kept in a locked file cabinet inside of the clinic 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 PI will enter protocol defined data into a web based Electronic Case Report Forms using an EDC-software that conforms to 21 CFR Part 11 (FDA guidance) requirements. Site staff will be given access to the EDC system after a training. The data are checked automatically for plausibility and discrepancies. The generated appropriate error messages allow the data to be confirmed or corrected before being saved in the database. At the end of the study, the PI must certify that the data entered into the Electronic Case Report Forms are complete and accurate. After database lock, the PI will receive a CD-ROM of the patient data for archiving at the site.

The CRF contains the following information:

Field	**Author**
Participant identification number	PI
Date of visit	PI
Subject birth year	PI
Date of Informed Consent	PI
Age	PI
Sex	PI
Otoscopy	PI
Standard audiometry	PI
Hearing loss classification	PI
Eligibility	PI
Trial information provided	PI
Inclusion / Exclusion Criteria	PI
Ear disease	PI
Hearing loss onset	PI
Musical history	
Real ear measure	PI
Investigational device serial numbers	PI
Randomization Program 2	PI
AMP results	PI

Questionnaires received	PI
IFU received	PI
Questionnaires returned	PI
Randomization assignment	PI
Devices returned	PI
Results from music questionnaire	PI
Results from preference questionnaire	PI
Results from product questionnaire	PI
AEs / SAEs, ADE / SADE	PI
Next appointment	PI
Name, date, signature of PI	PI

12.1.2 Specification of source documents

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

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

Subject clinical source documents include, but are not limited to subject clinic records, investigator's notes, appointment book, hearing test results, questionnaires, consultant letters, visit dates, signed Informed Consent Forms, randomisation numbers, SAEs, AEs, 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 immediately after the visit.

Source data 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 other investigator.

The entries will be checked by the Monitor and any errors or inconsistencies will be checked immediately. The Sponsor will collect original completed eCRFs on a USB flash drive at the end of the study. The USB flash drive with the completed and e-signed CRFs will remain on site and archived.

Source data must be available at the site to document the existence of the study participants. Source data must include the original documents relating to the study, as well as the medical treatment and medical history of the participant.

12.1.3 Record keeping / archiving

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

Trial documentation is stored in water- and fire-resistant locked boxes in the basement of the Sponsor's building.

12.2 Data management

A Data Management Plan is created by the Statistician according to the Sponsor's SOP ID103. This plan can be found in the TMF.

12.2.1 Data Management System

The CRFs in this trial are implemented electronically using a dedicated electronic data capturing (EDC) system, called Smart Trial. Smart Trial is designed according to IEC62304 and ISO13485 quality standards. The statistician creates the eCRFs and sets up the system for each trial. He then validates the system and records the validation in a report which is stored in the TMF. The EDC system is activated for the trial only after successfully passing this test procedure.

Data is coded when extracted for the analysis. The code values are found in the Codebook located in the TMF.

All data entered in the eCRFs are stored on a Windows server in a dedicated database located in Denmark.

12.2.2 Data security, access and back-up

The server hosting the Smart Trial EDC system and the database is kept in a locked server-room in Denmark. 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.

To enter data, a two-step verification system is used in addition toa permission-based access control with varying levels of access depending on the person's role within the trial. 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 data will remain anonymised during and after the statistical analysis. The database will be locked at this time, recorded in special archiving format and securely stored for at least 1 year. In addition, the PI will receive a USB flash drive of the trial 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. Additionally, the statistician creates the eCRFs with restrictions on data points that only allow expected number ranges, and furthermore, selected data points are cross-checked for plausibility with previously entered data for that participant.

Monitoring is used to validate entries with source data

12.3 Monitoring

The study site will be monitored by an employee of the Sponsor. A minimum of 3 visits will be performed; one site initiation visit, 1 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 at least 5 patients have been enrolled.

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

100% source data verification will be completed for 3 patients at the first interim visit. For any additional interim visits, another 3 patients of 100% source data verification will be completed at each visit.

Subject to SDV for all patients are: Patient Informed Consent Form Eligibility criteria

Diagnosis Visit dates

Study intervention details related to: Procedural success

Procedure date and time

(Serious) Adverse Events Device deficiencies

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

12.4 Audits and Inspections

CEC has the right to execute inspections at the study site. The Sponsor may at any time conduct an audit of the study site.
The study documentation and the source data/documents must 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 purposes of monitoring (12.3), audits and inspections (12.4) (ICHE6, 6.10) and only authorized persons involved in those activities will have access to source documents and must keep participants data strictly confidential. Only those involved with the trial (PI, statistician, monitor) will have access to the protocol, dataset, statistical code, etc. during the study and after the study the information will be made public through a publication of the results; however, trial participants' identities will remain coded.

12.6 Storage of biological material and related health data

No biological samples are taken or stored. Data collected during the trial will be stored and potentially reused for further analysis only with the participants' consent independent of the study. The data will remain encoded because results are only recorded using the identification code of the subject.

13. PUBLICATION AND DISSEMINATION POLICY

Trial results will be communicated to participants at the end of the trial. The trial results primary purpose is 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 the monitor 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

1. Declaration of Helsinki, Version October 2013, (http://www.wma.net/en/30publications/10policies/b3/index.html)
2. International Conference on Harmonization (ICH, 1996) E6 Guideline for Good Clinical Practice. (http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf)
3. International Conference on Harmonization (ICH, 1997) E8 Guideline: General Considerations for Clinical Trials http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E8/Step4/E8_Guideline.pdf)
4. Humanforschungsgesetz, HFG Bundesgesetz über die Forschung am Menschen (Bundesgesetz über die Forschung am Menschen, HFG) vom 30. September 2011/ Loi fédérale relative à la recherche sur l'être humain (loi relative à la recherche sur l'être humain, LRH) du 30 septembre 2011 / Legge federale concernente la ricerca sull'essere umano (Legge sulla ricerca umana, LRUm) del 30 settembre 2011
5. Verordnung über klinische Versuche in der Humanforschung (Verordnung über klinische Versuche, KlinV) vom 20. September 2013 / Ordonnance sur les essais cliniques dans le cadre de la recherche sur l'être humain (Ordonnance sur les essais cliniques, OClin) du 20 septembre 2013. Ordinanza sulle sperimentazioni cliniche nella ricerca umana (Ordinanza sulle sperimentazioni cliniche, OSRUm) del 20 settembre 2013
6. Heilmittelgesetz, HMG Bundesgesetz über Arzneimittel und Medizinprodukte (Heilmittelgesetz, HMG) vom 15. Dezember 2000 / Loi fédérale sur les médicaments et les

dispositifs médicaux (Loi sur les produits thérapeutiques, LPT) du 15 décembre 2000 / Legge federale sui medicamenti e i dispositivi medici (Legge sugli agenti terapeutici, LATer)
7. ISO 14155:2011 Clinical investigation of medical devices for human subjects -- Good clinical practice (www.iso.org)
8. ISO 10993 Biological evaluation of medical devices (www.iso.org)
9. MEDDEV 2.7/3 revision 3, May 2015
10. Medizinprodukteverordnung (MepV) vom 17. Oktober 2001 / Ordonnance sur les dispositifs médicaux (ODim) du 17 octobre 2001 / Ordinanza relativa ai dispositivi medici (ODmed) del 17 ottobre 2001
11. WHO, International Clinical Trials Registry Platform (ICTRP) (http://www.who.int/ictrp/en/)
12. European regulation on medical devices 2017/745.
13. Strahlenschutzverordnung (StSV) vom 26. April 2017 / Ordonnance sur la radioprotection (ORaP) du 26 avril 2017 / Ordinanza sulla radioprotezione (ORaP) del 26 aprile 2017.
14. Nabelek, A.K., Tampas, J.W., and Burchfield, S.B. (2004). Comparison of speech perception in background noise with acceptance of background noise in aided and unaided conditions. *Journal of Speech, Language, and Hearing Research*. *47*(5), 1001-1011.
15. Pocock, S. J. (1983). *Clinical Trials*. Chichester, England: John Wiley & Sons, Inc.
16. Kirchberger, M. J., & Russo, F. A. (201). Development of the Adaptive Music Perception Test. Ear and Hearing, 36(2), 217–228. https://doi.org/10.1097/aud.0000000000000112
17. Kochkin S. (2011). Marke Trak VIII Patients report improved quality of life with hearing aid usage. Hearing Journal, 64(6), 25-26, 28, 30, 32.
18. Chasin, M., & Russo, F. A. (2004). Hearing Aids and Music. Trends in Amplification, 8(2), 35–47. https://doi.org/10.1177/108471380400800202
19. Mussoi, B. S. S., & Bentler, R. A. (2015). Impact of frequency compression on music perception. International Journal of Audiology, 54(9), 627–633. https://doi.org/10.3109/14992027.2015.1020972
20. Madsen, S. M. K., Stone, M. A., McKinney, M. F., Fitz, K., & Moore, B. C. J. (2015). Effects of wide dynamic-range compression on the perceived clarity of individual musical instruments. The Journal of the Acoustical Society of America, 137(4), 1867–1876. https://doi.org/10.1121/1.4914988
21. Madsen, S. M. K., & Moore, B. C. J. (2014). Music and Hearing Aids. Trends in Hearing, 18, 233121651455827. https://doi.org/10.1177/2331216514558271
22. Creech, A., Hallam, S., McQueen, H., & Varvarigou, M. (2013). The power of music in the lives of older adults. Research Studies in Music Education, 35(1), 87–102. https://doi.org/10.1177/1321103x13478862
23. Leek, M. R., Molis, M. R., Kubli, L. R., & Tufts, J. B. (2008). Enjoyment of Music by Elderly Hearing-Impaired Listeners. Journal of the American Academy of Audiology, 19(6), 519–526. https://doi.org/10.3766/jaaa.19.6.7
24. Lehmberg, L. J., & Fung, C. V. (2010). Benefits of music participation for senior citizens: A review of the literature. Music Education research International, Vol. 4, 19-30.
25. Cohen, A., Bailey, B., & Nilsson, T. (2002). The importance of music to seniors. Psychomusicology: A Journal of Research in Music Cognition, 18(1–2), 89–102. https://doi.org/10.1037/h0094049
26. Humes, LE., Rogers SE, Quigley, TM, Anna K. Main, Kinney, DL. and Herring, C (2017): The Effects of Service-Delivery Model and Purchase Price on Hearing Aid Outcomes in Older Adults: A randomized Double-Blind Placebo-Controlled Clinical Trial. American Journal of Audiology, vol.26, 53-79.
27. Greasley, A. E., Crook, H. & Beeston, A. V. (2019). Hearing Aids for Music: Findings and recommendations for hearing aid users, audiologists, manufacturers and researchers. Final report of the AHRC-funded Hearing Aids for Music Project. 25 April 2019.
28. Fulford, R., Ginsborg, J., & Goldbart, J. (2011). Learning not to listen: the experiences of musicians with hearing impairments. Music Education Research, 13(4), 447–464. https://doi.org/10.1080/14613808.2011.632086

29. Fulford, R., & Ginsborg, J. (2014). Can you hear me? Effects of hearing impairments on verbal and non-verbal communication during collaborative musical performance. Psychology of Music, 42(6), 846–855. https://doi.org/10.1177/0305735614545196
30. Vaisberg, J. M., Martindale, A. T., Folkeard, P., & Benedict, C. (2018). A Qualitative Study of the Effects of Hearing Loss and Hearing Aid Use on Music Perception in Performing Musicians. Journal of the American Academy of Audiology. https://doi.org/10.3766/jaaa.17019

17. APPENDICES

1. Medical Devices: IB (according to ISO 14155)
2. Medical Devices: Declaration of Conformity
3. Case Report Form (e.g.) CRF
4. Instructions for Use
5. Statistical Plan
6. Patient Information and Informed Consent
7. List of study sites/PI
8. Questionnaires